ABSTRACT

IS ROBOT-ASSISTED GAIT TRAINING MORE EFFECTIVE ON IMPROVING GAIT VELOCITY AND BALANCE IN POST-STROKE PATIENTS COMPARED TO CONVENTIONAL OVERGROUND GAIT TRAINING? A META-ANALYSIS

Objective: This meta-analysis compared the effectiveness between robot-assisted gait training and conventional overground training on improving gait velocity and balance in patients in subacute and chronic phases of stroke.

Methods: Four databases were used to obtain studies to be included in this meta-analysis. Data analysis was completed using MetaAnalist software to determine treatment effect size and homogeneity between studies.

Results: Twelve studies were included in this meta-analysis. The results showed no statically significant difference between combination of robot assisted gait training and overground gait training versus overground gait training alone, or between robot-assisted gait training and overground gait training on improving gait velocity or balance.

Conclusion: This meta-analysis did not show significant differences between robot-assisted gait training and overground gait training on improving gait velocity and balance in subacute and chronic phases of stroke. However, is it suggested that lower functioning individuals or patients in the more acute stage may show more improvement from robot-assisted gait training compared to chronic stroke.

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A META-ANALYSIS

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BACKGROUND

Stroke, or cerebrovascular accident (CVA) is the 5th leading cause of death and the leading cause of long-term disability among adult in the United States. It affects almost 800,000 people in the U.S. every year.[1] Stroke results in a sudden, specific neurological deficit and happens when a blood vessel in the brain is either occluded by a clot or ruptures resulting in a bleed[2]. This vascular event can last for seconds, minutes, hours, or a few days.[2,3] There are two types of stroke: ischemic and hemorrhagic. Ischemic stroke is often caused by an obstruction of the blood flow in a cerebral blood vessel. It accounts for 87% of all stroke cases. Hemorrhagic stroke occurs when a weakened blood vessel ruptures. Both types of stroke cause disruption in the blood flow to an area (or areas) of the brain, resulting in tissue damage or tissue death. Studies show multiple declines in quality of life in stroke, and it is the leading cause of serious long-term disability.[4,5] The focal neurological deficit resulting from a stroke is determined by the size and location of the lesion and the amount of collateral blood flow. Signs and symptoms vary between types of stroke and between individuals, although, there are some common signs and symptoms. [6] Individuals who suffered a stroke can present with difficulty walking, weakness, problems with coordination, hypertonic muscles, paralysis, and reduced sensation in involved extremities, which can all lead to functional deficits. Many can also have difficulty with speech, swallowing, or vision. Hemiplegia, a paralysis of one side of the body, is the classic sign of neurovascular disease of the brain. The related hemiparesis is caused by disruption of descending neural pathways, with no direct lesion on the musculoskeletal system or spinal circuit in the acute phase.[7] Secondary changes in

the musculoskeletal system and spinal circuitry happen later, leading to increased deficits in mobility.[7]

Gait After Stroke

Walking dysfunction is a major problem for many stroke survivors,[3,8] and to improve walking function is the most often stated goal by patients following a stroke. About 80% of stroke survivors continue to experience walking problems 3 months after onset.[3] Muscle weakness and loss of voluntary movements are signs immediately following stroke. Gait deviations can be divided into primary and secondary deviations; primary deviations directly relate to the pathology and usually present at the beginning of the stroke, and secondary deviations can happen after a physical effect of the primary deviation (passive secondary deviations) or happen in order to actively offset primary deviations and secondary physical changes (active secondary deviations).[9] Primary gait deviations would be mostly related to the initial disruption of descending neural pathways while secondary deviations are a neural adaptive process. The asymmetric pattern may be a specific adaptation of the initial and on-going paresis of the affected side, as the cerebellum is usually intact in patients following a stroke.[9] Independent, functional, and safe walking is difficult to retrain in the early phases of stroke rehabilitation because it requires refined degrees of trunk and extremity control. Optimal gait requires proper trunk control, trunk alignment, lower extremity range of motion, and enough strength and control in the lower extremities to support body weight. Components of gait include movement of multiple joints in complex patterns, control of speed, momentum, and balance[2]. Stroke patients demonstrate a significant decrease in gait velocity compared to before stroke, and as expected, compared to the normal population.[10]

Gait Velocity

The patients who have experienced a stroke often demonstrate gait with slowed speed, uneven step and stride lengths, poor balance, abnormal posture, and dependence on assistive devices.[2] Reduced walking speed is a characteristic sign of post-stroke gait. For effective community ambulation, a gait velocity of at least 1.14m/s is suggested,[11] but post-stroke patients have an average gait velocity of 0.23m/s to 0.73m/s slower than able-bodied population.[12] Walking below normal gait speed is closely correlated with the risk of falling, hence causing additional injuries.[3,13] Seventy percent of community dwelling post stroke individuals fall during the first year due to loss of balance when walking.[3,14] Improving the quality of gait not only reduces a patient's disability, but also increases their safety in daily activities.

It is reported that gait velocity can still increase from 3 months to 12-18 months after stroke.[15] Therefore, gait velocity has been suggested to be one of the most important outcome measures of locomotor recovery for the post-stroke subjects.[3] A study detected real change in the majority of patients during the 8-week intervention period. It suggested that gait velocity was a cost-effective and simple measure to obtain in the clinical setting.[10] The 10-meter walk test has high reliability in evaluating improvement in various aspects of gait performance in individuals with chronic mild to moderate hemiparesis after stroke.[16]

Balance

Postural control and balance are usually impaired following stroke with change in alignment, stability, symmetry, and dynamic balance.[3] The patient may have difficulty with reactive postural control and/or anticipatory postural control. Therefore, the patients may have difficulty maintaining balance in sitting or standing or to move the posture. They often present with uneven weight

distribution and increased postural sway in standing. [3] The inability to utilize effective postural strategies and adapt postural movements to changing tasks and environment is due to the disruption in the central sensorimotor processing. Static and dynamic balance should be examined in patients with stroke.[8] The Berg Balance Scale (BBS) is proven to have high interrater and intrarater reliability, and is a valid outcome measure for balance.[8]

Rehabilitation After Stroke

Neuroimaging studies show that the premotor cortex and the supplementary motor cortex are activated prior to initiating stepping in human gait. Also, corticospinal inputs significantly facilitate muscular responses in lower extremities during swing phase. This indicates that cortical outputs play a significant role in the control of lower extremity during ambulation. However, the supraspinal outputs do not directly control the locomotion, rather, they regulate the synergy of walking.[3,7]

While locomotor control is distributed across certain regions in the central nervous system, walking is primarily controlled by the brainstem and the spinal cord. Patients with cortical stroke may be able to regain the ability to walk because the locomotor central pattern generators (CPGs) exist in the ventral spinal cord while integrating command centers have been identified in the medial medullary reticular formation. CPGs organize the activities of motor neurons to allow for alternating activation of agonist and antagonists and reciprocal movement during gait.[17,18] Through neuroplasticity, the adult brain can retain the ability to reorganize itself under the condition of peripheral stimulation, learning, and injury. Because of neural plasticity, the CNS is responsive to training-induced plastic changes in locomotor function and recovery; post-stroke neuroplasticity

can happen at levels ranging from synapses and neuron to brain network.[19] It is considered the most critical driving force of post-stroke motor recovery.[17,20] Task-oriented training is suggested to be an important element of rehabilitation of locomotion, and it is shown to significantly improve lower extremity function.[21,22] This type of training focuses on coordinating motor and cognitive functions - to maintain balance, to transfer and support body weight during stance phase, to clear the floor during swing phase, and to propel forward during ambulation. [23-25]

There are multiple interventions being used for gait training after stroke, and evidence shows that recovery of walking function occurs usually in the first 6 months after stroke.[26] Treatment options include task-specific overground locomotor training (conventional overground gait training or OGT), body weight support treadmill training, robotic-assisted gait training (RAGT) (i.e. Lokomat), functional electrical stimulation, and use of orthotics and assistive devices[8]. This Meta-analysis will compare RAGT and OGT, which are both types of task-specific locomotor training. [27]

