Document Date: 03/25/2019

The effects of swimming on elderly women with stage-2 hypertension : full study protocol and statistical analysis plan

NCT#03546270

Full study protocol

Participants

One hundred women (age, 67-85 y) with stage 2 hypertension (systolic/diastolic BP: 140-179 / 90-119 mm Hg) were recruited from multiple general practice centers. All participants had experienced the absence of menstruation for at least 1 year. They were not obese (body mass index >30 kg/m2) or smokers, did not have psychiatric conditions as assessed by medical history, and were not taking medications or hormone therapy during the year before the study. In addition, all participants were sedentary (<1 h of regular exercise per week in the previous year). All the participants gave written informed consent before their inclusion in the study. All protocols were approved by the Public Institutional Review Board designated by the Ministry of Health and Welfare (P01-201511-11-001), carried out in accordance with the Declaration of Helsinki, and registered in clinicaltrial.gov (NCT03546270).

Study design

Allocation was stratified randomly, and sequence was generated by a computer-based number. After baseline measurements, participants were randomly assigned to 20 weeks of SWM training (n=52) or to a no-exercise control (CON, n=48) group. Laboratory personnel were not aware of the allocation. Measurements were obtained at baseline and at 20 weeks during the same time of the day (±1 hour), in the morning, after an overnight fast and after abstaining from caffeinated drinks and alcohol between 48 and 72 hours after the last exercise session. Cardiovascular measurements were collected in a quiet temperature-controlled room (22-24 ^{0}C) after at least 10 minutes of rest in the supine position. After resting vascular measurements, body composition, muscular strength and cardiorespiratory fitness were assessed. Participants were instructed not to

alter their regular lifestyle habits during the study period (verified through food/physical activity logs).

Swimming training program

Participants performed SWM training (combination of free style, breast stroke, and backstroke) for 20 weeks with instructors. For the first 5 weeks, participants swam 25 to 30 minutes/day, 3 to 4 days/week at a relatively low intensity of exercise [~60% of maximal heart rate (HR)]. As their overall level of fitness and exercise skill improved, the intensity and duration of exercise increased to 40 to 45 minutes/day, 3 to 4 days/week at a moderate intensity of 70% to 75% of the maximal HR. Target HR was adjusted based on the observation that maximal heart rate during SWM is approximately 12 beats/min lower than that during running.[23] Each participant was instructed to swim continuously except during the time needed for checking target heart rate [by Polar heart rate monitor (Polar Electro, Lake Success, NY)]. The training protocol was adapted from prior literature on middle-age and older individuals.[14] Participants in the non-exercising control group did not participate in a supervised exercise program, visited the laboratory at the same frequency as participants in the swimming intervention and underwent recreational activities such as board games during this time. They were also encouraged to maintain their regular level of physical activity for the duration of the study.

Vascular function

BP was measured using an automatic oscillometric device (HEM- 705CP; Omron Healthcare, Vernon Hill, IL). A commercially available applanation tonometer (SphygmoCor; AtCor Medical Ltd, Sydney, Australia) was used with analysis software (version 8.0, SphygmoCor

Cardiovascular Management Suite, West Ryde, Australia) for the measurement of carotid-radial PWV [(crPWV), an indicator of brachial arterial stiffness] and pulse wave analysis components. Aortic pulse waveforms were derived using a validated generalized transfer function. The aortic wave is composed of a forward wave, caused by stroke volume ejection, and a reflected wave that returns to the aorta from peripheral sites.[24] Augmentation pressure (AP) is the difference between the second and first systolic peaks. The AIx was defined as the AP expressed as a percentage of the aortic pulse pressure. AIx was normalized to a HR of 75 beats/min (AIx@75), because it is influenced by HR.[25] Two measurements were collected at each time point and averaged as previously described.[26,27] The validity and reproducibility of noninvasive applanation tonometry measures derived from a SphygmoCor device has been previously shown.[28] The intraclass correlation coefficient for all measurements derived from tonometry, calculated on 2 separate days in a subsample, was >0.90.

Body composition

Height and weight were measured to the nearest 1.0 cm and 0.1 kg, respectively. Body fat (%) and lean body mass were determined in all participants by using a bioelectrical impedance meter (X-SCAN PLUS II; JAWON Medical, Seoul, Korea).[29] Bioelectrical impedance measurements have been shown to be valid and reliable predictors of body composition.[30] In our laboratory, the intraclass correlation coefficient for all measurements derived from bioelectrical impedance taken on 2 consecutive days in a subsample was >0.95.

Muscle Strength

To determine upper body muscular strength, maximal isometric handgrip strength of the dominant arm (with duplicate) was assessed unilaterally using a standard handgrip strength dynamometer (JAMAR, Patterson Medical/Sammons Preston, Bolingbrook, IL). The validity and reproducibility of handgrip strength dynamometry is well known.[31] In our laboratory, measures of maximal isometric grip strength calculated on 2 separate days in a subsample had an intraclass correlation coefficient >0.98.

Cardiorespiratory Fitness

The Cornell modification of the Bruce treadmill protocol was used to determine the maximal oxygen consumption (VO2max) for the participants.[32] The test was terminated when the participants were unable to continue exercise or the researchers could see adverse symptoms or changes in electrocardiogram or in BP. VO2max was defined as the highest 30 seconds value of O2 uptake.[32] The Cornell modification of the Bruce treadmill protocol has been shown to be valid and reproducible.[33] The intraclass correlation coefficient for VO2max determined with this protocol on 2 separate non-consecutive days in a subsample, was >0.98.

Statistical analysis plan

Data are expressed as mean ± standard deviation. All parameters were normally distributed as shown by the Shapiro-Wilk test. Differences at baseline between groups were evaluated using unpaired t tests. A two-way analysis of variance with repeated measures (group x time) was used to compare differences after SWM training within and between groups. All analyses were performed using SPSS 21.0 for Windows (IBM SPSS Analytics, Armonk, NY). Statistical significance was set at $P<0.05$. A power analysis calculation determined a minimum sample size

of 52 (26 each group) would allow for the observation of a difference of 3% to 5% between the groups (SWM vs control) on PWV and AIx with a power of 90%.[14,19] Because increases of 20% in PWV and 10% in AIx have been previously associated with respective increases of 1.3-fold and 31.8% in the risk for cardiovascular events,[34,35] an improvement of 3-5% in PWV and AIx would be considered clinically important.