

Evidence Based Therapeutic Exercise Recommendations for Patients with Multiple Sclerosis: A Physical Therapy Approach

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Abstract

Multiple Sclerosis (MS) is a chronic demyelinating disease of the central nervous system affecting over a million people worldwide. The demyelinating process begins when inflammatory T cells of the immune system attack the oligodendrocytes after infiltrating the blood-brain barrier, creating a cascade effect of neurological symptoms. MS presents itself through physical symptoms including fatigue, depressed mood and motor deficits. Current research has shown promise in using exercise intervention to curb the symptoms of this autoimmune disease.

This brief review evaluated studies that utilized exercise to decrease fatigue, improve quality of life (QoL), and improve ability to perform activities of daily living. Assessments utilized to examine efficacy of exercise include the Fatigue Severity Scale, Multidimensional Fatigue Inventory-20, and the Major Depression Inventory. These tests provide both an objective and subjective view of the MS disease process.

The purpose of this review is to provide information related to resistance exercise recommendations for physical therapists to use as a guide when prescribing exercise interventions to patients with MS. The training program aims to reduce mobility related impairments, decrease fatigue and improve QoL in individuals with MS. After review of this article the reader should ascertain a newfound comfort and knowledge for delivering progressive resistance training to persons with MS. This guide provides both novice and intermediate-advanced recommendations for exercise.

The exercise recommendations are indicated for patients with less than or equal to a 6.0 on the Expanded Disability Status Scale. MS patients should consult a physician before actively engaging in any exercise program.

Keywords: Multiple sclerosis; Patients

Introduction

Multiple Sclerosis (MS) is a neurological disease that presently affects over one million people in the world making it among the most common neurological diseases. Perhaps more concerning is that the incidence is growing [1,2]. MS is a degenerative autoimmune disease in which damage to the myelin sheath in the central nervous system (CNS) leads to a cascade of neurological effects [1,3-6].

Patients with MS either experience progressively worsening symptoms or they experience relapses [7]. Relapses are points in time when patient's symptoms become worse. A remission or recovery period follows the relapse and is characterized by symptom withdrawal and/or complete recovery. However, with any type of MS, as the patient ages the symptoms become harder to manage and the exacerbations become more severe [8]. Currently there is no cure for the disease.

Multiple Sclerosis presents with symptoms including, but not limited to: pain, fatigue, weakness, and altered coordination [9,10]. Symptoms related to mobility have been found to be severely debilitating. Symptoms are often managed with various pharmacological interventions [10,11]. Past recommendations suggest that any exercise could elicit symptoms of a relapse. However, patients with MS who have added aerobic and anaerobic routines have had positive outcomes in quality of life [2]. Considering that patients with MS typically are less active due to their fatigue, their subjective ratings of fatigue tend to be higher, in adjunct with lower QOL and IADL scores.

Currently, there is need for resistive exercise training recommendations for patients with relapsing remitting MS due to the dearth of literature. It is well known that exercise not only improves the psychosocial well-being of the healthy patient, but their overall muscular fitness [12]. It is also shown that exercise can have the same beneficial effects for the MS population including an overall reduction of fatigue, psychosocial benefits, and improved cardiovascular and muscular fitness pertaining to strength and endurance [5,7,12-15].

Our knowledge of cost dictates that it is cheaper to treat a patient on an outpatient basis than during an inpatient acute relapse [16]. Durable medical equipment, pharmacological interventions and in-hospital related cost can potentially be decreased with an exercise prescription that decreases fatigue, increases strength and improves QOL.

Pathophysiology

Multiple Sclerosis (MS) is a degenerative neurological disease affecting the central nervous system. The etiology of MS is believed to be both environmental and genetic [3]. A person with a family history of MS is more likely to develop the disease than someone without a family history. This disease specifically affects white matter in the central nervous system leading to degradation of the myelin surrounding nerves, especially the oligodendrocytes [3].

Patients with relapsing-remitting MS go through periods of exacerbations when their neurological symptoms worsen from days to several weeks due to inflammation and demyelination followed by time during which some of the myelin is replaced [3]. However, the myelin that is replaced is not as thick and there are more nodes of Ranvier [4]. It is known that lymphocytes in the periphery are activated which then penetrate the blood brain barrier and attack the body's own myelin sheath [2].

