Mass General Brigham

Jan 17
2024

Study Protocol and Statistical Analysis Plan

GUIDED MEDITATION TO DECREASE PERIOPERATIVE ANXIETY AND INCREASE PATIENT INTRAOPERATIVE COMPLIANCE IN VASCULAR SURGERY

NCT ID: 2021P002072

Institutional Review Board
Intervention/Interaction Detailed Protocol

Principal Investigator: Anahita Dua, MD

Project Title: **Decreasing Sedative Requirements for Peripheral Vascular Interventions using Preoperative Guided Meditation**

Version Date: Jan 17, 2024

For Intervention/Interaction studies, submit a Detailed Protocol that includes the following sections. If information in a particular section is not applicable, omit and include the other relevant information.

1. Background and Significance

Undergoing surgery is a life-altering event, and patients understandably often have severe anxiety prior to and during their surgical procedure. This can poorly impact procedural outcomes not only by causing perioperative hemodynamic instability, but in the case of patients undergoing conscious sedation, impact their ability to comply with perioperative provider instructions.[1] In addition to this, increased preoperative anxiety can result in increased anesthetic requirements in the form of short-acting benzodiazepines and opioids.[2] These pharmacologics not only have short term side effects including respiratory depression and possible apnea but can also in some cases result in addiction and long-term dependence.[3]

Guided meditation is a non-pharmacologic intervention that has proven to be effective in decreasing anxiety.[4, 5] This intervention has recently been adapted to the perioperative area, with several recent trials yielding promising results: meditation not only resulted in decreased perioperative biomarkers of anxiety and stress[6] but also resulted in decreased postoperative pain in the specialties of cardiac and spine surgery.[7] Several guided meditation techniques exist, including the body-scan technique which involves sequentially increasing one's awareness of each body part addressed, as well as breath-focused meditation which involves repeated controlled timed deep inhalations and exhalations – which is in contrast to the physiological effect of anxiety -- rapid and shallow breathing.

Of note, prior and currently ongoing trials have all involved general anesthesia, and none have enrolled patients under conscious sedation. It is worth noting that in vascular surgery, minimally invasive endovascular techniques have overtaken open surgical techniques in the management of Peripheral Vascular Disease (PVD). As these procedures do not require general anesthesia, many providers have moved from the operating room to ambulatory vascular centers or office-based laboratories to perform these procedures under conscious sedation.[8] At the same time, without general anesthesia or paralytics, patients are required to perform tasks such as keeping their extremity still or intermittently holding their breath for extended periods of time. Patients which are unable to completely comply can be subject to repeated imaging attempts, which result in additional doses of contrast administration and ionizing radiation.

Anecdotal data suggests that increased perioperative anxiety increases the likelihood that a patient is unable to hold their extremities still or hold their breath for extended periods of time during the catherization procedure. By extension, high perioperative anxiety is likely to be associated with increased contrast administration and radiation dose.

We propose to quantify the severity of perioperative anxiety in the form of State Trait Anxiety Inventory (STAI) scores, which we will then address via a guided meditation program that revolves around a body-scan and deep-breathing meditation. We will also collect data regarding Interoceptive Awareness using the Noticing subscale of the Multidimensional Assessment of Interoceptive Awareness (MAIA) score. The ultimate goal of this research is to decrease patient perioperative anxiety and thereby not only improve the perioperative patient experience but also increasing patient intraoperative compliance and thus reducing operative contrast administration and radiation doses.

2. Specific Aims and Objectives

We have one specific aim:

1. To test the feasibility and acceptability of a preoperative guided meditation program on patients undergoing vascular surgical procedures for peripheral vascular disease.

3. General Description of Study Design

This will be a prospective randomized controlled trial of patients undergoing peripheral vascular interventions. Participants will be randomized to receiving guided meditation during their preoperative history and physical exam versus a standard preoperative history and physical exam on the day of their procedure. Randomization will be performed based on a randomization mobile application.

