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November 11, 2012

Part A

**PICO: In patients age 30-60 with multiple sclerosis and impaired balance, are interventions to improve postural control more effective in decreasing falls risk than resistance exercise?**

**Introduction**

 Multiple Sclerosis (MS) is an autoimmune disorder of the central nervous system characterized by inflammation and neuro-degeneration1. The disease process causes progressive accumulation of neurologic deficits over several decades leading to varying levels of functional decline and increasing disability. MS is most often diagnosed in persons aged 15 to 45. In the US, 8,500-10,000 new cases are diagnosed each year and prevalence is estimated at 400,0001,2.

 MS causes demyelinization of nerves in the central nervous system (CNS) which interferes with nerve signal propagation to the peripheral nervous system1. The demyelinization can occur in any part of the CNS, but preferentially affects nerves that are highly myelinated. The myelin enables the nerves to conduct signals at high speeds, thus MS drastically slows nerve function. Symptoms of MS are dependent on the location of damage and can widely vary between persons with MS. Common symptoms include: fatigue, weakness, spasticity, gait, balance, and coordination dysfunction, problems with vision, dizziness, bladder and bowel dysfunction, pain, and emotional and cognitive changes1.

 People with MS (PwMS) commonly report loss of balance and more than half of PwMS have fallen in the past 6 months2. PwMS have increased risk of injury with falls3,4. Fracture risk is increased as a result of altered bone metabolism secondary to corticosteroid treatment and inactivity3. This is a concern at all levels of disability as bone density changes are often seen as early as time of MS diagnosis3. The mechanisms contributing to falls in PwMS are not well understood, but it is known that falls contribute to increased healthcare costs and increased disability. Findings indicate that better management and treatment of imbalance and gait instability in PwMS can result in decreased falls and thus decreased healthcare costs, increased mobility, and improved quality of life.

 The variability in presentation and progression of MS symptoms makes research challenging. This is especially true for falls prevention as multiple body systems are utilized for balance; vision, vestibular, musculoskeletal, and somatosensory systems all play a vital role. Further, research for similar symptoms in other neurodegenerative disease or aging populations has proven to not be generalizable to MS5.

 Resistance training to increase lower extremity strength improves balance in healthy adults, seniors, older adults with stroke, Parkinson's disease, and other neuromuscular diseases4,5. Likewise, postural control exercises are thought to improve balance and reduce risk of falls6. By comparing the effectiveness of resistance training to postural control for PwMS in an age range of 30 to 60, this literature review will serve as an evidence-based resource to design effective interventions for PwMS.

**Summary of the evidence**

*Background*

 Research finds that adults with MS have decreased lower extremity strength and decreased balance than their peers4. PwMS are capable of increasing strength with resistance training, but contrary to the effect in other populations resistance training to improve balance and gait in MS has shown mixed efficacy4,5.

Two articles, a research study and a literature review, have recently evaluated the role of postural control in standing balance and falls prevention for persons with MS6,7. The authors of both studies concluded that the primary mechanisms of imbalance in MS are slowed somatosensory conduction and impaired central integration6. These findings minimize prior theories that cumulative neurologic deficits and cerebellar lesions are major contributors to imbalance for PwMS6.

 In spite of the variable disease presentation, slowed somatosensory conduction and impaired sensory integration are common findings in PwMS6,7. In quiet stance, PwMS have increased sway than healthy controls6,7, likely related to the slowed somatosensory conduction6. In response to perturbations, PwMS react with more repetitive movement patterns and have reduced ability to move toward their limits of stability 6,7. This indicates reliance on past movement patterns and reduced adaptation to novel conditions6. Based on this research, postural control exercises should have a positive effect on balance and falls risk for PwMS.

*Literature Review*

 The evidence evaluating the effectiveness of resistance training and postural control exercise on falls risk in PwMS utilizes a variety of study design. Of the ten studies included in this review, six are randomized controlled trials, two are cross-sectional studies, one is a single-group repeated measure, and one is a literature review. All subjects have a diagnosis and Multiple Sclerosis and sample sizes range from 11 to 96. Expanded Disability Status Scale of the subjects range from 1.0 to 6.5. Mean age ranges from 46 to 51.

 Researchers use numerous outcome tools to assess change in balance, gait, and function. Gait speed is correlated with falls risk in the MS population10. Several studies measure gait speed with the 10 Meter Walk Test (10MWT) and Timed 25 Foot Walk Test (T25FWT)9-11. Balance measures include the Berg Balance Scale (BBS), Dynamic Gait Index (DGI), Mini-BestTest5,8,13-15. Dynamic posturography is utilized to measure postural sway, sensory organization (SOT) and limits of stability (LOS)4,15. The timed up and go (TUG) and cognitive TUG measure mobility and dual task8,13. The Activities-specific Balance Confidence scale (ABC) is also a frequently used measure as fear-avoidance can limit mobility8.