Conventional Overground Gait Training

Adequate overground gait training is recommended for stroke patients with gait disturbances. Overground physical therapy gait training is the most common strategy to improve gait function at any stage post-stroke. This strategy utilizes simple aids, such as parallel bars, and manual facilitation[3]. Conventional gait training typically consists of retraining weight bearing, weight shifting, and balance in static positions of the gait cycle, plus dynamic locomotor tasks. This strategy focuses on practicing a variety of activities and on improving the quality of walking and walking endurance. Patients practice tasks such as walking forward, walking backward, crossed stepping, step-up/step down, walking with

obstacles, walking with increased speed, walking with multi-task, and balance activities.[8] However, abnormalities and gait deviations have been found to persist following these conventional treatments.[28] A Cochrane Systematic Review of research on conventional locomotor training showed mixed results.[3,29] Improvements in walking speed and functional performance were found in some studies, but overall there was insufficient evidence to determine the benefits. Lack of high-quality research and limited data exist with subacute stroke patients.[30] Conventional overground gait training utilizes a significant amount of manual facilitation to target muscular dysfunction involved in ambulation. Manual rehabilitation techniques have limits in the quality and consistency of treatment due to overstrain of the physical therapist.[31] The one-to-one manual rehabilitation requires extra time and manual labor, which can potentially reduce the cost-effectiveness of the treatment provided.[31]

Robotic-Assisted Gait Training

To date, robot-assisted rehabilitation has been increasingly more involved in regaining the ability to walk in patients with neurological disorders, including stroke.[31] Lokomat, first approved by the FDA in March 2002, is a type of RAGT device developed to facilitate step training and to eliminate manual assistance. It is the first driven gait orthosis that assists movements of patients with impaired gait on a treadmill, with little to no manual labor from the therapist, as is required in other types of gait training.[23] It is a powered unit that attaches in parallel to the lower limb segments and moves in sync with the patient, to automate gait therapy on a treadmill and improve the efficiency of treadmill training.[28] It consists of a body weigh support system and two robotic orthosis to guide the patient's legs during ambulation on a treadmill.[32] The purpose of RAGT is to provide consistent

feedback and a safe environment to the patient, and eliminate the labor intensive manual facilitation provided by two or more therapists during gait training. When using RAGT, body weight, gait velocity, and shape of the computer program can be controlled. The patient can receive visual feedback from the screen in front of them.[28]

Many studies have reported that the use of RAGT devices can potentially reduce the health-care cost.[31]

Rehabilitation in Each Phase of Stroke

Recovery of stroke can be divided into three different phases: the acute phase, the subacute phase, and the chronic phase. In the acute phase, typically within 72 hours, low-intensity rehabilitation takes place to prevent or minimize the harmful side effects of bed rest and deconditioning. It is proven that early rehabilitation during the acute phase can lead to better survival rate, greater independence, and improved quality of life, though the therapist needs to be aware of the patient's medical status.[8,33,34] Patients with moderate to severe impairments or activity limitation resulting from a stroke can benefit from an intensive rehabilitation program to improve functional abilities during the subacute phase, from 3 days after the onset of a stroke to 6 months post-stroke.[8,22,34] In the chronic phase, rehabilitation usually takes place in an outpatient rehabilitation facility, community setting, or at home, and is the continuation and/or progression of the treatment received in inpatient rehabilitation facility during the subacute phase. The treatment focus in the chronic phase is to improve flexibility, strength, balance, locomotion, endurance and upper extremity function.[8,35,36] The timing of rehabilitation services is very important in the prognosis of the patients who have suffered a stroke; evidence has shown that early interventions can lead to better

long term functional outcomes and less failure; however, promising results have also been shown in the patients with chronic stroke. [8,37] Therefore, this Meta-Analysis will focus on the treatments received during both the subacute and chronic phases.

Purpose

Based on current literature, conventional overground gait training is the most common strategy used in rehabilitation facilities but the effectiveness is inconclusive.[38] RAGT devices such as Lokomat are slowly being integrated in gait training, and has proven to be effective. It also substitutes manual rehabilitation provided by the therapists and improves cost-effectiveness of stroke rehabilitation. While studies have shown effectiveness in both treatments, there is limited research comparing both of them to determine if there is a significant difference.[3,39,40] Evidence shows that OGT may not be effect on restoring normal gait pattern in most patients post stroke.[31] The purpose of this Meta-analysis is to compare the effectiveness of RAGT to OGT on gait velocity and balance in patients in the subacute and chronic phases of stroke.

The null hypothesis is that there is no significant difference between RAGT and OGT on improving gait velocity and balance in patients with subacute and chronic stroke. The alternative hypothesis is that RAGT is significantly more effective than conventional OGT on improving gait velocity and balance in patients in the sub-acute and chronic phases of a stroke.[23,28,41,42]

METHODS

Searching Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used as a guideline for the design of this study. Four different databases were used to conduct the search of studies and they included the U.S. National Library of Medicine National Institutes of Health (PubMed), Cochrane Library database, the Cumulative Index of Nursing and Allied Health Literature (CINAHL), and the ProQuest database, using the following search terms: stroke OR cerebrovascular accident AND Lokomat gait training, stroke OR cerebrovascular accident AND robot assisted gait training, and overground gait training AND stroke OR cerebrovascular accident. The search was conducted from July, 2016 to October, 2016, and only included studies written between the years of 2006 and 2016.

Inclusion and Exclusion Criteria

Studies that included patients who suffered a stroke at least 3 weeks prior to receiving intervention, aged between 18 to 80 years old, and presenting with gait abnormalities were considered eligible for further review. Inclusion criteria also included studies that used gait velocity or balance as outcome measures, and studies that included robot assisted gait training and/or conventional overground gait training for patients who had suffered a stroke. Studies were excluded if they were single subject studies, or if they included subjects with cognitive deficits, subjects who suffered a stroke less than 3 weeks prior to intervention, or subjects with lower extremity injuries not related to stroke, that limits their ability to ambulate. Upon further review, studies were eliminated based on title, abstract, and the availability of usable data for analysis.

Outcome Measures

The outcome measure data collected from the studies were gait velocity, measured by 10-meter walk test (10MWT), or 8-meter walk test (8MWT), and balance, measured by the Berg Balance Scale (BBS). The 10MWT is proven to have excellent interrater/intrarater reliability, contrast validity, criterion validity, and responses in patients recovering from a stroke.[16,43-46] It is also reported to be highly correlated with BBS.[47] The walking test can be done at a distance of 6 meters, 8 meters, or 10 meters, although 10MWT is the most common. The test can be done at preferred walking speed or fastest walking speed possible, the time to complete the distance is recorded. Gait velocity is calculated by dividing the distance covered by the time, resulting in m/s.[48]

The Berg Balance Scale (BBS) is a 14-item objective measure assessing the static and dynamic balance through activities of varying difficulties, and determining whether an individual is at risk for falls.[49] Research has proven the BBS to have excellent criterion validity, interrater/intrarater reliability, and test-retest reliability for stroke patients.[50,51]

Data Collection Process

Statistical data used for analyses were extracted from means and standard deviation for the desired outcome measures (gait velocity and balance). In circumstances where studies directly comparing the two interventions were not found, the data for the control group (overground gait training) and the experimental group (robotic gait training) were pulled from separate studies and matched by similarity in subject demographics and baseline measurements before treatment.

Quality Assessment

The quality of the studies used for the meta-analysis were assessed using the 10-point Pedro Scale (see Appendix). The purpose of the Pedro scale is to help reviewers determine whether the studies have met the criteria for good internal validity, or whether or not they have the sufficient statistical information for data interpretation.[52]

Statistical Analysis

The data collected was statistically analyzed for effect size of treatment outcomes, homogeneity, and heterogeneity analysis among studies using the Open Meta-Analyst software. The effect sizes were calculated based on means of outcome measures and standard deviations and categorized as follows: less than equal to 0.2 = small effect size, 0.2 – 0.5 = moderate effect size, and larger than 0.80 is considered a large effect size. Heterogeneity or homogeneity of studies was determined by the Q-statistics and the associated p-value. If the Q-statistic was less than degrees of freedom and/or the associated p-value for heterogeneity is greater than 0.05, and the I^2 is 0, there was homogeneity between studies; otherwise, it was considered heterogeneous.[53] The results were considered significant if the p-value (95% confidence interval) was less than 0.05 and the upper and lower limits of confidence interval did not cross the zero line.