Schema:

<table>
<tr><td rowspan="4">Patient consents to vascular procedure AND consents to trial</td><td></td><td rowspan="4">Randomize</td><td>=></td><td>Intervention group: Guided meditation program preoperatively</td><td>=></td><td rowspan="4">Vascular Procedure</td></tr>
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<tr><td></td><td>=></td><td>Control group: No guided meditation preoperatively (standard of care)</td><td>=></td></tr>
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4. Subject Selection

Inclusion Criteria: Patients who are >18 years of age who are undergoing an endovascular procedure for a peripheral vascular disease indication with an anesthetic plan for conscious sedation

Exclusion Criteria:

Patient related:

1. who have an associated significant psychiatric disorder such as anxiety, panic disorder, depression, psychosis, or bipolar disorder
2. patients who are unable to give informed consent
3. patients who are non-English speaking
4. patients who are pregnant
5. patients with a prior lower extremity amputation
6. patients with chronic sensorimotor deficits of either lower extremity

Procedure related:

1. procedures that are booked as urgent or emergent;
2. procedures that are a combination of an open and endovascular procedure (e.g. an angiogram with a toe amputation)

Recruitment Procedures:

Providers: All vascular surgical attendings and trainees that perform PVIs at Massachusetts General Hospital, Newton Wellesley Hospital, Salem Hospital and Southern New Hampshire Hospital will be notified of this study at an in-person research meeting prior to enrollment of any patients. Should they give verbal consent, they and their patients will be eligible to participate in this study moving forward. The vascular surgery attending will likely be the provider answering the post-procedure provider survey, unless they for some reason are not the attending provider during the procedure; if such is the case, the provider performing the procedure will fill out the post-procedure provider survey- if they had been part of the group that had consented during the in-person research meeting. Otherwise, they will not be requested to fill out the post-provider survey. These will be the same providers that fill out the post-procedural provider questionnaire, which will be completed electronically, in person using an iPad and anticipated to take no longer than 3 minutes to fill out.

Patients: All patients will be personally screened by the vascular surgical attending who they are known to or had been referred to in the case of new patient. This vascular surgical attending will then (1) give approval for his/her patient to be contacted for research purposes, (2) initially introduce the study to the patient AND (3) obtain the patient's permission to be contacted by study staff. Patients will be consented initially either at the preoperative surgical clinic visit or prior to the day of surgery in person if they are inpatient or via telephone if they are not inpatient. If the patients are not inpatient, they will be provided the fact sheet prior to their procedure and intervention on the day of their intervention. Subjects will be given the details about the study and given adequate time to ask questions and talk the study over with family that accompanies them.

The principal investigator or the co-investigators will be responsible for enrolling the patients.

Specific recruitment methods will not be used to enhance recruitment of women or minorities – we aim to enroll a patient population which is representative of the PVD demographic. Members of a minority race and Hispanic patients will be included in this study in a manner exactly the same as white patients and non-Hispanic patients so long as they meet the inclusion criteria. Given that the Massachusetts General Brigham has a large catchment pool, we expect the recruitment pool will adequately reflect the prevalence rates in the community, including proportions of minorities of race or ethnicities.

5. Subject Enrollment

All patients will be screened initially either at the preoperative surgical clinic visit or prior to the day of surgery in person if they are inpatient or via telephone if they are not inpatient. Subjects will be given the

details about the study and given adequate time to ask questions and talk the study over with family that accompanies them.

There will be no separate description for children as they will not be enrolled.

Given that the script for the guided meditation is in English, non-English speakers will not be enrolled.

Given the cognitive requirements to perform meditation, any patient who is unable to provide their own surgical consent will not be enrolled.

The investigators' own patients will be enrolled; however in this situation, a co-investigator will perform the enrollment to minimize the potential for coercion. It will additionally be emphasized that the decision to enroll in the study will not in any other way affect their perioperative clinical care. They will also be advised that they may withdraw from the study at any point at their request.

The post-consent intervention randomization method will be via a randomization application – with block randomization per study site.

