Protocol Synopsis

Singing and Cardiovascular Health in Older Adults PRO: 35864

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Protocol Synopsis

Brief Summary (up to 5,000 characters)

Cardiovascular disease (CVD) claims more lives each year than cancer and chronic respiratory disease combined. Participation in cardiac rehabilitation (CR) reduces mortality and risk of a major cardiovascular event in secondary prevention populations, including older adults. Older adults are less likely to participate in CR, as comorbidities in this population, including arthritis and chronic obstructive pulmonary disease, make participation difficult. Singing is a physical activity that involves components of the vagal nerves manifested as changes in cardiac autonomic regulation. Unlike physical exercise, the effects of singing on cardiovascular health has not been well-studied. To our knowledge, no studies have evaluated the impact of singing on important cardiac biomarkers. Our hypothesis is that older patients with CVD will have favorable improvement in cardiovascular biomarkers, including, endothelial function and heart rate variability (HRV), after 30 minutes of singing. Our pilot data in 23 subjects provides proof of principle, with a small, but significant, improvement in peripheral vascular endothelial function (measured by peripheral arterial tonometry) after 10 minutes of singing. This pilot study has helped us optimize the clinical trial design for this proposal, which will include a more targeted population, incorporation of personal music preferences, increased duration of singing, inclusion of a music therapist and measurement of brachial artery flow-mediated dilation (FMD), the "gold standard" measurement for vascular endothelial function, as our primary outcome. Our proposal seeks to create, optimize and test two different singing interventions in older patients with CVD.

The study will consist of three arms, according to a randomized, single-blind, crossover, sham procedure-controlled design. Sixty-five total participants will each have three visits on three different occasions for the following interventions: (1) a 30-minute period of guided singing from an in-person music therapist, (2) a 30-minute period of singing along to an instructional video including a professor of voice and "inexperienced, older singing student" and (3) a 30-minute rest period without any intervention. We will use biofeedback (target heart rate and BORG Rating of Perceived Exertion) to help subjects optimize the cardiovascular impact of the music interventions. The (2-year) R61 phase of this proposal will assess the feasibility (implementation, practicality, and acceptability) of executing the proposed study design (Aim 1). We anticipate that the R33 phase will take 3 years to complete. The combined R61/R33 phases will be statistically powered to assess changes in FMD and HRV (primary and secondary outcomes, Aims 2a and 2b). An alternative mechanism in Aim 3 will explore the impact of singing on mental health and well-being by measuring salivary cortisol and cytokines and by using a validated visual mood score designed to evaluate performing arts activities in healthcare settings. We will determine which singing intervention, if any, is superior to the other – as this would be important to guide longer and larger clinical trials in the field. Knowledge gained from this proposal will improve our understanding of biologic mechanisms of singing behaviors, as it relates to CVD.

Study Design Narrative Study Description (up to 32,000 characters)

The intent of this protocol is to evaluate the impact of singing on important cardiac biomarkers, including endothelial function, a marker of cardiovascular health and future cardiac risk.

The study is designed to consist of an initial phone screen and three study visits. The study will consist of three arms, according to a randomized, single-blind, crossover, sham procedure-controlled design. Sixty-five total participants will each have three visits on three different occasions for the following interventions: (1) a 30-minute period of guided singing from an in-person music therapist, (2) a 30-minute period of singing along to an instructional video showing

a professor of voice and “inexperienced, older singing student” and (3) a 30-minute rest period without any intervention.

Study staff will be provided a list of already pre-qualified subjects via an Honest Broker Tool through The Medical College. Study staff will then screen potential subject’s charts to determine eligibility. Providers will be messaged asking if they are appropriate. If yes, potential subjects will learn of this study via phone call or email from the study team. If a potential subject indicates that they are not interested, their information will not be saved, and they will not be contacted further. All private health information will be kept in a locked file cabinet in a locked office. All electronically stored information will be stored on a password protected computer with standard encryption software only accessed by those working directly on this project. The study team will first screen the potential subject via a phone conversation.

Once the subject is deemed eligible based on the eligibility criteria, he/she will be mailed a copy of the Institutional Review Board consent form to review. If after reviewing information about the study, the potential subject remains interested, randomization will occur and the first study visit (in the Adult Translational Research Unit) will be scheduled. Recruited subjects will be advised to remain fasting (for a minimum of at least 3 hours) until their research study appointment has been completed. The FMD procedures require an 8 hour fast, and the PAT procedures need only at least a three hour fast. For all study visits the subjects will be asked to remain fasting for 8 hours prior to their scheduled visit, they can have as much water as needed.

The informed consent signing/review will occur at the first study visit. Baseline vital signs (resting heart rate, blood pressure, pulse oximetry), weight and height will be obtained. Blood pressure will be measured from the subject's control arm (dominant arm preferred). The appropriately-sized (Bluetooth-capable) Heart Rate Variability (HRV) heart rate sensor strap will be applied to the subject. Subject's positional comfort will be maximized in the supine position. Baseline measurements of heart rate variability (HRV), brachial artery flow-mediated dilation (FMD) and peripheral arterial tonometry (PAT) will be collected by the research coordinator and specialized vascular sonographers as per detailed protocols.

The research team member will assist the subject in completing the study questionnaire, including demographics, medical history, current medications, current exercise and singing habits and physical limitations and/or mobility issues. A target heart rate (60% of 220-age) will be calculated. The subject will be educated on the BORG Rating of Perceived Exertion and target heart rate goals for singing. A visual analog mood score (ArtsObs) will be obtained prior to singing (or sham) intervention. Baseline salivary samples will be obtained (for cortisol and cytokines). The subject will be moved to a seated position for the singing intervention.