RESULTS

Study Selection

Through searching in 4 different databases, 317 studies published between 2006 and 2016 were found using the search terms identified in the methods section. After a review of titles and abstract, 257 studies were eliminated due to irrelevance to the topic, subjects falling outside of inclusion criteria, or unwanted types of articles. Twenty articles were eliminated from the remaining 60 because of duplication. After eliminating duplicates, 9 studies were excluded from the 40 studies due to absence of at least one of the outcome measures. Studies that did not include RAGT as one of the interventions were eliminated. Finally, 16 studies were eliminated because they did not provide the mean or standard deviation for the data being analyzed or the full texts were unable to be obtained. After eliminating studies that did not qualify for the meta-Analysis, 5 studies were used for the final analysis of data for gait velocity and 5 studies were used for BBS data analysis. Within the 5 studies used for BBS data, only 2 directly compared RAGT to OGT and provided data for both groups; 3 of them compared RAGT to other gait training strategies. Two additional studies that used OGT as the control intervention were pulled from the eliminated studies to pair with the 3 studies that did not include OGT. A total of 12 studies were included in the meta-analysis. A summary of the searching process is provided in Figure 1.

Characteristics of Included Studies

The quality of each study was analyzed by using the PEDro scale (0-10). The 12 studies included had scores ranging from 5-8 out of a 10-point scale. None of the studies blinded subjects or therapist, and only 2 of the studies blinded the

evaluator. Most of the studies found were randomized controlled trials except for 4. The PEDro score of each study is provided in Tables 1 and 2.

When reviewing each individual study, they all consisted of subjects with similar pre-treatment important prognostic characteristics. When comparing pre-treatment data of subjects between studies, the average ages of subjects ranged from 53.67 to 66.5 years. However, there was a significantly wide range in duration after stroke, from an average of 21.6 days to more than 6 years post stroke. As seen in Tables 3 and 4, the treatment protocols between studies were different as well. Among the studies used to collect data for gait velocity, 3 of the studies used RAGT plus OGT as the intervention, whereas the other 2 studies used robotic-assisted gait training only as the intervention. Similarly, 2 of the articles used for BBS meta-analyses compared the effects of combining RAGT to OGT with OGT alone. There is lack of consistency in treatment duration and frequency between studies. The treatment duration ranged from 4 weeks to 8 weeks with treatment time being from 30mins to 60 minutes, which took place 3 to 5 times a week. In terms of treatment protocol, there were differences in the amount of guidance provided during RAGT and the operational definition of OGT. Westlake et al. and Hornby el al. provided 100% guidance in bilateral lower extremities throughout all treatment sessions while all the other studies provided higher amount of guidance and slowly reduced the amount based on the patient's improvement and tolerance.[54,55] Also, there was slight variability in the outcome measures used to collect data. All the first 5 studies used gait velocity as one of their primary or secondary outcome measures, although they did not all use the same measuring tool. Fisher et al. used the 8-minute walk test while the other four studies used the 10MWT to obtain gait velocity.[56] However, all the studies that measured balance used BBS as one of the outcome measures. The variation

between studies also included the subject size. 4 out of 5 studies included 10-15 subjects in each treatment group, but Schwartz et al. had a total of 67 subject in their study and Dundar et al included 107 subjects in the study;[57,58] however, Schwartz et al. only included data regarding gait velocity from 30 subjects, who scored at least a 3 in the functional ambulatory capacity scale (FAC), indicating independent ambulation.[57,59]

Data Analysis

Primary Outcome Measure: Gait Velocity

The meta-analysis comparing RAGT plus OGT vs. OGT alone showed homogeneity between studies with a Q-statistic of 0.085 (2 degrees of freedom) and an associated p-value of 0.958. The forest plot comparing the means and standard deviation of post treatment gait velocities between two groups showed an effect size of -0.05, with an overall p-value of 0.787, indicating insignificance, as shown in Figure 2. The upper and lower limits of the ES crosses zero (95%CI [-0.313,0.414]), indicating that not all subjects responded the same; some responded better to RAGT + OGT while some responded better to OGT alone. Table 3 shows the effect size, CI upper, and CI lower of each of the individual studies, as well as the grand effect size of the combined data for RAGT + OGT versus OGT alone.

A separate meta-analysis was run using studies that compared RAGT alone with OGT alone. The result shows heterogeneity, with a Q-statistic of 2.097 (1 degree of freedom); the associated p-value = 0.149 and $I^2 = 51.9\%$. The grand effect size comparing intervention alone vs. control alone was small, ES = 0.117, with a p-value of 0.787, indicating statistical insignificance. CI upper and lower

limits for individual studies, as well as for the grand ES crossed 0 (95% CI [-0.734, 0.898]). With the CI crossing 0, it is indicated that not all subjects responded better to RAGT and some subjects responded better to OGT. Figure 3 shows the forest plot of the meta-analysis while Table 4 shows the data for each individual study.

Secondary Outcome Measure: Berg Balance Scale

The data for BBS were collected by pooling control and experimental statistics from different studies by controlling the ages, chronicity of stroke, and subject sizes, if possible. As was conducted for gait velocity, two meta-analyses were run for BBS. One meta-analysis was run comparing the combination of RAGT and OGT to OGT alone, while the second analysis was run comparing RAGT alone versus OGT alone. The first meta-analysis had a grand effect size of 0.279, with an p-value of 0.127, indicating insignificance. CI upper and lower limits for individual studies and grand ES also crossed zero (95% CI [-0.0079,0.637]), indicating the subjects responded differently to the intervention and control. The studies were homogeneous with a Q-statistics of 0.910 and I^2 =0, the associated p-value was 0.34.

When comparing only RAGT to OGT, the grand effect size was small; ES = -0.228, the p-value of 0.477 and CI crossing the line of zero (95% CI [-0.850,0.402]) indicated insignificance of the result. Heterogeneity existed between the studies with a Q-statistic of 2.735 and I^2 = 31.7%. Statistical data of the meta-analyses are shown in Tables 5-8, and the forest plots are shown in Figures 2-5.

DISCUSSION AND CONCLUSION

The purpose of this meta-analysis was to compare the effectiveness of robot-assisted gait training versus conventional overground gait training in improving gait velocity and balance in patients with subacute to chronic stroke. Although studies have shown the benefits of both treatment strategies, there is lack of evidence showing one is superior to the other. This meta-analysis takes a closer look to compare the two treatment strategies and analyzes the effectiveness in the stroke population. It provides additional information on both treatments and gives clinicians a better idea of which treatment to use for which purpose and population. This meta-analysis shows no statistically significant difference between using the combination of RAGT and OGT versus OGT alone, or between using RAGT alone versus OGT, in both outcome measures. However, a combination of RAGT and OGT showed the greatest effect size in improving BBS score, though it was not statistically significant. The null hypothesis that there is no significant difference between those who received RAGT versus those who received conventional OGT in improving gait velocity and balance is supported. The alternative hypothesis that RAGT is significantly more effective than OGT in improving gait velocity and balance in stroke patients is rejected.

This discussion provides an interpretation of the meta-analysis results of the two outcome measures, gait velocity and BBS. It also examines the limitation of the research and addresses the gaps that need to be covered. Finally, it provides application to the physical therapy clinical practice in treating patients with gait abnormalities in the subacute and chronic phases of a stroke.

Review of Results

The first meta-analysis comparing RAGT plus OGT vs. OGT alone and their effect on gait velocity included subjects in the subacute phase of stroke and showed a very small effect size that favored OGT. The second analysis comparing RAGT vs. OGT and their effect on gait velocity included subjects in the chronic and subacute stages, and it showed an effect size that favored RAGT for improving balance. The third analysis, which compared the effect of RAGT plus OGT vs. OGT on improving balance showed an effect size that favored the RAGT plus OGT, in patients in the subacute stage of stroke. The last analysis, which compared the effects of RAGT vs. OGT on balance, showed an effect size favoring OGT alone, in patients in the chronic phase of stroke. There were no statically significant results in any analysis, with all the p-values greater than 0.05 and the CI upper and lower limits crossing the 0 line. This indicated that neither of the two treatment interventions were significantly better than the other in subacute or chronic stage of a stroke, and that the subjects responded differently to either treatment. Therefore, the null hypothesis was accepted.

