Official Title: Unblinded Quasi-Randomized Pilot Study Exploring the Benefits of the ZeroG TRiP System to Improve Patient Balance Following an Acute Stroke

Clinical Trial Number: NCT04919161
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STUDY PROTOCOL
AND
STATISTICAL ANALYSIS PLAN

Participants

All participants were admitted to the hospital under the inpatient stroke rehabilitation program after receiving a stroke diagnosis at a regional acute care hospital. Participant recruitment occurred over 12 months from October 2019 through September 2020. Patients admitted under the inpatient stroke rehabilitation program were evaluated by physical and occupational therapy within the first 72 hours of admission, at which point, an initial Berg Balance Scale (BBS) score was obtained as appropriate. To be considered, patients had to be classified as a "Moderate" fall risk, or better, shown by a BBS score of 21 or greater during their initial physical therapy evaluation. Patients who did not meet this inclusion criteria during their initial evaluation were able to screen-in at a later time pending a BBS reassessment. If the reassessment showed a sufficient functional improvement, and the patient had a discharge date of greater than two-weeks after the reassessment, the patient was recruited for the study.

In addition to meeting the BBS score criteria, participants needed to be 18 years of age or older, be able to understand and respond to simple verbal instructions in any language, and be able to tolerate and actively participate in at least three, 30 minute, weekly sessions in the ZeroG body-weight support system (BWSS). Patients were ineligible to participate if they presented one or more of the exclusion criteria shown in the table provided below.

Exclusion Criteria for Study Participation

Cognitive deficits that would disrupt the ability to provide informed consent
Berg Balance scale score < 21
Seizure
Spinal stabilization with use of Halo device
Uncontrolled hypo/hypertension
Unstable skin structures (i.e. skin grafts, chest tubes)
Unstable rib or lower extremity fractures
Osteoporosis
Active enteric infection control precautions
New limb amputations
Need for >50% high flow oxygen
Bodyweight of more than 450 lb. (structural limitation of the ZeroG BWSS)

After providing informed consent, participants were assigned in an alternating fashion by the investigators to either the BWSS control or BWSS with perturbation (BWSS-P) group.

Outcome Measures

The BBS and the Activities-Specific Balance Confidence (ABC) scale were the primary study endpoints. Both assessments have been validated for the stroke population and have high inter-rater reliability.[1,2] The BBS is a standardized balance assessment that uses various balance tasks to objectively measure a person's balance, and determine if a participant is a low, moderate, or high fall risk. The ABC Scale subjectively measures a person's self-perceived balance-confidence to perform various tasks without losing balance or experiencing a sense of unsteadiness; it is based on a rating scale from 0% (no confidence) to 100% (completely confident).[2,3]

To identify eligible candidates for the study, chart reviews were conducted to collect the admission BBS scores of recently admitted stroke patients. The progression of patients who were disqualified from the study by just their admission BBS score were tracked through periodic chart reviews to determine if they had sufficiently improved to be re-considered for the study. During their

regular treatment, modified functional independence measure were collected used to assess each participant's assistance needs while ambulating and undergoing toilet transfers.[4] A final chart review was conducted at the end of the study to collect participants' BBS score and modified functional independence measures from their physical therapy discharge documentation. The ABC scale was administered pre and post-intervention by site investigators at the time of consent and immediately after the last intervention session.

BWSS Equipment and Interventions

For this study, the BWSS used was the FDA listed ZeroG Gait and Balance System (Aretech, LLC, Ashburn, VA).[5] We first introduced ZeroG to our institution in September 2019. Unlike some BWSSs, this device is mounted on an overhead track that follows patients as they ambulate.[5,6] Like other BWSSs, this system is designed to unload the patient of up-to 200 pounds of their body weight while simultaneously protecting patients from falling. For this study, 10 pounds of participants' body-weight, the system minimum required to engage the BWSS, was continuously displaced. If a patient were to fall, the system would detect the change, decelerate, and stop the descent after a set distance; the fall distance was set between 8 to 12 inches for the purpose of this study.