6. STUDY PROCEDURES

Study Visits:

Timing	Location	Procedure/Data Collected
At least one day prior to day of vascular intervention: When decision is made to proceed with vascular intervention	Outpatient Clinic vs Inpatient Ward	Screening and consent for enrollment into trial Preoperative Quality of Life survey (PROMIS-10)
Day of vascular intervention: 30 minutes preoperatively, after surgical and anesthesia consents are obtained	Pre-operative holding area	Randomization Pre-meditation STAI-6 if randomized to intervention arm Guided Meditation if randomized to intervention arm Pre- procedural STAI-6 Pre-procedural MAIA (Noticing subscale)
Day of vascular intervention: 2 hours after vascular intervention	Post-anesthesia care unit	Post-procedural Patient Questionnaire Post-procedural Provider Questionnaire Post-procedural MAIA (Noticing subscale)
Outpatient follow-up Typically between two weeks to one month after procedure	Outpatient Clinic	Follow-up Patient Questionnaire Followup Quality of Life survey (PROMIS-10)

Study Intervention: A guided meditation using the body scan technique, which will have two sessions- the first session while the patient is in the perioperative holding area and the second session after the patient has been positioned on the operating room table, however this second session will still be completed prior to the beginning of the surgery. This will be administered via a set of Bluetooth headphones (with bone-conduction technology so they do not cover the patients ears), with the associated audio recording being played from an MGB iPad. This protocol, specifically regarding having one session in the perioperative holding area and one session in the operating room was designed by a multidisciplinary panel which included vascular anesthesiologists, perioperative nurses, integrative medicine clinicians and surgeons. this expert panel agreed that the protocol in this form would be most beneficial to the patients and simultaneously cause minimal (if any) disruption to the current operating room workflow.

We will use a transcription modified from one of Jon Kabat-Zinn's body scan meditation videos, with his explicit approval. Dr. Jon Kabat-Zinn is a Professor Emeritus of Medicine and the creator of the Stress Reduction Clinic and the Center for Mindfulness in Medicine, Health Care, and Society at the University of Massachusetts Medical School. As the creator of mindfulness-based stress reduction and the author of two national bestsellers on the topic, he is regarded as one of the thought-leaders in the mindfulness field.

Data collection logistics: These sheets will be completed electronically, in person using an MGB iPad . Each sheet is anticipated to take no longer than 3 minutes to fill out.

PROMIS-10 score: The PROMIS-10 is a measurement system developed by the NIH to assess health and wellbeing in adults and children from the general population, as well as those living with chronic conditions. The PROMIS 10 is a comprehensive and accessible set of tools used to measure self-reported physical, mental and social health; including symptoms, function and general perceptions of health and wellbeing. This score will serve to collect baseline and post-intervention quality of life data.

STAI-6 score: The STAI-6 includes six questions with a Likert scale from 1 to 4 for a range of 6 to 24. For context, the original STAI has two components; a state portion which evaluates the current state of anxiety a patient has in a clinical setting, and a trait portion which evaluates how the patient generally feels unrelated to the clinical setting. Each of these sections has 20 items to answer and approximately takes 10-15 minutes to complete. There exists a shortened six question version of the state portion which only takes a few minutes to complete and is highly correlated with the full state STAI.[9] As such, we will be using the STAI-6 form questionnaire to measure anxiety levels in our patient population.

MAIA score (Noticing subscale): The Multidimensional Assessment of Interoceptive Awareness is self-reported multidimensional instrument with eight separately scored scales. The three scales each have between three and seven questions that combine to provide an assessment of a patient's interoception (awareness of bodily sensations). Each subscale can be separately administered with the retention of its psychometric features; we chose to administer the first subscale "Noticing" to strike a balance between assessment fidelity and question-fatigue.

Return of Study Results: The study data will be collected by study staff and electronically converted into a spreadsheet to be stored in LabArchives. The principal investigator will be responsible for managing incidental findings.

Primary outcome: Patient pre-procedural anxiety as measured by STAI-6 scores

Secondary outcome: Secondary outcomes will include provider and patient satisfaction scores, intraoperative patient ability to perform breath holds and to maintain leg immobility, and the extent to which additional contrast or radiation was required during the procedure. These will be assessed in the form of post-procedure questionnaire and measured on a Visual Analogue Scale.

Study termination criteria:

Individuals may withdraw from the study at any time without impact to their care. They may also be discontinued from the study at the discretion of the Investigator for lack of adherence to intervention or study procedures or AEs. It will be documented whether or not each subject completes the study.

Should the subject's participation in the trial be terminated early, the rest of their care, namely their vascular intervention, will proceed as if they had not been in the trial to begin with.

The study itself will be terminated should there be serious adverse events resulting directly from the intervention as described in the Monitoring and Quality assurance section.

No remuneration will be offered to the trial participants.

There will be no plans to send or receive data with research collaborators outside Mass General Brigham.