Limitations Leading to Heterogeneity

Heterogeneity existed in 2 out of 4 meta-analyses included in this study, and there are several reasons that could contribute to this outcome.

Because this meta-analysis looks at subacute and chronic stroke patients, chronicity of stroke played an important role in leading to heterogeneity between the studies. In the study by Kelley et al., the average years since stroke before the treatment were 2.87 in the control group, and 3.71 in the intervention group. The patients participating in this study were in the chronic phase when they started the treatments[60]. In the study by Ochi et al., the patients were in subacute stage of stroke recovery. The average duration after stroke was 26.1 (+/- 8.0) days in the

control group and 22.9 (+/- 7.4) days in the intervention group. There was clearly a significant difference in the chronicity between the two studies. The data from the control group was pulled from the study conducted by Park et al., who recruited participants who were at least 6 months post stroke; the average duration since stroke was 16.5 (+/-8.8) months in the control group. In another study, which the control data was obtained from, Llorens et al. recruited patients who were also at least 6 months post stroke, but the average duration in their control group was 587.6 (+/-222.1) days, which was equivalent to almost 20 months. In studies from which interventional data was collected, the chronicity varied compared to the control data. Patients who participated in the study by Bang et al. were 11.56 months post stroke on average[61], Hornby et al. recruited patients who were 50 months post stroke on average[55], and Westlake et al. conducted a study with patients who were 43.8 months post stroke on average[54]. The different chronicity can indicate patients are in different stages of recovery, and therefore having different functional levels. This can be a threat to internal validity because it can affect the subject's response to the treatments.

The treatment dosing differed greatly between the studies. When comparing Kelly et al. to Ochi et al., the amount of RAGT provided ranged from 7 hours to 27 hours total. When comparing RAGT vs. OGT alone for balance, the total treatment time ranged from 6 hours to 20 hours. In addition to the difference in the duration of intervention provided, 2 studies included subjects in the inpatient settings while others included subjects in the outpatient setting; the subjects in the inpatient setting received 60 minutes of physical therapy, occupational therapy, and speech if needed, in addition to the intervention provided for the study. [42,56] The large variability in treatment duration and intensity between studies can

contribute to the heterogeneity because patients who received more treatments could have demonstrated a greater improvement in post-treatment measures.

Besides treatment duration and intensity, the treatment protocol differed between studies as well. Westlake et al. and Hornby et al. provided 100% guidance in bilateral lower extremities throughout all the treatment sessions in RAGT, while other studies started with a greater amount of guidance and reduced based on patient's tolerance. One of the techniques to improve motor learning is by reducing the amount of guidance and making the task more difficult.[40] However, one of the features of RAGT is that it provides high intensity repetitive training with consistent feedback. [28,56] Based on these two theories, providing different amounts of guidance throughout the treatment sessions can affect the post-treatment results.

The last factor that may have led to heterogeneity between studies is the difference in sample sizes. One example is the comparison between Westlake et al and Hornby et al.; Westlake et al. included 16 subjects and Hornby et al. included 48 subjects. A smaller subject size can lead to exaggeration in the variation in the results, which can lead to a greater range in the CI. Also, a study with a larger subject size can be "weighted" more heavily when running a meta-analysis and may affect the grand effect size more by pulling the grand effect size one way or the other, compared to the study with a smaller effect size.

Limitations to Meta-Analysis

The meta-analyses failed to yield a statistically significant difference between treatment intervention and control data. As shown in the forest plots, all of the p-values indicating significance were greater than 0.05, with the CI crossing 0, meaning there is no significance in the data, and some subjects benefited more

from the control and some from the intervention. There are many reasons that can contribute to these results. Small sample size is one of them. Most of the studies included less than 20 subjects, while there are hundreds of thousands of patients affected by stroke. It is difficult to generalize results found in a study with such a small sample size. Another reason is that there are too many confounding variables that are difficult to control in treating patients following stroke. A lesion in different parts of the brain can affect the outcome of the treatment. For example, if the lesion happened in the motor cortex, the patient may have more difficulty in ambulation compared to a lesion in the temporal lobe, which controls language and memory more than motor function. A patient with left sided neglect can also respond to treatment differently than a patient who does not have neglect. Because of the variations in stroke presentation and cause of gait deviations, there is lack of standardization of treatment dosage. This is a threat to internal validity as it leads to great variability in treatment protocol, especially in OGT.

Therapist experience could potentially affect the outcome of gait training, especially with overground training, which requires a great amount of manual facilitation. Fisher et al. suggested that OGT may require a highly trained therapist specializing in neurological rehabilitation, and these specialized therapists are more likely to be found at inpatient rehabilitation facilities or neurology-based outpatient clinics. [56] In addition, the intensity of gait training in inpatient rehabilitation facilities versus outpatient facilities may vary. Currently there is no evidence based guideline on the optimal dosing of gait training for patients with stroke. The variability in treatment intensity and frequency can lead to different treatment outcomes.

Although all of the studies used in this study were considered moderate to high quality, with PEDro score of 5 to 8 out of 10, some studies were not

randomized controlled trials and all of the studies lacked blinding of subjects, therapists, and accessors except for 2. Randomization can ensure that intervention group and control group were comparable. Lack of randomization can lead to the subjects with similar demographics ending up in the same group, which is not a good representation of the general population. The inability to blind subjects, therapist, or accessors may lead to bias in the results, if they were hoping for a certain result. This is another threat to internal validity. Dundar et al. conducted a retrospective comparative study, which started after the subjects had received the interventions. This not only made it difficult for randomization, but could also lead to great variety of treatment protocol just within the same study.[58]

Because of the limited research, this meta-analysis required pooling of data from different studies, and that lead to difficulty in controlling variables in terms of patient demographics, pre-treatment measurements, and treatment protocol. In addition, the selection criteria were not very well controlled and there was a wide range of chronicity and baseline measurements. This meta-analysis also included studies using different types of RAGT devices. These are all flaws to study deigns, which are threats to internal validity. The inconsistency in pre-treatment data and sample sizes could also contribute to the heterogeneity between studies. Among the studies that provided pre-treatment data, a test of means data analysis was run to examine the significant difference between pre-test means. Pre-treatment BBS means were taken from Westlake, Llorens, Bang, Park, and Hornby as heterogeneity was present among these studies. [54,55,61-63] The test of means showed a significant difference among the pre-treatment BBS means, with a p-value of less than 0.001, as shown in Figures 6 and 7. With the pre-test measurements being significantly different, this could have contributed to the differences in post-

treatment scores. Subjects who started with a lower baseline score may also end up with a lower post-treatment score, despite the amount of improvement made.

Effectiveness of Either Treatment Strategy

Although the overall meta-analyses comparing both treatment strategies did not reveal significant difference between them, the participants in the studies improved significantly after receiving either treatment. When the pre-treatment and post-treatment gait velocities were compared between interventions in each study that compared combination treatment to OGT alone, almost all treatment groups showed a significant improvement after receiving either the experimental (RAGT + OGT) or the control treatment (OGT). The minimal clinically important change for the 10MWT or the 8MWT was 0.06m/s for a small meaningful change and 0.14m/s for a substantially meaningful change. In the study conducted by Fisher et al., the patients in the control group showed an average improvement of 0.087m/s and the patients in the intervention group showed an average improvement of 0.064m/s, which are both higher than the threshold for small meaningful change in gait velocity[56]. In the study conducted by Husemann et al., the average improvement on gait velocity of the control group was 0.08m/s and 0.06m/s in the intervention group, which were also large enough to be clinically significant[23]. In the study by Kelley et al., the control group made an average improvement of 0.09m/s; however, the intervention group showed no difference in pre-test and post-test gait velocity[60].

In the 2 studies included in the meta-analysis comparing RAGT versus OGT on improving gait velocity, neither of those provided pre-treatment gait velocity, so the change in gait velocity from pre-test to post-test was unable to be determined. The participants in the study by Ochi et al., were unable to ambulate

independently prior to treatment, and all of them had a functional ambulation classification (FAC) of less than 3, which indicated that the subjects either (1) were unable to ambulate, required more than 1 person to ambulate safely outside of parallel bars, or (2) required continuous manual contact of 1 person during ambulation.[59] After 4 weeks of treatment, 10 out of 13 patients from the OGT group and 12 out of 13 patients from the RAGT group scored at least a 3 in FAC, which indicated that they (3) required continuous or intermittent light touch to assist balance or coordination, (4) required supervision only, or (5) were fully independent ambulators[59]. It was suggested that both treatment strategies resulted in improved ability to ambulate in most of the patients[42].

