STUDY TITLE:

A Randomized Controlled Trial of Music vs. No Music During Cesarean Delivery on Patient Satisfaction

STUDY SPONSOR:

Department of Anesthesiology and Perioperative Medicine, Tufts Medical Center

PRINCIPAL INVESTIGATOR

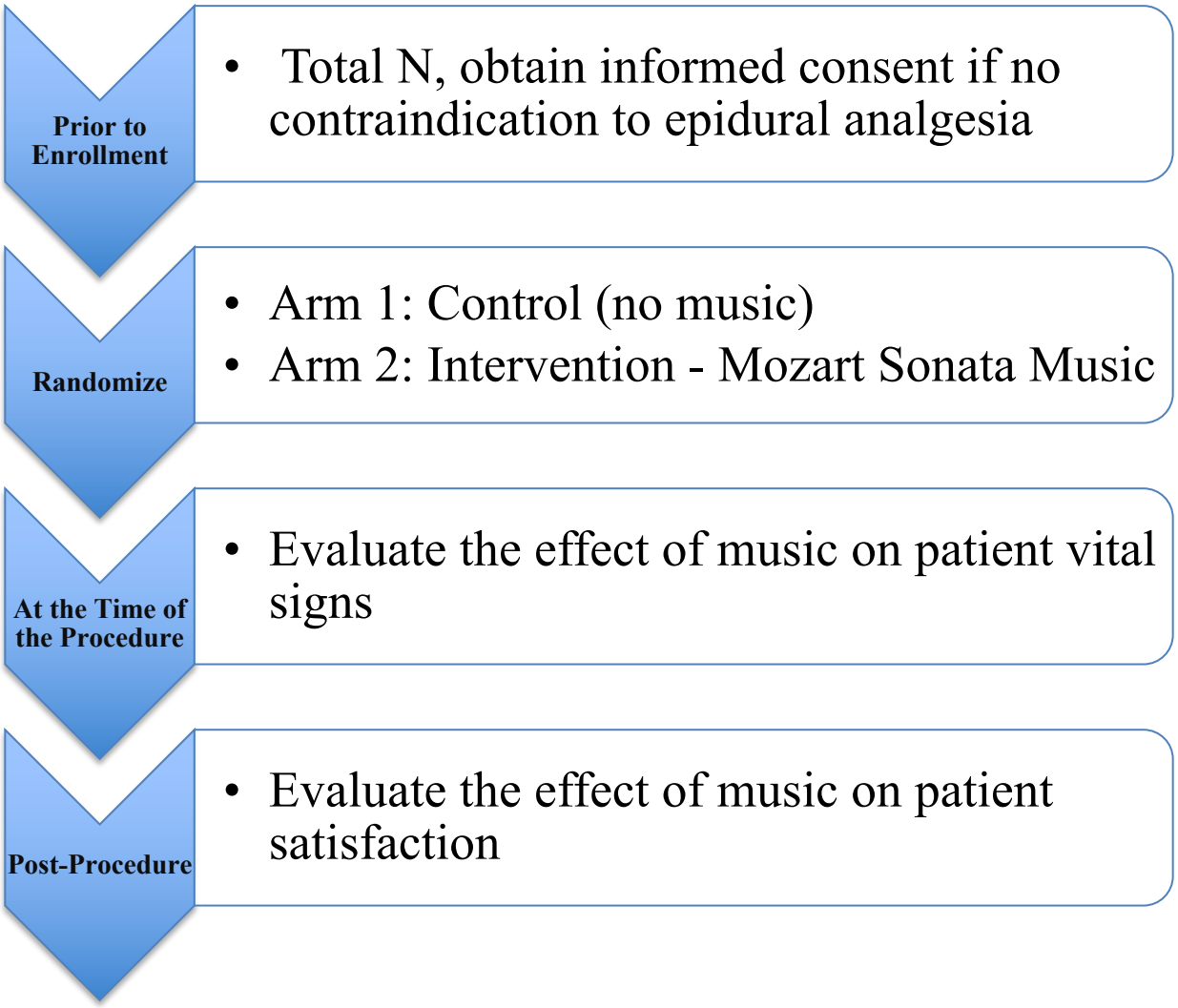
Dan Drzymalski, MD
Assistant Professor
Tufts University School of Medicine
Department of Anesthesiology and Perioperative Medicine
Tufts Medical Center
Phone: 617-913-8168
Email: ddrzymalski@tuftsmedicalcenter.org