*Resistance Exercise*

 Five studies evaluated the effect of resistance training on balance or balance-related outcomes4,5,9-11. Two of these, designed by Dalgas and Romberg10-11 provide evidence in favor of resistance training to improve balance. Studies by Hayes, Dodd, and Debolt did not show a significant effect on balance and falls prevention4,5,9.

 The studies by Dalgas and Romberg are both randomized controlled trials10-11. Dalgas's study occurred over 12 weeks with 2 days a week of supervised training in a gym setting10. Romberg's study occurred over 26 weeks divided into a 3 week period of inpatient rehabilitation followed by 23 weeks of home exercise11.

 Significant improvements in gait speed occurred in all subjects in both studies. The exercise group in the Romberg study demonstrated a 12% decrease in time to perform the T25FWT whereas the control group took 6% longer than baseline11. Similarly, the exercise group in the Dalgas study demonstrated a 12.3% decrease in the 10MWT and the control group increased 6.7%10. The 12.3% change corresponds to a 0.2m/s increase in gait speed which is clinically meaningul at reducing risk of falling10.

 As expected for their different settings, the intervention design differed between Dalgas's and Romberg's studies. Dalgas uses weight machines to provide resistance whereas Romberg uses theraband resistance for the home exercise period10. In the Dalgas study, resistance training was performed 2 days a week consisting of leg press, knee extension, hamstring curl, hip flexion, and hip extension10. In the Romberg study, resistance exercise was performed 3 days a week and consisted of 6 exercises: 2 exercises each for the lower extremities, upper extremities, and trunk11. Additionally, aerobic exercise was performed 1 day a week11.

 In contrast to the findings by Dalgas and Romberg, studies by Hayes, Debolt, and Dodd did not show a significant effect of resistance training to decrease fall risk4,5,9. The intervention in Hayes's RCT occurred over 12 weeks with 3 days a week of supervised training in a gym setting5. Dodd's study, a RCT, also occurred in a gym setting with supervised training 2 days a week for 10 weeks9. Debolt's study, a cross-sectional design, began with 6 sessions of exercise instruction in a 2 week period followed by 8 weeks of home exercise4.

 Debolt's results showed the most benefit for balance and mobility, but findings were not significant4. There was a 10.3% decrease in anterior-posterior sway and 4.0% decrease in medial-lateral sway in the exercise group4. The exercise group also demonstrated a 12.7% decrease in time to complete the Up and Go Test (similar to the TUG)4. The control group results showed little improvement or a decline over the same time period4. Resistance exercises included chair raises, forward lunges, step ups, heel and toe raises, and leg curls and weighted vest and ankle weights were used to progress intensity4.

 Dodd's study utilized weight machines to perform leg press, knee extension, calf raises, leg curls, and reverse leg press9. Two sets of 10 to 12 reps were performed of each exercise9. While strength did improve, there was no effect for gait speed, balance, or falls prevention9.

 Hayes's study included aerobic training, stretching, and balance exercise with the treatment group adding a single lower extremity resistance exercise5. The results in Hayes's study were in favor of the control group whose BBS scores increased by 6 points compared to only 1.3 points in the treatment group5. Similarly, performance in ascending and descending a flight of stairs improved in the control group and declined in the treatment group5.

 There are no glaring differences between these five studies to easily explain the inconsistent results. Home exercise versus supervised exercise and weight machines vs alternative methods of providing resistance were utilized in both the successful and unsuccessful studies4,5,9-11. Aside from the 26 week Romberg study, the 10-12 week timeframes may have been insufficient for changes in strength to carryover to functional changes. Variables of intensity, duration, and frequency are also a factor. Whereas the Romberg study had the benefit of time11, the Dalgas study used a higher exercise intensity: 3-4 sets of 8-12 reps with a load at 8-12 rep max10. The other studies primarily used only 2 sets of each exercise4,5,9.

*Postural Control Exercise*

 Five studies evaluated the effect of postural control exercise on balance or balance-related outcomes for PwMS. Two articles compared postural control exercises to other physical therapy interventions: a literature review by Hogan12 evaluated physical therapy interventions compared to exercise including aerobic and resistance training and a RCT by Cattaneo14 compares balance rehabilitation with motor and sensory strategies to conventional therapy. The final three articles evaluate the effectiveness of home balance training, group kickboxing, and Wii Fit gaming8,13,15.

 The Hogan article included four studies on specific physical therapy interventions for balance rehabilitation12. The interventions with successful balance outcomes used sensory and motor strategies, a task oriented approach, and facilitation techniques. The other articles included in the literature review used body weight supported treatment training, aerobic exercise, resistance training, and yoga. Of these, only the body weight supported treadmill training showed benefit while the others had no effect on balance outcomes.