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It is believed that auto-reactive T cells are the cause of the inflammation and demyelination. Studies show that patients with MS and healthy patients have the same number of T cells (CD4+ and CD8+), however the cells differ in activity. The T cells in patients with MS have an active phenotype and the T cells in the healthy population have a phenotype with no memory. In patients with MS the myelin specific T cells produce cytokines such as interferon- γ which are suggested to cause inflammation. Cytokines cause many T cells to evolve into inflammatory Th1 (type 1 helper T cells) lymphocytes rather than the Th2 anti-inflammatory lymphocytes which are seen in the healthy population. The inflammatory Th1 lymphocytes attack the body's myelin sheath in the central nervous system [1]. This process draws macrophages and granulocytes to the area to further mediate the inflammatory process [2].

The purpose of the myelin sheath is to increase conduction velocity along the white matter tracts, called axons, as well as to increase the capacity for action potentials. Nodes of Ranvier exist between sections of myelinated axon to increase the speed of the action potential, however the node can only be so wide before the action potential is unable to cross the node. Demyelination begins at the Node of Ranvier making these gaps wider. This decreases the current that is available for the nerve to depolarize, thus affecting muscular action. This process causes slow conduction speeds and conduction block [2]. As the myelin deteriorates some re-myelination occurs. However, much of the myelin it is replaced by scar tissue, referred to as plaque, which further interrupts the conduction of the nerve.

In patients with multiple sclerosis the slowed conduction speed presents as awkward or uncoordinated movements [1]. Due to the demyelination of patients with MS, a lower tetanic and twitch tension are realized along with greater fatigue during stimulated contractions [17]. To produce the same amount of force as a healthy person, patients with MS need to recruit more motor units per contraction. This could lead to the peripheral fatigue in patients with MS due to increased work [2]. Weakness and atrophy contribute to a decline in mitochondria concentration in contractile units [17]. This explains the importance of incorporating a strengthening program into the MS patient's multidisciplinary treatment plans. Strengthening muscles that still have strong innervation will help compensate for the weaker or denervated muscle groups. This will improve baseline strength and function, and expedite recovery after exacerbations. Treatment should focus on coordination, balance, strength and functional rehabilitation.

Another factor that can increase the symptoms of MS is core temperature. MS patients have difficulty regulating their autonomic nervous system; therefore they have difficulty regulating their core temperature. An increase of at least 0.5 degrees Celsius will slow and ultimately block nerve impulse conduction in demyelinated fibers. This results in a temporary increase in neurological symptoms that can worsen fatigue and prevent the patients from being able to perform their ADLs [2]. When treating patients with MS it is important to incorporate a work to rest ratio that is patient specific to avoid overheating. One suggestion to incorporate this into a training program is to break up aerobic exercise. For example: if the patient wishes to do 20 to 30 minutes of aerobic exercise, they can do 2 periods of 10-15 minutes with a rest period of 10 to 15 minutes. Patients can be monitored with the RPE scale and should not exceed a moderate intensity for aerobic exercise, corresponding to 11-14 on the Borg Scale of Perceived Exertion [18]. When performing resistance training it is important to take breaks between each set and allow the patient to fully recover before moving on. This will significantly lengthen treatment times and there may not be time to do as many exercises per treatment. Therapists should plan

their treatments prior to patient contact, choosing resistance exercises that will yield the best results. Therapists need to account for work to rest ratios and any necessary reassessment before progressing exercise.

There are still many unanswered questions regarding the pathology of multiple sclerosis. However, it is clear that the neuronal damage significantly effects patient's strength, energy level and motor control. High intensity resistance training may play a pivotal role in maintaining functional capacity and improved quality of life.

Epidemiology

Over 350,000 people in the United States have been diagnosed with multiple sclerosis and it is estimated that 1,080,000 people worldwide have the disease [2]. Petajan and White reported that in 1999 approximately 8,000 new cases of MS were diagnosed per year in the United States. An article by Rumrill in 2009 indicates approximately 10,000 new cases of MS are diagnosed each year [1,2]. This shows an increased incidence of MS within the past decade, leading to higher health care cost associated with this disease. The incidence of this disease is much greater in temperate zones, and in areas of higher latitude. Areas closer to the equator have very little incidence of MS [2].

MS is typically diagnosed between the ages of 20 and 40, but most often before the age of 30. MS is occasionally diagnosed in children and the elderly. MS is three times more prevalent in women than in men [1,3,19]. MS is uncommon among African Americans and rarely seen in the Asian population. Those of German, Anglo Saxon, and Scandinavian decent have an increased prevalence of MS [1].