CO-INVESTIGATORS

Mohammad Dahlawi, MD
Post Doctoral Research Fellow
Tufts University School of Medicine
Department of Anesthesiology and Perioperative Medicine
Tufts Medical Center
Phone: 202-285-6420
Email: mdahlawi@tuftsmedicalcenter.org

Table of Contents

1. Study Schema



2. Introduction

2.1. Background and Rationale

Several studies have demonstrated that music can improve various outcomes during labor and delivery. However, many of these studies suffer from severe methodological flaws. In particular, patient satisfaction is often measured on a simple VAS scale, where 0 is no satisfaction and 10 is the highest satisfaction. However, patient satisfaction is a complex parameter to measure, and may be affected by a number of different factors. This will be the first study performed on the labor and delivery unit to assess patient satisfaction with a validated, reliable, 22-question survey developed by Morgan et al. (Morgan 1999), in the setting of music or no music during the cesarean delivery.

Although "music" is an all-encompassing term that describes sound with different pitches and rhythms that comes together as a harmonious whole, not all music is the same. Using "music" for therapeutic purposes would be the equivalent of using "antibiotics" to cure an infection; it is too general of a term, and unlikely that such a general use of music would show a valid therapeutic benefit. However, Conrad et al. demonstrated that specific selections of Mozart piano sonatas, which have a specific rhythm and mode, improve patient anxiety through a biochemical mechanism (changing the plasma levels of IL-6 and epinephrine). Therefore, in this study, when we refer to "music," we will specifically plan on using the same Mozart sonatas as described in Conrad's prior studies.

2.2. Risks to Subjects

Participation in this study will include a risk that if the music is too loud, injury to the tympanic membrane may occur. This complication will be avoided with the patient's active participation at all times to report if the music is too loud, and volume will be adjusted according to the patient's preference.

Psychosocial (non-medical) risks include the concern for coercion to participate. To minimize this risk, the co-investigator of the study, who is an anesthesia research fellow, will recruit all participants greater than or equal to one hour prior to participation in the study.

Other risks may include the unintentional loss of patient confidentiality. In order to minimize that risk, all paperwork will be stored in a secure location. Furthermore, all electronic data will be held in a Tufts Medical Center provided, password protected, encrypted, Box storage account.

2.3. Potential Benefits to Subjects

There is no direct benefit for participation in the study.

Subjects being randomized to the intervention arm, Mozart music, may receive greater overall satisfaction with their delivery experience.

2.4. Alternatives

The alternative is not participating in the study.

3. Objectives

The objective of this study is to determine the effect of music on patient satisfaction and anxiety during cesarean delivery. We will evaluate this objective by studying the following outcomes:

- The primary outcome of this study is patient satisfaction. This outcome will be measured using Morgan's "Maternal Satisfaction Scale for Cesarean Section" (MSSCS) on post-operative day one during the hours of 8am-1pm.
- The secondary outcome will include anxiety at several time points (immediately prior to and after neuraxial technique placement as well as at the end of surgery). This will be evaluated using a simple numeric rating score from 0-10, where 0 is no anxiety and 10 is the greatest anxiety.

We hypothesize that parturients exposed to music during cesarean delivery will have greater overall satisfaction and less anxiety.

4. Enrollment and Withdrawal

4.1. Inclusion Criteria

- Age: 18-50 years old
- Scheduled for elective cesarean delivery
- Nulliparity
- Singleton pregnancy
- Planning cesarean delivery
- Full term fetus (≥37.0 weeks gestational age)
- Healthy fetus (no known congenital diseases at the time of surgery)
- Requesting neuraxial anesthesia for the procedure
- Able to provide informed consent
- Spontaneous labor

4.2. Exclusion Criteria

- Patient refusal
- Prior history of extensive abdominal surgery
- Active labor
- Contraindication to neuraxial anesthesia
- Uncorrected coagulopathy
- Infection at the skin site of epidural placement
- Increased intracranial pressure
- Untreated hemodynamic instability
- Known hypersensitivity to local anesthetics (a.k.a. amide or ester allergy)
- Patients with impaired hearing
- Patient on anti-anxiolytic medication

4.3. Withdrawal of Subjects

- Withdrawal of study subjects without their consent may occur in parturients who consent to the study but do not undergo neuraxial placement.
- Patients who decide to withdraw prematurely will be withdrawn and provided the standard of care at Tufts Medical Center.