The MCID for BBS in patients with stroke is not established, but the minimal detectable change (MCD) for chronic stroke patients is 2.5. It is suggested that an individual in the chronic phase of stroke will need to improve at least 2.5 points in order to be a confident result.[16,50] The participants in the experimental group who received RAGT in the study by Bang et al. showed an average improvement of 5.67 points in BBS after treatment[61]. Kim et al. also presented results that showed significant improvements in BBS in patients who received RAGT. The average improvement in the group after treatment was 14.62 points.[64] Dundar et al., who compared the combination of RAGT and OGT to OGT alone, showed that both the intervention group (improved 11.5 points) and the control group (improved 7.4 points) demonstrated improvements that were higher than 2.5 in BBS.[58] The other studies that looked at BBS did not show significant changes from pre-test scores to post-test scores.

Pros and Cons of Each Treatment

While both the RAGT and OGT were shown to be significantly effective in some studies but not in others, they each have their advantages and disadvantages. Some advantages of RAGT devices include providing a safe and secure environment to the patients as they are being strapped into a harness with body weight support, providing consistent and easily adjustable guidance during treatment, providing visual feedback on the screen, and reducing the need for manual assistance. However, as discussed previously, a RAGT unit is very costly. For example, a newly invented Lokomat device can cost from $200,000 to $400,000. In addition to the purchasing price of the device, a facility will need to consider the amount of other expenses including electricity, warranty, premises, and insurance. An example showed that it can take a clinic more than 2 years to reach the breakeven point between expenses and income, even with frequent use of Lokomat. Another disadvantage of a robotic gait training device is that it does not mimic functional ambulation such as walking on uneven surfaces or walking in narrow space. Studies have shown that, because patients are put in a harness, RAGT devices may lead to restraint in pelvic and trunk movement, and most of the RAGT devices only provide assistance in the sagittal plane for hip and knee trajectories.[55,56] For patients with sensory deficits, wearing a harness for long periods of time may cause skin breakdown or irritation.[60] Compared to RAGT, OGT with manual assistance allows the therapist to facilitate any specific muscle during a specific phase of the gait cycle. It also allows easy change of environment to let patients practice ambulating on sidewalks, ramps, or grass, which mimics functional ambulating. Most importantly, OGT is far less costly than using a RAGT device. However, there are some disadvantages to OGT as well. It puts a high amount of strain on the therapist, which may lead to burn out or injury.

Unlike RAGT, OGT does not provide as safe of an environment for the patient, which may increase their fear of falling. It is likely to be more difficult for patients to ambulate during OGT because it lacks body weight support.

Clinical Application

Previous studies and studies included in this meta-analysis suggest improvements in motor function and balance can be achieved by patients with stroke following RAGT or OGT. However, different types of treatment can benefit different levels of severity and chronicity of stroke. Hornby and Ochi believed RAGT would be more beneficial to patients in the subacute phase of a stroke; Ochi suggested that RAGT training should be initiated within, at most, 5 weeks after stroke onset to provide enough gait training.[42,55] Kelley and Dundar both discussed in their studies, that patients with lower functional level or patients who are non-ambulatory would have a greater gain using a RAGT device. The patients in the early phases of stroke, and those who experience greater ambulation difficulties tend to be more fearful of walking and require a greater amount of practice to regain locomotor function. With body weight support, the patients will have an increased sense of security and are more likely to practice ambulating.[58,60] Kim suggested that in a 20-min session of RAGT, at a walking cadence of 100 steps/min, it allows the patient to repeat the gait training for postural and locomotor control up to 2000 times, which is sufficient to provide plasticity of motor neurons and to achieve a recovery of locomotor function.[65] In a systematic review completed to examine the effectiveness of mechanically assisted gait training with body weight support in non-ambulatory stroke patients in the acute to subacute phases of stroke, the results showed that mechanically assisted training resulted in more independent walking than overground gait training in an inpatient

rehabilitation facility.[66] Kelley also indicated that use of Lokomat greatly reduced PT burden; however, it may increase the chance of skin breakdown.[60] Therefore, although skin integrity or sensation was not one of the inclusion/exclusion criteria for this present study or the studies analyzed in this paper, therapists should take into consideration possible skin breakdown during RAGT and make sure to assess skin integrity frequently.[60] It is recommended that RAGT should be initiated no later than 5 weeks after a stroke onset for the most optimum recovery in gait.[42] The study conducted by Schwartz et al. and other studies showed that a combination of RAGT and OGT might result in greater improvement in terms of reducing disability and improving gait function in subacute stroke.[41,57,67] A Cochrane review including 8 trials (414 participants) found that RAGT in combination with conventional OGT increased the odds of becoming independent in walking, and increased walking capacity, but did not increase in walking velocity.[68] Park et al. compared the effects of OGT in the patients with fast walking speed to those with slower walking speed, and found that there was a greater improvement in gait velocity, endurance, and balance in the fast walking group. [63]It is indicated that higher level ambulators may benefit more from OGT than those at a lower level. [63] Mayr et al. suggests improving walking ability requires 4 components in gait training: 1) reduction of body weight support, 2) increasing walking duration, 3) increasing speed of walking, and 4) reduction of guidance.[69] Overground training can potentially be used as a progression after RAGT to ultimately eliminate body weight support. Bang et al. states that their study provided these factors in their gait training with robotic device and concludes that RAGT produces more significant improvement in both the quality of gait and balance in chronic stroke, when compared to treadmill training.[61] Morone et al., who also studied lower function patients, found that RAGT

combined with OGT may be more effective than OGT alone. The study suggested that patients with greater motor impairment may have more discomfort and fear of falling during locomotor training, therefore increasing the likelihood of overstraining the therapists. When comparing the effectiveness of RAGT and OGT in higher level patients, Morone et al. found no significant difference. It is suggested that higher level patients have more voluntary control and allow more intensive training,[70] therefore they could potentially benefit more greatly from OGT.[57]

Future Research

Future research is needed to compare the effects of different treatment dosage, duration, and intensity for patients in different stages of stroke rehabilitation. As mentioned, there are many different types of robotic-assisted gait training devices being used clinically. There is lack of research comparing the advantages and disadvantages of different devices. Also as important, more high quality RCTs should be conducted comparing RAGT to OGT and/or BWSTT, which are the most commonly used gait training strategies, to allow for a better meta-analysis. Financial analyses to weigh the large initial cost of RAGT against the potential reduction in manpower should also be conducted.

Conclusion

The result of this meta-analysis did not show a statistically significant difference between the effects of RAGT and OGT on improving gait velocity and balance in patients with subacute and chronic stroke. It is suggested that RAGT can be more beneficial to patients with lower functional level and those in acute to subacute stages.[42,56,58,65] This is because of the fact that patients with greater dependence in ambulation often have more discomfort and a greater fear of

falling, which will lead to more strain to the therapist providing the assistance in either conventional OGT or therapy-assisted treadmill training. [39,42,58] It is recommended that higher level patients would benefit from more intensive OGT because they have more voluntary control and require less assistance. Studies also indicated that skin breakdown is more likely with the use of RAGT device, therefore long periods of RAGT training may not be the best treatment strategy for patients with sensory deficits. Therapists should choose treatment strategies based on the duration since onset and baseline ambulation and pay attention to risks of injury in the patients and the therapists.