80% of people that are diagnosed with MS have a subtype called relapsing-remitting multiple sclerosis. This subtype is defined by periods of exacerbations of worsening neurological symptoms which can last for up to two months. Symptoms then fade or are completely relieved [20].

Cost

Cost associated with the treatment of MS is an important factor in the treatment regime of the health care team. It is imperative to have rationale for treatment when billing payers. Cost can be considered either direct or indirect, while direct cost refers to resources consumed by MS interventions, and indirect cost correlates to productivity and functional loss. Also, with an estimated 1,080,000 people in the United States that have MS, much of our health care spending is devoted to these patients [2]. Cost associated with an inpatient hospital stay due to a relapse is six times greater than treatment on an outpatient basis [16]. Patients with MS require multiple medical services and as of 2007 the greatest amount has been spent on drugs, hospitalization and other direct costs such as equipment for their disability and nursing services [1]. It costs nearly 50,000 dollars per patient with multiple sclerosis to be treated annually. On average over 3 million dollars are spent on each patient throughout their lifetime [6].

By improving physical therapy services and inevitably improving their quality of life through exercise, we can potentially decrease some of the cost for drugs, hospitalization and equipment. For example, if we can improve or maintain strength, the person is less likely to need a wheelchair and can better perform their work.

Anti-depression and anti-anxiety medications are widely used by patients with MS. If the health care team can make these patients more mobile and able to complete their activities of daily living, they will be less likely to suffer from anxiety or depression. Exercise and functional training should eradicate the need for these medications. Improving the

quality of physical therapy services for MS patients can reduce health care spending for patients with MS.

History of exercise training for patients with multiple sclerosis

Resistance training has often been avoided in patients with multiple sclerosis because it often initiates an immediate increase in neurological symptoms. However, this increase in symptoms, which appears in approximately 40% of patients, is shown to last only half an hour post-training [21]. There remains a necessity to educate the patients and the health care team about this ephemeral increase in symptoms due to exercise, and that there are no lasting consequences related to relapse. The long term benefits of a comprehensive treatment program outweigh the short term fatigue and increase in symptoms. Resistance training however, is not for patients who have recently experienced an acute exacerbation (see Appendix-B).

Most successful studies have involved subjects that have been in remission for at least 8 weeks [22]. Most studies with successful outcomes used a 2-4 minute rest period between sets of resistive exercise to avoid adverse effects [21]. For many years it was idealized that an increase in core body temperature caused symptom instability in the MS population, thus physical activity beyond ADLs was not advised. Also, by foregoing exercise, these patients were thought to conserve energy for ADLs [23]. To help prevent an exacerbation of symptoms due to an increase in core temperature, room temperature should be set lower than usual, careful attention should be paid to the work: rest ratio, cool garments should be worn when possible- and patients should be well hydrated throughout exercise [2]. It can help if patients take a cool bath or shower prior to exercise [24].

The benefits of resistance exercise include muscle hypertrophy, improved cardiovascular and respiratory fitness, increased arousal, improved mood and reduced fatigue [25]. Past exercise routines have included a “muscular fitness pyramid” moving up from the base of passive range of motion to active flexibility, then resistive exercise, and lastly a specific muscle strengthening and integrated strength grading program. Tai Chi and yoga have been found useful in flexibility- and body weight exercises have been shown to strengthen patients who are physically able.

Aquatic programs, endurance training and resistance exercise using high reps and low to moderate exertion have been a traditional therapeutic exercise approach to care for MS patients [2]. There is limited access to exercise recommendations involving progressive resistance training for MS. It has been shown in a study by Kraft et al. that progressive resistance training improves patient’s ability to perform activities of daily living and improves their overall mood and health [26]. In addition former exercise programs focused on lower extremity training [27]. Rather than challenging the potential of MS patients, rehab specialists have stopped progressing MS patients before they have reached their maximal exertion.

Effects of Resistance Training on Type II Muscle Training vs. Type I Muscle Training

Muscles are made up of different percentages of fiber types. Type I or slow twitch fibers and are highly oxidative with the greatest amounts of mitochondria. They are highly resistant to fatigue and have a slow velocity of shortening. Type II fibers are divided into subtypes. Type IIa muscle fibers are less oxidative than type I fibers, and are considered highly anaerobic. They fatigue more quickly than type I fibers and have a higher velocity of shortening. Type IIb fibers are the fastest to fatigue but

can produce the greatest force and velocity of shortening. Type IIx is found to be an intermediate fiber type between type IIa and type IIb [28].