4.4. Recruitment and Retention

4.4.1. Local Recruitment Methods

Faculty in the Obstetrics and Gynecology Department at Tufts Medical Center will be informed about the study at one of the departmental meetings. They will be asked to inform their patients about this study in their clinic visits. The co-investigator, Dr. Dahlawi will review medical records and schedule of medical procedures to know their time and date. Once the patients arrive to the labor and delivery unit, he will meet with the patients and discuss the study with them further. If they agree to participate, informed consent will be obtained.

4.4.2. Study-Wide Recruitment Methods

Is this is a multicenter study where subjects will be recruited by methods not under the control of the local Tufts site (e.g., call centers, national advertisements)?

☐ **Yes** ☑ **No**

4.4.3. Payment

Will subjects receive money, gifts, or any other incentive for participating in this study?
This does not include reimbursement for expenses, which is considered in the next section.

☐ **Yes** ☑ **No**

4.4.4. Reimbursement

Will subjects be reimbursed for their expenses, such as travel, parking, meals, or any other study related costs?

☐ **Yes** ☑ **No**

5. Study Design

5.1. Study Timelines

- Participation begins at the time of consultation for cesarean delivery on the day of surgery, where the co-investigator Dr. Dahlawi will approach the participants and ask them to sign the ICF, and it ends after the post-anesthesia check on postoperative day 1. After recruitment and consent, patients will be randomized using a computer-generated randomization scheme will be used to allocate patients to one of the arms of the study.
- The two arms of the study are as follows:
  - Control group: baseline hemodynamics and anxiety screen; no music
  - Intervention group – Mozart: A study investigator will turn on a playlist of pre-selected Mozart music.
- Given our sample size calculation and that not all women who are approached will consent to the study, we expect recruitment to take 12 months.
- The estimated date for primary analyses will be November 2018
- We estimate that it will take an additional 12 months to complete the study, including statistical analysis and manuscript preparation.

5.2. Procedures

- Is there a placebo control arm?

☐ **Yes** ☑ **No**

After reviewing their medical records, the co-investigator, Dr. Dahlawi, will approach parturients meeting inclusion criteria on the day of admission for scheduled cesarean delivery at Tufts Medical Center. The

research study will be explained and parturients will be given an informed consent form to read. After the parturient read through the informed consent form, think about the risks and benefits, and ask questions, she will be asked to sign the form if she wishes to participate in the study. The informed consent form will then be stored in the principal investigator's locked office. Once a study subject is enrolled, the anesthesia provider, obstetric provider, as well as the nurse will be informed that this parturient is part of the study.

Once the subject is recruited, patient demographic data and baseline vitals signs (including anxiety levels) will be collected. All parturients will receive a standardized spinal technique using 1.6 mL of 0.75% hyperbaric bupivacaine with 15mcg fentanyl and 200mcg morphine, which is the typical standard dose at Tufts Medical Center in nulliparous parturients.

Upon entry into the operating room, parturients who are randomized to music will start to listen to the Mozart piano sonatas during the entire procedure, while those randomized to no music will not listen to any music. After at least 5 minutes of listening to music and immediately after the spinal anesthetic is placed, anxiety levels and vitals signs will be assessed again. At the end of surgery, after coming into the PACU, anxiety and vitals will be assessed. Finally, on postoperative day 1, during the hours of 8AM – 1PM, patient satisfaction will be assessed by administering the MSSCS, which should take about 10 minutes to complete. After that, her participation in the study will end.

5.3. Evaluations

Will you perform any laboratory tests for this study?

☐ **Yes** ☑ **No**

5.4. Collection and Storage of Human Biological Specimens (Tissue Banking)

Will biological specimens be stored for future, unspecified, research?

☐ **Yes** ☑ **No**

6. Ethics and Protection of Human Subjects

6.1. Informed Consent Process

Will subjects be required to provide informed consent?

☑ **Yes** ☐ **No**

- The parturients will be informed about the study during a clinic visit before being admitted for surgery.
- The informed consent will be taken in a private room in the labor and delivery unit on the day of the procedure.
- The patient will have one hour before the start of the procedure to make a decision regarding enrollment.
- The consent will be obtained in person and documented in writing following "SOP: Informed Consent Process for Research (HRP-090)".
- Non-English speakers will be enrolled using interpreters and IRB approved Short Forms per the IRB's Short Form policy

6.2. Waiver or Alteration of Consent Process

- Is a waiver or alteration of the consent process being requested for this study?
  ☑ **Yes** ☐ **No**
- Is a waiver of the consent process being requested for parents for research involving children?
  ☐ **Yes** ☑ **No**
- Is a waiver of the consent process for planned emergency research being requested?
  ☐ **Yes** ☑ **No**

6.3. Confidentiality

In order to maintain confidentiality, the following measures will be taken:

- All study related materials, including consent forms and data collection forms, will be stored in the principal investigator's locked office
- The principal investigator and co-investigators will have exclusive access to the forms
- Digital data will be stored in a hospital provided, password protected, Box account
- Data will not be coded, as it will be stored in a protected online account.
- Records will be stored for 7 years after the study is closed with the IRB, as per IRB policy.
- A certificate of confidentiality will not be obtained.