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TABLES

Table 1. PEDro Scores for studies used in gait velocity analysis

PEDro Criteria	Fisher 2011	Husemann 2006	Kelley 2013	Ochi 2015	Schwarz 2009
Subjects were randomly allocated to groups	1	1	1	1	1
Allocation was concealed		1	1	1	1
Groups were similar at baseline regarding the most important prognostic indicators	1	1	1	1	1
Blinding of all subjects					
Blinding of all therapists					
Blinding of all assessors					
Measure of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	1	1	1	1	
All subjects from whom outcome measures were available received the treatment or control condition as allocated	1	1	1	1	1
Results of between-group statistically comparisons are reported for at least one key outcome	1	1	1	1	1
Study provides both point measures and measures of variability for at least one key outcome	1	1	1	1	1
Total	6	7	7	7	6

Table 2. PEDro scores for studies used in BBS meta-analysis

PEDro Criteria	Park 2013	Llorens 2015	Hornby 2008	Westlake 2009	Dundar 2014	Bang 2016	Kim 2015
Subjects were randomly allocated to groups	1	1	1	1		1	1
Allocation was concealed	1	1	1	1		1	
Groups were similar at baseline regarding the most important prognostic indicators		1	1	1	1	1	1
Blinding of all subjects							
Blinding of all therapists							
Blinding of all assessors						1	
Measure of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	1	1		1	1	1	1
All subjects from whom outcome measures were available received the treatment or control condition as allocated	1	1	1	1	1	1	1
Results of between-group statistically comparisons are reported for at least one key outcome	1	1	1	1	1	1	1
Study provides both point measures and measures of variability for at least one key outcome	1	1	1	1	1	1	1
Total	6	7	6	7	5	8	6

Table 3. Characteristics of studies included in gait velocity analyses

Study	Study design	Sample Size	Intervention	Control	Outcome measures	Treatment Dosing
Fisher (2011)	Pilot study	N=20	Robotic training + Conventional PT	Overground gait training	gait velocity (8m walk)	24 sessions, each consisted of either 1 hour of OGT or 1 hour of RAGT + OGT
Husemann (2007)	RCT	N=30	Robotic training + Conventional PT	Overground gait training	gait velocity	20-30 sessions total, 4 weeks, 30 minutes of OGT or 60 minutes of combination
Kelley (2013)	RCT	N=20	Lokomat Gait training	Overground gait training	Gait velocity	5 days a week for 8 weeks, 40 total sessions, 35 – 40 minutes of active intervention each
Ochi (2015)	RCT	N=26	Robotic training	Overground gait training	gait velocity	4 weeks, 20 treatment sessions, 60 mins of standard PT and 20 minutes of RAGT or OGT each
Schwartz (2009)	RCT	N=67	Robotic gait training + overground	Overground gait training	gait velocity	6 weeks, 30 treatment sessions, 60 mins each session

Table 4. Characteristics of studies included in balance data analyses

Study	Study design	Sample size	Intervention	Control	Outcome Measures	Treatment Dosing
Park (2013)	RCT	N=20	Body weight supported treadmill training	Overground gait training	BBS	2 30min training per day, 5 days a week. 4 weeks
Bang (2016)	Randomized controlled pilot trial	N=18	Robotic gait training	Body weight supported treadmill training	BBS	4 weeks, 20 treatment sessions, 1 hour each session
Llorens (2015)	RCT	N = 20	virtual reality-based training	Overground gait training	BBS	4 weeks, 20 treatment sessions, 1 hour each session
Westlake (2009)	Pilot study	N 16	Robotic gait training	Body weight supported treadmill training	BBS	4 weeks, 12 treatment sessions, 30 mins each session
Hornby (2008)	RCT	N= 24	Robotic gait training	Therapist assisted treadmill training	BBS	12 treatment sessions, 30 mins each session
Dundar (2014)	Retrospective comparative study	N=107	Robotic gait training + overground	Overground gait training	BBS	6 or more weeks, at least 30 treatment sessions, 60 mins each session
Kim (2015)	RCT	N = 26	Robotic gait training + overground	Overground gait training	BBS	4 weeks, 40 treatment sessions, 40 mins x 2 per day

Table 5. Effect sizes and confidence intervals (CI upper and lower) of individual studies and grand effect size of overall comparison between RAGT plus OGT vs. OGT alone – Gait velocity

Studies		
Fisher (2011)	ES	0.028
	CI Upper	0.905
	CI Lower	-0.848
Husemann (2007)	ES	0
	CI Upper	0.716
	CI Lower	-0.716
Schwartz (2009)	ES	-0.097
	CI Upper	0.385
	CI Lower	-0.578
Grand ES	ES	-0.05
	CI Upper	0.313
	CI Lower	-0.414

Table 6. Effect sizes and confidence intervals (CI upper and lower) of individual studies and grand effect size of overall comparison between RAGT vs. OGT – Gait velocity

Studies		
Kelley (2013)	ES	-0.344
	CI Upper	0.543
	CI Lower	-1.231
Ochi (2015)	ES	0.526
	CI Upper	1.308
	CI Lower	-0.256
Grand ES	ES	0.117
	CI Upper	0.968
	CI Lower	-0.734

Table 7. Effect sizes and confidence intervals (CI upper and lower) of individual studies and grand effect size of overall comparison between RAGT plus OGT vs. OGT alone – Balance

Studies		
Dundar (2014)	ES	0.19
	CI Upper	0.592
	CI Lower	-0.212
Kim (2015)	ES	0.62
	CI Upper	1.407
	CI Lower	-0.167
Grand ES	ES	0.279
	CI Upper	0.637
	CI Lower	-0.079

Table 8. Effect sizes and confidence intervals (CI upper and lower) of individual studies and grand effect size of overall comparison between RAGT vs. OGT – Balance

Studies		
Westlake vs. Llorens	ES	0.322
	CI Upper	1.258
	CI Lower	-0.613
Bang vs. Park	ES	-0.794
	CI Upper	0.141
	CI Lower	-1.729
Hornby vs. Park	ES	-0.216
	CI Upper	0.626
	CI Lower	-1.057
Grand ES	ES	-0.228
	CI Upper	0.402
	CI Lower	-0.859