Type I and type II muscle fiber diameter and mass is decreased in patients with multiple sclerosis. In a study by Kent-Braun JA et al., it has been shown that there is greater atrophy in type II fibers vs. type I fibers in patients with MS [17]. The combination of decreased strenuous activity and past suggestions to only participate in low intensity activity propagate muscle atrophy in the MS population. This phenomenon combined with decreased strenuous activity is likely to be reason for muscle atrophy in patients with MS. Allowing type II fibers to atrophy can lead to difficulty performing activities of daily living, reinforcing the necessity of a resistance strengthening program [29].

Adequate intensity should be considered when prescribing a resistance training program for patients with MS. Intensity can be described in terms of a percentage of age predicted maximal heart rate (APMHR) [22]. It is important to understand that people with MS may have a decreased average maximal heart rate compared to a healthy person. One study showed that with cycle ergometry peak heart rate was 10 less beats per minute than the age predicted estimate [30]. To measure intensity objectively, the health care professional can use a HR monitor to track the patient’s performance over time. The patient can also report their perceived intensity subjectively using the Borg scale of rate of perceived exertion (RPE). A score of 11-14 on the Borg Scale of Perceived Exertion is considered moderate intensity training [27].

“Henneman’s size principal” indicates that larger motor neurons innervate type II muscle fibers and are activated with moderate to high intensity exercise. In MS patients the larger motor neurons are not triggered as often since they do not typically engage in moderate to high intensity exercise or activity. In one study by Dugas et al., it was shown that resistance training increased type II muscle fiber cross sectional area. Isokinetic muscle strength was improved especially in fast muscle contractions. For example, there was a significant increase in the knee extensor group with fast contractions at 180 degrees per second, and in the knee flexor group with fast and slow contractions at 180 and 90 degrees per second, respectively [31].

In a study by Bacou et al., who denervated fast and slow twitch muscles in rabbits, it was found that type IIb muscle fibers were the most affected by neural influence. After 5 months of denervation, muscles with 70% type IIb fibers and 22% type IIx/d converted to 2% type IIb fibers and 98% type IIx/d fibers. Muscles consisting of type I fibers only, were hardly affected by denervation with respect to fiber numbers and size [Bacou]. Therefore it is important to train type II muscle fibers in patients with neurological disorders considering anaerobic fibers are most affected by neural degeneration. If the integrity of these fibers is maintained or even improved, MS patients should experience less fatigue with activity.

Additionally, women have a smaller cross sectional area of all fiber types, especially type II. This is true for both the healthy population and people with multiple sclerosis. Since MS primarily affects women, type II fibers need to be targeted during exercise to maintain strength. Another factor affecting type II muscle fibers is age. It has been shown that type II muscle fibers are more affected by aging than type I fibers [32,33]. Skeletal muscle high in type II muscle fibers showed a decrease in size and number of type II muscle fibers with aging [29]. This study shows that age further deteriorates the MS patient’s ability to perform quick muscle contractions which are needed daily to perform activities required for their role in society.

Age is an additional factor leading to decreased strength. A review

by Faulkner et al., shows that muscle mass, and resultant strength and power, gradually decline starting as early as age 40. This is known widely as sarcopenia- and is caused by the cross sectional area of type II muscle fibers decreasing with age. Type I fibers tend to maintain their cross sectional area [34]. The normal decline in power with age, in combination with the neurological effects of MS accentuates the severe motor deficits seen in the MS population. Resistance training can help reduce the functional deficits resultant from weakness from the aging and disease process.

Resistance Training in Patients with Multiple Sclerosis

Since type II muscle fibers are more affected by multiple sclerosis and aging, it is important to perform resistance training to hypertrophy the tissue. These muscles need to be able to produce the adequate fast contractions that MS patients need in order to independently perform activities of daily living.

The goals of resistance training are: to increase cardiorespiratory fitness, strength and endurance, reduce fatigue, improve ability to perform ADLs, improve mood and better the quality of life. Resistance training reduces the risk of obesity, vascular disease, heart disease and individual propensity to osteopenia. Failure to perform resistance exercise leads to decreased bone strength, an increase risk of fracture, decreased breathing efficacy and a greater amount of fatigue [25].