6.4. Provisions to Protect the Privacy Interests of Subjects

Subjects will be assured that their interaction with any member of the research team is optional, as well as the information they share.

6.5. Provisions to Monitor the Study to Ensure the Safety of Subjects

- The standard of care at Tufts Medical Center is to collect safety information on all patients undergoing surgery through an established computerized system called Anesthesia Touch. Safety information and adverse events that will be collected includes failure of spinal analgesia. For the purposes of this study, the principal investigator will periodically (every 6 months) evaluate the safety data and assess the risks and benefits to assess subject safety. The purpose of obtaining this information is to ensure that no untoward events are occurring. This information will be obtained after signing the ICF. The statistical tests that will be performed on the safety data to determine whether harm is occurring will include a chi-squared test, to compare proportions between groups.
- Stopping rule: we do not anticipate a stopping rule to this study.
- No Data and Safety Monitoring Board will be used in this study.

6.6. Compensation for Research-Related Injury

Does the research involve greater than minimal risk to subjects?

☐ **Yes** ☑ **No**

6.7. Economic Burden to Subjects

Does the research involve any costs to subjects?

☐ **Yes** ☑ **No**

6.8. Vulnerable Populations

Will pregnant women be enrolled?

☑ **Yes** ☐ **No**

- The procedure in the study is not a part of the standard care at Tufts Medical Center for parturients. However, it is not uncommon for music to be played in the operating room during cesarean delivery, at the patient's request.
- This study's risk to the fetus is NOT greater than Minimal Risk.
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy and that in the case of a fetus; the fetus is not the subject of a planned abortion.
- Research team will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy or in determining the viability of a neonate.

Will the research involve neonates of uncertain viability or non-viable neonates?

☐ **Yes** ☑ **No**

Will subjects who are not yet adults (neonates, children, teenagers) be enrolled?

☐ **Yes** ☑ **No**

Will minors who are:

i) married, widowed, divorced; or
ii) the parent of a child; or
iii) a member of any of the armed forces; or
iv) pregnant or believes herself to be pregnant; or
v) living separate and apart from his/her parent or legal guardian, and is managing his/her own financial affairs

be approached for study participation for either themselves or their child?

☐ **Yes** ☑ **No**

Will wards of the state and/or children at risk of becoming wards of the state be enrolled (this includes foster children or any child that is in state custody)?

☐ **Yes** ☑ **No**

Will cognitively impaired adults (adults with impaired-decision making capacity) or adults who may lose the capacity to consent be enrolled?

☐ **Yes** ☑ **No**

Will prisoners be enrolled?

☐ **Yes** ☑ **No**

Will students and/or employees be enrolled in this research?

☐ **Yes** ☑ **No**

7. Adverse Event Monitoring

7.1. Definitions

The study does not carry a higher risk of adverse events than typically expected. Also, there is a risk of injury to the tympanic membrane if the music is too loud. The risks to the infant, which will initially be intra-uterine during the study and eventually delivered by the end of the study will be minimal.

Unanticipated problems: any incident, experience, or outcome that meets **all** of the following criteria: unexpected; related or possibly related to participation in the research; and suggests that the research places subjects at a greater risk of harm than was previously known or recognized.

7.2. Reporting Procedures

The co-investigator, Dr. Dahlawi, will be responsible for contacting the principal investigator to report the occurrence of adverse events. The principal investigator will then complete any necessary safety forms, include the Anesthesia Department's Quality Assurance form. Reportable new information will be reported to the IRB per the Tufts Health Sciences IRB's Reportable New Information policy within 5 business days of an event.

8. Statistical Considerations

8.1. Study Endpoints

- Primary endpoint: measurement of patient satisfaction
- Secondary endpoint: measurement of patient anxiety levels, hemodynamics, and postpartum analgesics requirement.

8.2. Statistical Analysis

- Given that our primary outcome is the satisfaction between two groups, we will use a statistical test to compare proportions (the Chi-squared test).
- Given that our secondary outcomes include mean patient anxiety levels and mean blood pressure, we will use a statistical to compare means (Student's t-test).