FIGURES

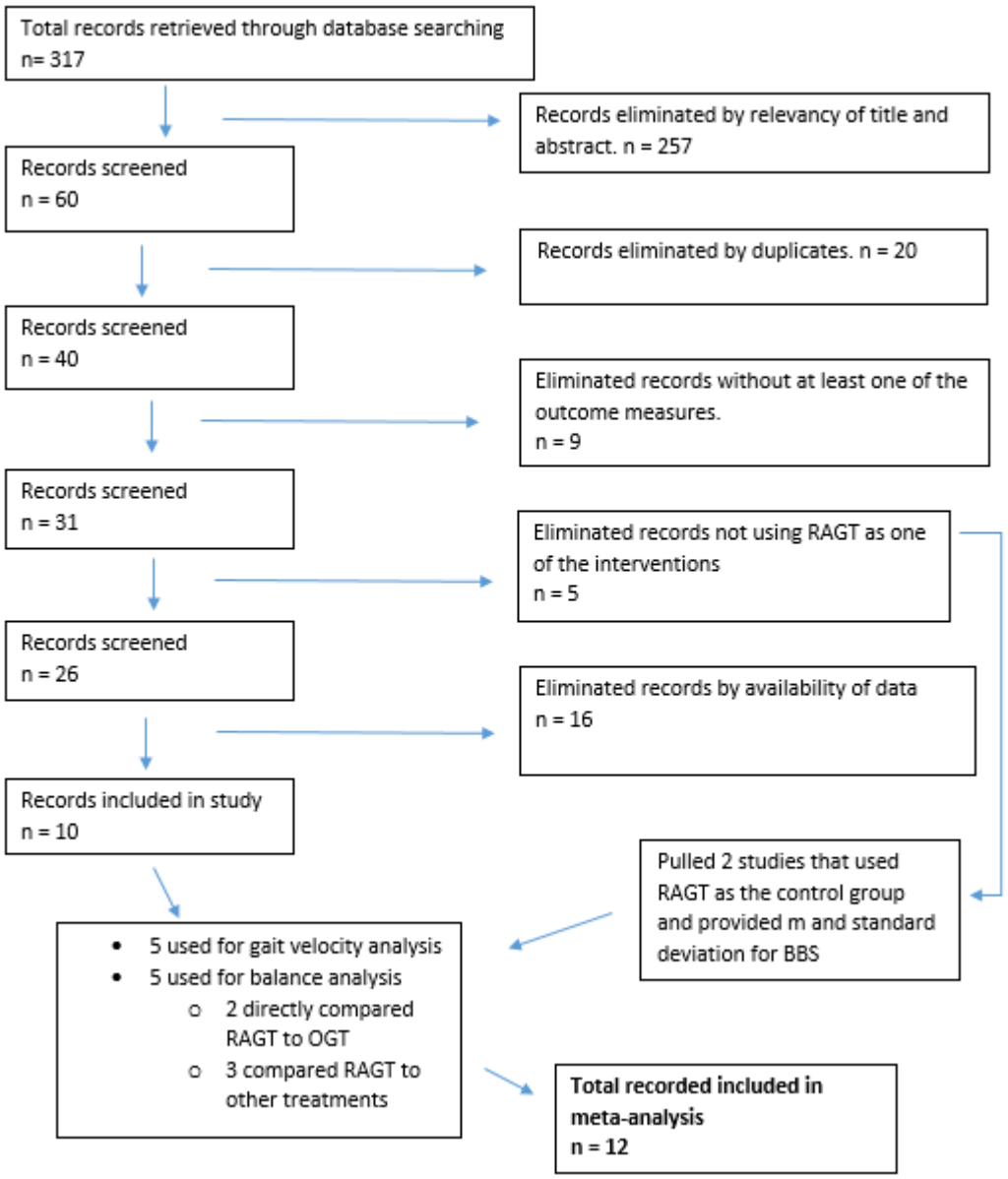

Figure 1. Data collection flowsheet

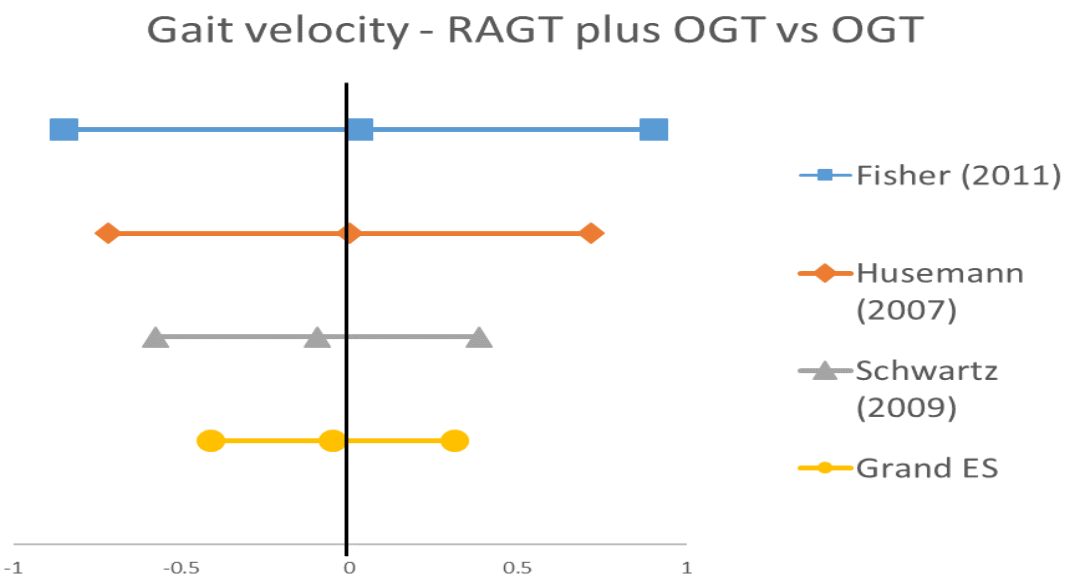

Figure 2. Forest plot for comparison between RAGT plus OGT vs. OGT alone on gait velocity

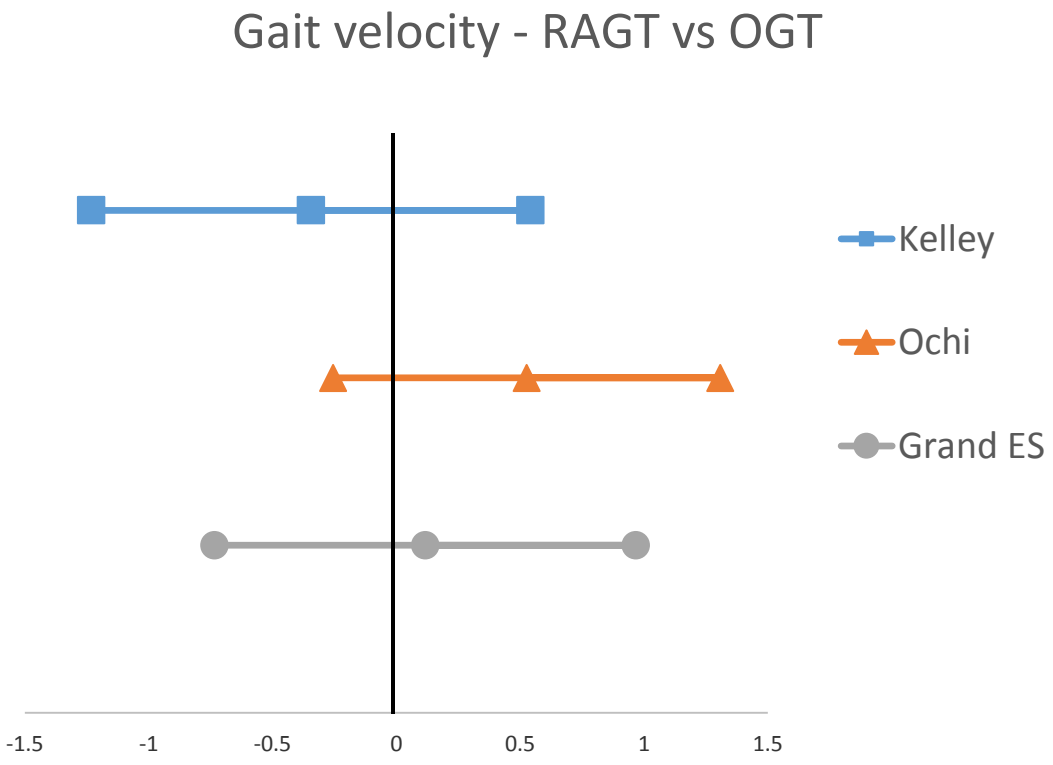

Figure 3. Foret plot for comparison between RAGT vs. OGT on gait velocity

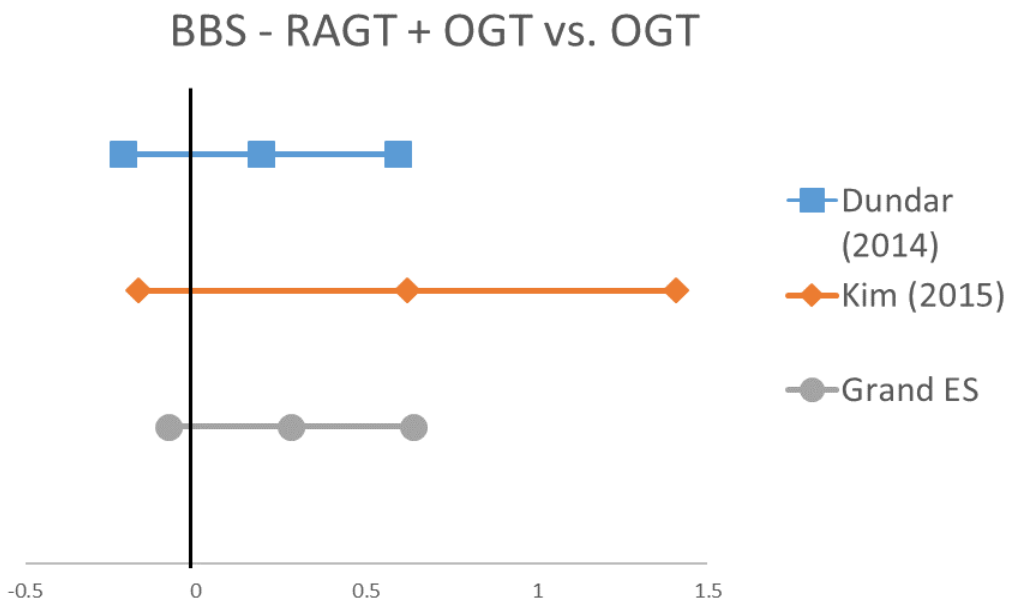

Figure 4. Forest plot for comparison between RAGT plus OGT vs. OGT alone on balance