Subjects will undergo the following three interventions (separate Visits 1-3) in a cross-over design, separated by a minimum of 2 days (to allow for wash-out effects of the prior intervention):

1. Singing intervention 1 (instructional sing-a-long video): A video series will be created and recorded for the purposes of the study. The videos will include a vocal warm-up (10 minutes long). The subject will then have the option to select and sing two songs (10 minutes each), with offerings in four music genres including Folk, Pop, Country, and a Hymn. Each piece will vary in tempo, melodic contour, and rhythm. The total duration of singing via this format will be 30 minutes. The videos will be led by Dr. Tanya Kruse, Associate Professor of Voice and Voice Area Head at the University of Wisconsin-Milwaukee, with an inexperienced, older singer participating in the music making.

2. Singing intervention 2 (in-person music therapy session): Intake forms will be distributed to participants prior to starting music therapy for these sessions. These forms are used

to assess musical preference, prior music experiences as well as any medical conditions to take into consideration. Music therapy sessions will begin with vocal and breathing warm-up exercises for about 10 minutes. Upon completion of these exercises, subjects will choose a preferred song to sing from the multi-genre binder that the music therapist (MT) created specifically for this research based on age and preferences of patients. The MT will play the songs for the subject to sing along to and will alter the characteristics of the music (volume, tempo, level of support) to ensure a successful experience for subjects and motivate them to put forth more effort into singing the song. The music therapist will continue to coach throughout the 30-minute session, reminding subjects of strategies practiced and how to implement those strategies while singing (i.e. maintain proper body alignment, breathe with the diaphragm as opposed to chest and shoulders, etc). Music therapy sessions will be led by Erica Flores, MT-BC, WMTR, Owner of Healing Harmonies Music Therapy, or a member of her team. Erica and her team of MTs were trained in Neurological Music Therapy by Dr. Michael Thaut, one of the workshop panel of experts at the 2016 John F. Kennedy Center for the Performing Arts event that served as the catalyst for the current funding opportunities to promote research on music and health.

3. Control/sham intervention: Subjects will have a 30-minute period of rest sitting upright (as they would be positioned for the singing interventions). During this "rest" period, they will not be allowed to sleep, watch television, read, listen to music, converse with research team members, or even use their smart phones. This arm is meant to isolate the specific effects of the treatment rather than the potential "incidental" effects related to the research setting and measurements.

Target goals for both singing interventions will include at least one the following: (1) achieving at least 60% of maximum age-predicted heart rate (calculated as 220-age), or (2) reaching Borg Rating of Perceived Exertion intensity of 11 or higher. This will ensure at least a light-moderate level of exertion for singing activities to strengthen impact on cardiovascular biomarkers and outcomes. HRV recordings will be obtained or the duration of the singing interventions (or 30 minutes for the control intervention). One set of vitals signs (heart rate, blood pressure, and pulse oximetry) will be recorded within the last 5 minutes of the singing intervention). After 30 minutes of intervention/control, the subject will be moved to the supine position where repeat measures of brachial artery flow-mediated dilation (FMD) and peripheral arterial tonometry (PAT) will be obtained. Additional salivary samples will be obtained (for cortisol and cytokines) after singing. A third set of vital signs will be recorded .A "post-singing" visual analog mood score (ArtsObs) will be obtained after the intervention. The entire ArtsObS instrument will be completed. Two reactions (relaxation and distraction) will be scored by the research coordinator nurse based on direct observation of the subjects during the singing intervention. The qualitative portion of this instrument enables the collection of personal feedback and quotations from subjects. Observers (research team) can also gather more detailed accounts of subjects' responses to activities, including experience and perceptions. At Visit 3, the research team will subjectively ask each subject about which (if any) singing intervention they preferred and why.

Interventions (<1,000 characters)

1. Singing intervention 1 (instructional sing-along video): Videos will include a vocal warm-up (10 minutes). The subject will select and sing two songs (10 minutes each), with offerings in four music genres including Folk, Pop, Country, and a Hymn. The total duration of singing will be 30 minutes. The videos will be led by Dr. Tanya Kruse, Associate Professor of Voice, with an inexperienced, older singer participating in the music making.

2. Singing intervention 2 (in-person music therapy session): Music therapy sessions will begin with a 10-minute warm-up. Subjects will choose songs to sing from a multi-genre binder. The music therapist (MT) will play the songs for the subject to sing along to while coaching the subject for a total of 30 minutes.

3. Control/sham: Subjects will have a 30-minute period of rest sitting upright, during which they will not be allowed to sleep, watch television, read, listen to music, converse with research team members, or use their smart phones.

FMD description

FMD is considered the gold-standard for non-invasive measurements of endothelial function. Vascular function is an important factor in the pathogenesis of atherosclerosis, hypertension and heart failure. Endothelial function, a marker of cardiovascular health and future cardiac risk, can be measured non-invasively with minimal to no risk to the subject. Brachial artery FMD is also highly predictive of coronary endothelial function and is a powerful indicator of vascular inflammation and future cardiovascular events. FMD measurement is attractive because it is non-invasive and allows for repeated measurements. Both diameter and blood velocity are assessed before and after brachial artery occlusion with a blood pressure cuff and results are reported as a change from baseline. Observational data from large population studies have demonstrated that abnormal FMD is associated with a higher rate of incident adverse cardiovascular disease events during a 5-year follow-up period.