 Cattaneo's research builds on Hogan's findings by comparing three interventions: balance rehabilitation to improve motor and sensory strategies, balance rehabilitation to improve only motor strategies, and treatment not aimed at improving balance14. This study took place within an inpatient rehabilitation facility with 10 to 12 physical therapy sessions occurring over 3 weeks14.

 Over the course of Cattaneo's study, patients in all groups reported reduced number of falls, but a greater reduction was seen in the groups receiving balance rehabiliation14. On the BBS, the motor and sensory strategies group improved 6.7 points and the motor strategies only group improved 4.6 points14. The non-balance intervention group only improved 0.8 points14. There was a significant difference between scores in groups 1 and 3 and groups 2 and 3 indicating that the addition of motor strategies was beneficial, but not to a statistically significant degree14.

 Hogan and Cattaneo's research findings support the motor learning principles of transfer and specificity12,14. The interventions focused on balance rehabilitation were logically most successful at improving balance. The 6.7 and 4.6 point improvements on the BBS likely correlate with a clinically meaningful reduction in falls risk for the majority of subjects in those treatment groups12,14. Their results are also consistent with the proposed mechanisms of imbalance in MS - slowed somatosensory conduction and impaired central integration6,7.

 With the goal of improving exercise adherence, a randomized controlled trial evaluated a 6-7 week Nintendo Wii Fit program to improve balance for PwMS13. A physical therapist was in control of the remote, but participants were allowed to choose the Wii games they enjoyed13. After 12 thirty minute sessions, participants showed a significant improvement in TUG cognitive, timed chair stand, and the DGI13. However, there was not a significant difference between the Wii group and the control group as a level of contamination may have occured13.

 Capitalizing on another popular activity, a 2012 pilot study evaluated the effect of a group kickboxing class on balance8. The class met 3 times a week for 5 weeks and progressed through a series of punching, kicking, and kneeing movements8. The participants hit padded targets as well as held targets for one another.8 An overhead harness was used for safety and allowed participants to move without fear of falling8. Significant improvements were seen in gait speed, TUG, DGI, Mini-BESTest, and the ABC which correlate with a reduced risk of falls8.

 Lastly, Jackson designed a 2007 study based on specific impairments associated with MS: vestibular dysfunction, weakness, sensory disturbances, and decreased range of motion15. The home-based program includes 11 exercises performed in either seated and standing to improve static and dynamic postural control, vestibular and visual systems, ankle strategy, strength, and posture15. The exercises performed 3 times a week for 6 weeks resulted in an average 6 point improvement on the BBS, significant improvement on the SOT and improved excursion to limits of stability15. The results likely indicate a reduced risk of falls for the study participants.

 Of these studies, there is extreme variability in intervention design, however, postural control exercises showed a positive effect in nearly every balance outcome for improving balance and reducing falls.

*Results and limitations*

 The design of the studies included in this literature review limit the direct comparison of the effectiveness of resistance training versus postural control exercise to decrease falls risk. A primary limitation in making comparisons is the inconsistent outcome measures used in each study. That said, the evidence in favor of postural control interventions was overwhelming positive compared to the mixed results seen in the research for resistance training.

 The progressive and variable nature of multiple sclerosis provides an additional challenge to research. Several of the postural control interventions provided a greater amount of customization to the specific impairments of the patient than the resistance training protocols. For example, Cattaneo's balance rehabilitation interventions are little more than a conceptual framework that allow significant leeway for the discretion of the physical therapist14. The home exercise program in the Jackson study includes lower extremity strengthening even though balance is the primary outcome15. Since balance involves the integration of multiple systems, the ability of any single intervention to have an effect on balance is unlikely.

 Sample sizes are often small in MS research. Several of the studies in this literature review have small group sizes that limit the ability to detect significance. In the Hayes study groups only included 9 and 10 subjects and the treatment group and control group participated in the same 45-60min exercise program with the addition of a single exercise for the treatment group5. The results were largely in favor of the control group for several outcomes, however, the raw data of the individual subjects showed wide variability5. Thus, the strength of the author’s conclusions is limited.

*Clinical Relevance*

 This review of literature finds strong support for postural control exercise and moderate support for resistance training to improve balance and reduce falls in persons with multiple sclerosis. In clinical practice the individual impairments and needs of the patient need to be considered when planning an intervention. The interaction of multiple body systems in context of the individual patient and their environment warrant consideration with intervention design.

*Capstone Prospectus*

 For physical therapists working with patients with Multiple Sclerosis, the chronic, progressive, and variable nature of the disease creates a challenge for the design of effective interventions. The amount of research for physical therapy interventions is growing, but has historically been lacking. As such, many practicing physical therapists are not up to date on the evidence for treating MS. The results of this literature review will be included in a module to educate physical therapists on physical therapy assessment and treatment for persons with MS. A portion of the module will focus on intervention ideas. Several studies referenced in this paper have well described interventions supported by evidence and theory.

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