Although there are barriers to resistance training such as spasticity, tone, fatigue and ataxia, it is important to perform resistance training specifically to meet the needs of each patient [35]. Exercise should be planned to avoid overheating for MS patients. Some things that the therapist can do include turning down the temperature in the room and giving the patient frequent breaks. Research suggests 2-3 min rest between sets during resistance bouts [12,15,31].

To cool core body temperature before resistance exercise patients can take a cold bath for half an hour. This will allow for approximately 40 minutes of sustained exercise without significant increase in core temperature [24]. Patients can also use cryotherapy during a session of resistance training on body parts that are not being exercised [2]. In addition to resistance training, therapists should include stretching and tone reduction techniques in their treatments such as rhythmic rotation and sustained deep pressure.

One study by Dalgas U, et al. showed that biweekly progressive resistance training in MS patients leads to an increase in type II fiber cross sectional area without any deviation from the original fiber proportions in respect to fiber number [21,31]. This shows that the individual type II muscle fibers increased in diameter. Other populations with weakness have showed improvements with a resistive training regime. These populations include arthritis patients, nursing home residents and life care community residents [2]. After several months of training it is possible for all patients to reach a plateau [2]. The resistance training program should be progressed to provide a continuous overload by adding new exercises to target neglected muscle groups.

Not only has resistance training been shown to increase muscle volume and strength in patients with MS, but studies show that it improves the quality of functional activities such as gait. A study by Gutierrez GM, et al. showed that after 2 months of resistance training in patients with MS their gait was improved. Specifically, patients demonstrated a longer swing phase (less time spent in double limb support), longer step and stride length and better toe clearance. Also, a decrease in the amount of fatigue was reported by the patients in this study [13]. In addition, one study showed that knee extensor and flexor

strength is an important indicator for ambulation. It shows that people with improved knee extensor and flexor strength have more advanced gait. This implies the necessity for strength training of the quadriceps and hamstrings [36,37].

In a study by Gehlsen GM, et al. patients performed an aquatic exercise program working up to 75% of their maximal heart rate. Results from the study showed that these patients had improved muscle strength and endurance in the upper and lower extremities. Specifically, upper extremity arm power was increased and fatigue was reduced after performance of lower extremity exercise [14]. Decreased fatigue with daily activities will lead to improved mood and greater ability to be a part of larger social groups.

A study by Kraft GH, et al. found that after progressive resistance exercise three times a week for twelve weeks comparing mild to severely impaired MS patients that walking, climbing, and chair mobility all improved as a measure of function in both groups. Improved ability to perform these activities results in increased participation in society and improved quality of life. Studies also reported that there were no sustained increases in neurological symptoms during progressive resistance training trial periods [34].

Psychosocial Benefits of Exercise

Among psychosocial aspects of this disease condition, fatigue is considered the most limiting to a patient's daily activities. The Social Security Administration recognizes fatigue as a criterion for MS disability. 67% of MS patients reported fatigue as limiting their social and occupational responsibilities; healthy adults had null reports in comparison [38]. Fatigue and depression have a high correlation of coexistence in the MS population [39]. MS patients have less of a tolerance for exercise, ADLs, social activities etc. all contributing to a decreased quality of life. As their motivation to exercise declines, their strength decreases contributing to a deconditioned state that continues its morbid cycle over time.

Patients with MS were previously discouraged to exercise, leading to a decrease in baseline ability and social capacity, further implicating depression.

Physical therapy exercise recommendations for individuals with multiple sclerosis

When treating patients with multiple sclerosis a thorough assessment should be performed prior to intervention. This assessment should be inclusive of the Expanded Disability Severity Scale (EDSS) and the Fatigue Severity Scale (FSS). The design of this protocol is targeted for MS patients who are still ambulatory, and score equal to or less than a 6.0 on the EDSS. Each patient presents differently with the disease and it is important to know what the patient is capable of doing and where they need strengthening. A baseline assessment and a reassessment after every four to five treatments are crucial to goal setting and objective outcome measurements. Exercises should be targeted to improve the patient's ability to proficiently perform ADLs and social responsibilities.

The prescribed exercises aim to strengthen and decrease fatigue so that the patients can participate in recreational activities and enhance their quality of life. Fatigue and depression decrease the patient's activity levels, leading to deconditioning over time. As clinicians it is important to consider psychosocial factors such as depression, difficulty with sleeping, and decreased motivation when prescribing an exercise regimen [39]. Patient education is crucial, along with reassurance of the benefits of exercise. Guidance should be provided by

the rehab team to resolve psychosocial matters. In addition, clinicians need to be sure to recognize any contraindications and precautions to treatment, which defines common precautions or contraindications to the MS population. This chart is not all inclusive; be aware of any other contraindications or precautions to exercise pertaining to your specific patient.