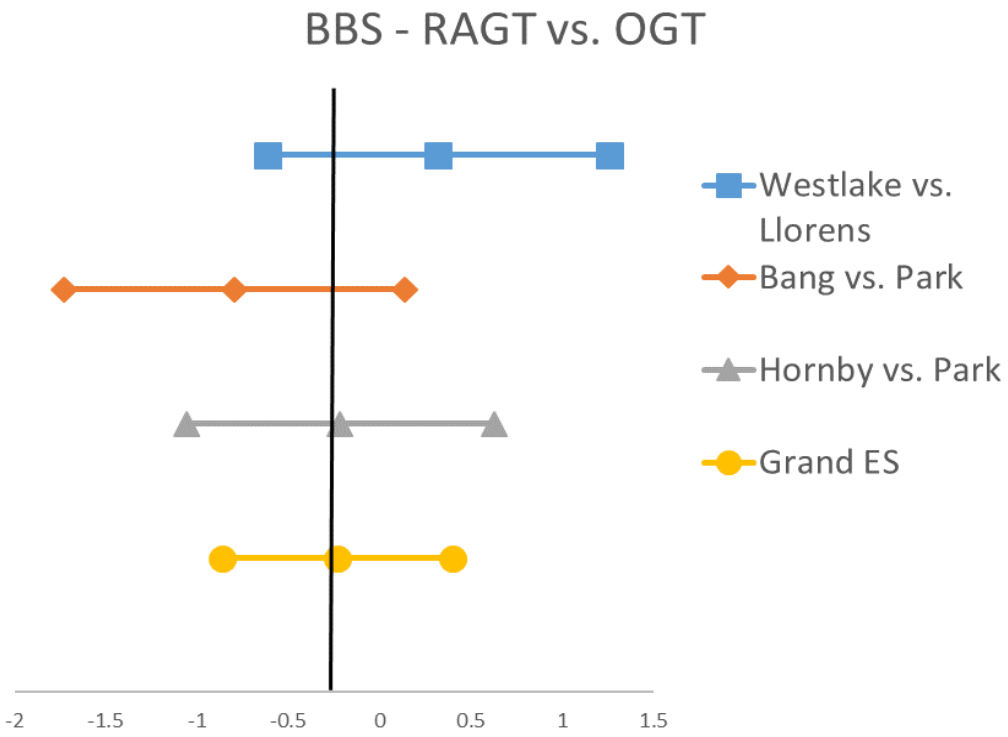

Figure 5. Forest plot for comparison between RAGT vs. OGT on balance

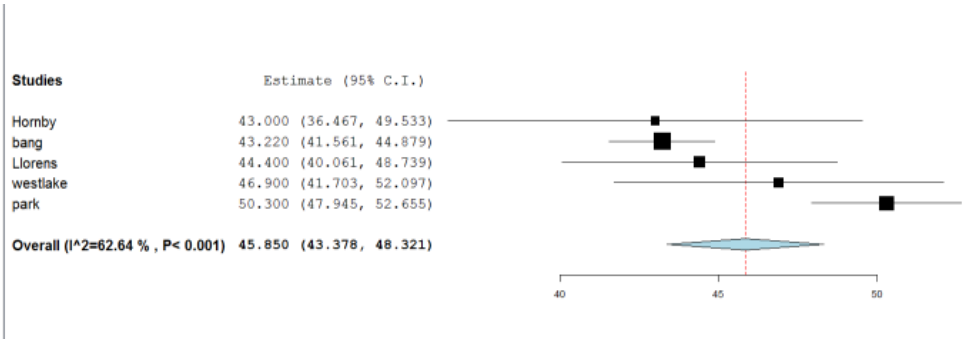

Figure 6. Forest plot showing difference in baseline BBS between studies.

Summary

Continuous Random-Effects Model

Metric:

Model Results

Estimate	Lower bound	Upper bound	Std. error	p-Value
45.850	43.378	48.321	1.261	< 0.001

Heterogeneity

tau^2	Q(df=4)	Het. p-Value	I^2
4.369	24.291	< 0.001	62.639

Figure 7. Statistical data showing difference in baseline BBS between studies. p-value < 0.001.

APPENDIX: PEDRO SCALE

PEDro scale

1.	eligibility criteria were specified	no ❑ yes ❑ where:
2.	subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	no ❑ yes ❑ where:
3.	allocation was concealed	no ❑ yes ❑ where:
4.	the groups were similar at baseline regarding the most important prognostic indicators	no ❑ yes ❑ where:
5.	there was blinding of all subjects	no ❑ yes ❑ where:
6.	there was blinding of all therapists who administered the therapy	no ❑ yes ❑ where:
7.	there was blinding of all assessors who measured at least one key outcome	no ❑ yes ❑ where:
8.	measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	no ❑ yes ❑ where:
9.	all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	no ❑ yes ❑ where:
10.	the results of between-group statistical comparisons are reported for at least one key outcome	no ❑ yes ❑ where:
11.	the study provides both point measures and measures of variability for at least one key outcome	no ❑ yes ❑ where:

The PEDro scale is based on the Delphi list developed by Verhagen and colleagues at the Department of Epidemiology, University of Maastricht (*Verhagen AP et al (1998). The Delphi list: a criteria list for quality assessment of randomised clinical trials for conducting systematic reviews developed by Delphi consensus. Journal of Clinical Epidemiology, 51(12):1235-41*). The list is based on "expert consensus" not, for the most part, on empirical data. Two additional items not on the Delphi list (PEDro scale items 8 and 10) have been included in the PEDro scale. As more empirical data comes to hand it may become possible to "weight" scale items so that the PEDro score reflects the importance of individual scale items.

The purpose of the PEDro scale is to help the users of the PEDro database rapidly identify which of the known or suspected randomised clinical trials (ie RCTs or CCTs) archived on the PEDro database are likely to be internally valid (criteria 2-9), and could have sufficient statistical information to make their results interpretable (criteria 10-11). An additional criterion (criterion 1) that relates to the external validity (or "generalisability" or "applicability" of the trial) has been retained so that the Delphi list is complete, but this criterion will not be used to calculate the PEDro score reported on the PEDro web site.

The PEDro scale should not be used as a measure of the "validity" of a study's conclusions. In particular, we caution users of the PEDro scale that studies which show significant treatment effects and which score highly on the PEDro scale do not necessarily provide evidence that the treatment is clinically useful. Additional considerations include whether the treatment effect was big enough to be clinically worthwhile, whether the positive effects of the treatment outweigh its negative effects, and the cost-effectiveness of the treatment. The scale should not be used to compare the "quality" of trials performed in different areas of therapy, primarily because it is not possible to satisfy all scale items in some areas of physiotherapy practice.

Last amended June 21st, 1999

Notes on administration of the PEDro scale:

All criteria	**Points are only awarded when a criterion is clearly satisfied.** If on a literal reading of the trial report it is possible that a criterion was not satisfied, a point should not be awarded for that criterion.
Criterion 1	This criterion is satisfied if the report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study.
Criterion 2	A study is considered to have used random allocation if the report states that allocation was random. The precise method of randomisation need not be specified. Procedures such as coin-tossing and dice-rolling should be considered random. Quasi-randomisation allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.
Criterion 3	*Concealed allocation* means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for this criteria, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was "off-site".
Criterion 4	At a minimum, in studies of therapeutic interventions, the report must describe at least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups' outcomes would not be expected to differ, on the basis of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented.
Criteria 4, 7-11	*Key outcomes* are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy. In most studies, more than one variable is used as an outcome measure.
Criterion 5-7	*Blinding* means the person in question (subject, therapist or assessor) did not know which group the subject had been allocated to. In addition, subjects and therapists are only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In trials in which key outcomes are self-reported (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind.
Criterion 8	This criterion is only satisfied if the report explicitly states *both* the number of subjects initially allocated to groups *and* the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time.
Criterion 9	An *intention to treat* analysis means that, where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated.
Criterion 10	A *between-group* statistical comparison involves statistical comparison of one group with another. Depending on the design of the study, this may involve comparison of two or more treatments, or comparison of treatment with a control condition. The analysis may be a simple comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another (when a factorial analysis of variance has been used to analyse the data, the latter is often reported as a group × time interaction). The comparison may be in the form hypothesis testing (which provides a "p" value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval.
Criterion 11	A *point measure* is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. *Measures of variability* include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges), and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a Figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.