Unlike other BWSSs, a newly developed balance perturbation module known as the Training Responses in Postural rehabilitation or TRiP, is directly integrated to the ZeroG BWSS. This perturbation module is different than other systems as the balance perturbations are elicited directly through the BWSS and do not require a treadmill,[7–10] tilt-table/shaking platform,[10,11] or manual exertion by a therapist.[12] Further, they can be induced during normal gait and balance exercises during therapy. The BWSS control group interventions consisted of various balance activities, including: marching, side-stepping, retro-ambulation, step-taps, and step-ups. The BWSS control group also practiced various gait tasks, including: ambulation over the ground, going up and down stairs, and performing sit-to-stand transitions. The BWSS-P intervention group performed the same activities as the control group, with just the addition of lateral, anterior, and posterior perturbations. Assistive devices and equipment were used during intervention sessions as recommended by the participant's primary therapist, including: canes, rolling walkers, hemi-walkers, and ankle-foot-orthoses, ankle support braces, and upper extremity slings.

Therapists/Investigators administered perturbations using a Wi-Fi-enabled handheld device linked to the BWSS and these consisted of a sudden and brief assistive or resistive force in the desired direction. Lateral perturbations were issued while participants were in a static stance, while anterior and posterior perturbations were issued during ambulation; eight perturbations, two in each direction, were completed each session.

All participants started at perturbation level "one" and progressed up to a maximum perturbation level of "ten" through the course of the study. The amount of force exerted at each perturbation level is pre-set by the manufacturer. The perturbation level (i.e. intensity or force) used each session was based on the participant's progress and observational analysis made by the therapist of the participants' response to the perturbation level. If the participant was able to tolerate the initial perturbation level without exhibiting a balance reaction, the perturbation level was incrementally increased until an appropriate balance reaction was exhibited. If a participant was unable to recover and elicited a fall response in the system, the perturbation level was decreased by one level to ensure patient safety, and the exercise repeated to reinforce the exercise mechanics and participant confidence. The highest perturbation level achieved was recorded after each session is what is reported.

Time frame and number of sessions

Participants in both study groups received a total of eight treatment sessions over two weeks. As necessary, participants received up to two sessions in one day to ensure they completed the

required eight sessions before discharge. These sessions were incorporated into the participants' regular care. At our institution, treatment sessions are broken into 30 minute blocks. This time includes patient transportation, equipment set-up, and in the case of this study, donning the BWSS harness. On average, participants received 20 minutes of active time in the BWSS for each 30 minute treatment block. All sessions were analyzed equally despite the length of time in the BWSS.

Data Analysis

Data was analyzed using GraphPad Prism version 9.0.0 (GraphPad Software, San Diego, CA). To compare the observed proportion of males and females in the BWSS groups, a Binomial Test and Fisher's exact test were used. The 95% CIs reported for the proportion of males and females in the BWSS-P group were calculated using the Wilson-Brown Method.

BBS and ABC measurements changes between the pre- and post-intervention were compared directly, as well as between groups. The degree of change made by each individual was shown by calculating the *percent change*:

$$\frac{(Post\ assessement) - (Pre\ assessment)}{(Pre\ assessment)} \times 100\%$$

BBS data of stroke rehabilitation patients from fiscal year 2018 served as a historical standard of care (SOC) baseline control. The SOC data was sorted to consist of patients with initial BBS scores of 21 or greater and who were admitted and discharged before the launch of the institution's BWSS in September 2018. This resulted in the inclusion of retrospective BBS data from 30 patients. Shapiro-Wilk testing was first used to test for normality; if one or more of the data-sets in the group failed ($p<0.05$), nonparametric tests were used going forward. For hypothesis testing between two groups, unpaired or paired two-tailed Student's t-test were conducted as appropriate. When indicated by an F-test for variance ($p<0.05$), Welch's correction was applied for unequal standard deviations between groups.

When comparing three or more groups, if one or more groups were abnormally distributed, non-parametric Kruskal-Wallis analysis of variation (ANOVA) test and Dunn's multiple comparison test for statistical hypothesis testing were used. When normally distributed, an Ordinary one-way ANOVA with a Tukey's multiple comparisons test for statistical hypothesis testing was used. If Brown-Forsythe's test for variance indicated the variance of the groups were significantly different ($p<0.05$), a Brown-Forsythe correction was applied and Dunnett's T3 multiple comparisons test for statistical hypothesis testing was used instead.

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