8.3. Number of Subjects

- A previous study demonstrated that the total satisfaction score in parturients who get midazolam pre-operatively vs. those who do not is 130.3 ± 10.5 vs. 113.6 ± 11.9, respectively. Although we do not have similar data for music, we expect that the effect of Mozart music will be similar to that of midazolam because both music and midazolam work as anxiolytics and may play an important role in patient satisfaction. Therefore, we will expect to see a similar difference in patient satisfaction.
- Using G*Power 3.1, we determined that in order to detect a difference between the two groups using a two-tailed T-test with power of 80% and alpha of 0.05, the total number of subjects needed is 18. In order to account for 20% attrition rate, the total number of subjects that would be required to complete study aims is **22**.

8.4. Data Management

- Data collection forms and an excel spreadsheet with all of the analyzed data will be stored during the study period in the PI's private locked office and hospital approved Box account, where access is exclusive to the research team.
- Name, date of birth and medical record number, vital signs and dates of service will be collected. Data sheets used in the collection of PHI and generation of the database will be destroyed after generation of the database.

8.5. Randomization

Will subjects be randomized?

☑ **Yes** ☐ **No**

In order to randomly allocate study subjects to one of three arms entirely by chance, we will use the on-line randomization tool "Research Randomizer Version 4.0, www.randomizer.org," which is a computer-based "random number generators," the numbers are generated by use of a complex algorithm (seeded by the computer's clock) that gives the appearance of randomness. This tool has been studied and validated as an adequate randomization tool, to generate a randomization list. Allocation concealment will be maintained by preparing sequentially numbered, sealed, opaque envelopes, which will contain the randomization assignment consistent with the generated randomization list. The study is not blinded.

9. Drugs or Devices

Will the research involve drugs?

☐ **Yes** ☑ **No**

Will the research involve devices?

☐ **Yes** ☑ **No**

10. Study Administration

10.1. Setting

Tufts Medical Center will be the sole research site.

10.2. Registration

The co-investigator, Dr. Dahlawi, will ensure the eligibility of subjects and obtain their consent before receiving any study related interventions.

10.3. Resources Available

The research team is composed of the following members:

- Principal Investigator: Dan Drzymalski, MD Assistant professor of Anesthesiology. Primary investigator responsible for the preparation, design, conduct, and administration of the study.
- Co-investigator: Mohammad Dahlawi, MD Research fellow. Responsible for writing the study's protocol under the PI guidance, obtaining the informed consent, managing data collection and coding and coordinating various sectors in the study.
- Tufts Medical Center facilities provide medical resources that might be needed by study subjects.

10.4. IRB Review

- An appropriate IRB registered with the OHRP, will review and approve this study.
- Any amendments to the protocol or informed consent documents will be reviewed and approved by the IRB prior to use, unless required to eliminate an apparent immediate hazard to subjects.

10.5. Multi-Site Research

Is this a multi-site study where Tufts is the sponsor, primary grant recipient, or coordinating site?:

☐ **Yes** ☑ **No**

10.6. Community-Based Participatory Research

Will this study involve community-based participatory research?

☐ **Yes** ☑ **No**

10.7. Sharing Results with Subjects

Will results (overall study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) be shared with subjects or others (e.g., the subject's primary care physician or the subject's treating physician)?

☐ **Yes** ☑ **No**

References

- Morgan PJ, Halpern S, Lo J. The development of a maternal satisfaction scale for caesarean section. Int J Obstet Anesth 1999;8:165-70.
- Drzymalski, DM, Tsen, L, Palanisamy, A, Zhou, J, Huang, CC, Kodali, B. "A Randomized Controlled Trial of Music Use during Epidural Catheter Placement on Laboring Parturient Anxiety, Pain and Satisfaction." Anesth Analg. 2017 Feb;124(2):542-547.
- Koch ME, Kain ZN, Ayoub C, Rosenbaum SH. The sedative and analgesic sparing effect of music. Anesthesiology 1998;89:300-6.
- Barnett SF, Alagar RK, Grocott MP, Giannaris S, Dick JR, Moonesinghe SR. Patient-satisfaction measures in anesthesia: qualitative systematic review. Anesthesiology 2013;119:452-78.
- Conrad C, Niess H, Jauch KW, Bruns CJ, Hartl W, Welker L. Overture for growth hormone: requiem for interleukin-6? Crit Care Med 2007;35:2709-13.