7. Risks and Discomforts

Meditation is widely accepted as a harm-free intervention, though one potential risk of the guided meditation is increased anxiety due to increased awareness of their limitations with breath-holds, if applicable. This will be mitigated by excluding patients with known anxiety disorders.

From a privacy standpoint, the results of the questionnaires including anxiety scores will not be added to the patient's medical record, as such only pre-authorized research staff will have access to them.

There are no foreseeable additional risks other than the risks inherent to the vascular intervention itself which is standard of care and patients will separately consent to.

8. Benefits

Potential benefits:
Intervention group: Possible benefits include potentially decreased perioperative anxiety, reduced operative contrast administration and reduced radiation doses.
Healthy controls: No potential benefit

Potential benefits to study population in society:
Should our intervention prove to be effective in reducing patient anxiety, the adoption of preoperative guided meditation programs will likely benefit a significant fraction of the PAD patient population and by not only decreasing patient perioperative anxiety but also increasing patient safety by reducing operative contrast administration and radiation doses.

9. Statistical Analysis

Statistical analyses will be performed using STATA 15 statistical software (College Station, TX). Demographic or other categorical data will be analyzed using T test or Fishers exact test as appropriate. Interval measurements (STAI-6 scores) will be analyzed by using the t-test or Mann-Whitney test as appropriate.

Power Analysis:
This is a pilot study to assess the feasibility and acceptability of an intervention and to gather preliminary data to adequately power a future trial, and as such there will not be any power analysis for this study.

10. Monitoring and Quality Assurance

Adverse event criteria

Adverse Event

any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

Serious Adverse Event

any event temporally associated with the subject's participation in research that meets any of the following criteria:

- results in death;
- is life threatening (places the subject at immediate risk of death from the event as it occurred);
- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in a persistent or significant disability/incapacity;
- results in a congenital anomaly/birth defect; or

any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the outcomes listed above (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

Adverse Event Reporting: The Principal Investigator and study staff will review all adverse events experienced by any subjects as a result of this study. The PI will supervise the assessment of relationship of each adverse even to the study procedures. The adverse events, if any occur, will be classified as definitely related, probably related, possibly related, unlikely or unrelated. Additionally, all adverse events will be reported following the Mass General Brigham IRB guidelines for Adverse Event Reporting.

Data and Planned Safety Monitoring: The PI, Dr. Dua and her collaborator Dr. Png will be responsible for data safety and monitoring. All paper data will be kept in a locked cabinet in the MD collaborator's office. Safety and outcomes reviews will be performed after each consecutive enrollment of 25 patients.

Termination of Study: The study itself will be terminated should there be serious adverse events that are classified as definitely related to and directly resulting from the intervention.

Internal Monitoring of Source Data and Protocol Adherence: All monitoring and quality assurance will be done through Harvard Catalyst every 3 months and more frequently as needed. This will be performed through a statistician who works closely with the vascular surgery department through our research office. They will be responsible for reviewing data and verifying its accuracy and completeness.

11. Privacy and Confidentiality

- ☐ Study procedures will be conducted in a private setting
- ☒ Only data and/or specimens necessary for the conduct of the study will be collected
- ☒ Data collected (paper and/or electronic) will be maintained in a secure location with appropriate protections such as password protection, encryption, physical security measures (locked files/areas)
- ☐ Specimens collected will be maintained in a secure location with appropriate protections (e.g. locked storage spaces, laboratory areas)
- ☒ Data and specimens will only be shared with individuals who are members of the IRB-approved research team or approved for sharing as described in this IRB protocol
- ☒ Data and/or specimens requiring transportation from one location or electronic space to another will be transported only in a secure manner (e.g. encrypted files, password protection, using chain-of-custody procedures, etc.)
- ☒ All electronic communication with participants will comply with Mass General Brigham secure communication policies
- ☒ Identifiers will be coded or removed as soon as feasible and access to files linking identifiers with coded data or specimens will be limited to the minimal necessary members of the research team required to conduct the research
- ☒ All staff are trained on and will follow the Mass General Brigham policies and procedures for maintaining appropriate confidentiality of research data and specimens
- ☒ The PI will ensure that all staff implement and follow any Research Information Service Office (RISO) requirements for this research
- ☐ Additional privacy and/or confidentiality protections

12. References

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