The American College of Sports Medicine recommends that resistance exercises should be done two to three times per week [11]. The first to occur are physiological in nature and are the result of neurological adaptation. More rapid changes may be seen initially, with a decrease in the speed of results as they progress with the program.

To determine the amount of weight for each exercise a one repetition maximum (1RM) needs to be calculated. This is calculated using the following formula:

$1RM = (0.03 \times \text{repetitions} \times \text{weight (lbs)}) + \text{weight (lbs)}$. Prior to finding the 1RM, manual muscle tests should be performed to obtain a baseline strength measurement. To further evaluate their capacity a thorough history of functional and recreational activity should be taken into account when choosing a starting weight.

Repetitions represent the frequency of the exercise and the number of sets represents the duration of the exercise. Once a full evaluation and 1RM are assessed, the patient is ready to begin exercise training. Exercise should begin the second session. During the next session, when exercise training begins, the weight for each exercise should be set at 60-70% of the patient's 1RM for the muscle groups being trained. At this weight the patient should be able to perform approximately 10-12 repetitions. Once the patient can perform 15 repetitions with correct posture at this weight, the weight should be increased to by 2-5% of what they were previously lifting. If the patient can perform up to 15 repetitions with correct posture at the new weight, this patient needs to be reevaluated for their 1RM. Prior studies that have used a 2-3 minute rest period between sets have had successful outcomes with no adverse effects from exercise [12,15,31].

Task Specific Strength Training

Task specific training is exercise designed to directly improve a specific task that a patient has difficulty performing. Research shows that doing parts of the task in isolation to strengthen movements that are weak or uncoordinated, followed by practicing the complete sequence of movements involved in the task is more beneficial than strengthening alone. When muscles are trained in the correct position and sequence of the task that needs improvement, patients have more successful goal related outcomes [34,40,41]. An example of training in the correct position with the correct sequence would be squats to improve sit to stand.

Prior to focusing on task specific training it is important to determine where to focus interventions. Functional assessments such as the Dynamic Gait Index, Functional Independence Measure, Timed up and Go, 6 minute walk, and Berg Balance Test will objectively measure functional activity. These tests can also be used to document functional outcomes. Once deciding what area of function is most important to focus on, the physical therapist should incorporate task specific training. When prescribing exercise to patients with multiple sclerosis, strengthening should be followed by an activity that targets patient-specific goals [42].

When doing task specific training, movements should be practiced repeatedly and positive reinforcement from the therapist should be used. Tasks can be progressed from blocked practice, doing the task

the same way multiple times, to performing the task in a randomized fashion in varying conditions [34]. To avoid fatigue, strength training should last no longer than 45 minutes to an hour with periods of rest incorporated. Resistance training should be followed by 10 minutes of task specific strength training. This functional training can include tasks such as gait training on uneven surfaces, stair climbing, swimming, or other tasks that are important to the patient.

Conclusion

It is important for clinicians to realize that Appendix A is a suggested protocol for exercise and that this study is a review of literature, not a randomized controlled trial. Therefore, it is important to realize any contraindications and precautions to exercise especially in this population. Recent research shows statistically significant gains in functional ability when exercising patients with MS whose EDSS score is less than 6.0. Those patients whose EDSS score is more than 6.0 should be carefully monitored when performing any resistance exercise. This study shows no conclusions pertaining to the benefits of exercise for the severely disabled- due to the inability exercise these patients at a moderate intensity.

Clinicians are reminded to prioritize the safety of their patients, as well as to closely monitor their symptoms before and after exercise. Physical therapists should establish short and long term exercise goals with their patients, and ensure patient adherence through verbal contract. The patient is more likely to experience psychosocial gain if they can achieve mini-milestones during rehabilitation. It is necessary for the clinician to educate patients of the benefit of resistance training and its positive effect on fatigue. It is important for the patient to draw correlate to an improvement in all aspects of fatigue and a better quality of life.

In order for health care providers to decrease cost, a thorough assessment of the literature is always recommended when working with special populations. In particular, keeping the cost of inpatient relapse stays down can reduce the total expenditure per capita in this population. This review provides exercise guidelines to follow in order to improve baseline function of the individual in order to decrease the demand for further specialty care.

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