The University of Texas Medical Branch at Galveston

Research Protocol #18-0265

Title: Antimicrobial Dressing versus Standard Dressing in Obese Women Undergoing Cesarean Delivery: A Randomized Control Trial

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1. Introduction and Purpose:

Surgical site infection (SSI) is a major cause of morbidity in obstetrics. Cesarean delivery is the most common surgical procedure performed in pregnancy. Cesarean delivery rates are on the rise worldwide. At the same time, obesity, a known risk factors for SSI, has become an epidemic. Interventions which prevent SSI could have a significant impact on maternal health, as well as the cost of maternity care. Incisional SSI can be affected by multiple pre- or intra-operative variables, but there is little data regarding the impact of postoperative wound care, especially type of postoperative wound dressing, on SSI. Our objective is to evaluate the effect of a novel antimicrobial dressing on patient's satisfaction and health related quality of life before beginning the pivotal trial about its efficacy in decreasing SSI rates.

2. Background:

Cesarean delivery is the most common surgical procedure in the USA. Despite a concerted effort to decrease the cesarean delivery rate, it continues to hover around 30%, and is unlikely to decrease. SSI is a major contributor to obstetrical morbidity, hospital readmission, and higher health care cost. Risk factors that have been associated with incisional SSI include surgery type, administration of perioperative antibiotic prophylaxis, and patient's comorbidities. In contrast, the relationship between postoperative wound care, especially wound dressing types, and SSI remains to be elucidated. Recently, a post-operative dressing that integrates the antimicrobial properties of chlorhexidine gluconate (CHG), the practicality of absorbency, and the convenience of transparency has been approved by the FDA. Its antimicrobial and absorption properties in conjunction with its convenient features (transparent and adherent) makes it an optimal dressing for our obstetrical population. At UTMB, these dressings are available to surgeons and may be used at the physician's discretion. They have been evaluated in 20 post-cesarean patients with very positive feedbacks from patients and medical staff. As there are no clinical trials focusing on these novel dressing types, and because the risk factors and pathogenesis for post-cesarean SSI may not mirror other surgical procedures, level 1 evidence specific to pregnancy is needed before extrapolating the results from other types of surgeries to cesarean procedures.

3. Concise Summary of Project:

This will be an open label pilot randomized controlled clinical trial. Women undergoing cesarean delivery will be randomized to have standard wound dressing care or CHG impregnated wound dressing (ReliaTect™ Post-Op Dressing). We will exclude women with chorioamnionitis, immunosuppression, active skin infection, contraindication to

CHG (allergy), those unlikely to be followed-up after delivery, or unable to provide consent.

Subjects requiring cesarean delivery and without exclusion criteria will be informed by the obstetrical team about the study and asked for permission to contact the study personnel. Written informed consent will be obtained by person-to-person contact. The research staff will be responsible for the informed consent.

Subjects who agree to participate in the study will be randomized to one of the two groups below in a 1/1 allocation:

- Standard Wound Care: Wound dressing and care as per our current practice. Compression dressing consisting of gauze, tefla and adhesive tape will be placed intraoperatively. Dressing will be removed after 24 hours from surgery completion and subjects will have an absorption pad with overlying garments for the remaining postoperative days until standard postoperative visit for wound check.
- CHG Wound Care: ReliaTect™ Post-Op Dressing will be applied as per the manufacturer's instructions (Appendix A) intraoperatively. The dressing will be in place until the postoperative clinic visit on postoperative day 7.

The remainder of the subjects' care will be similar for both arms and will follow current standard clinical practice at the University of Texas Medical Branch (UTMB). The study period will be between February 2019, and February 2020. The number of subjects to be studied at UTMB will be 160. A subject will be withdrawn from the study if she wishes to discontinue participation.

4. Study Procedures:

After a subject who meets eligibility criteria agrees to participate in the study, the obstetrical team will contact the research staff who will obtain a signed informed consent.

The data collected will be kept on a password-secured UTMB computer. An encrypted USB flash drive will be used to transfer data. The data will be linked to the subject by subject's MRN number. This identifier is needed to access and analyze demographic data. During analysis of the data, all identifiers will be deleted.

4.1 Screening Recruitment and Consenting:

Under the direction of the PI, trained research staff will be available 24/7 to screen and consent subjects. Subjects will be enrolled at the time of admission to labor and delivery (L&D) for delivery or thereafter. Medical records of all potential subjects will

be reviewed and those who satisfy eligibility criteria will be approached and written informed consent obtained. A screening log will be used to track all subjects approached for the study. Women will be randomized in the operating room when the decision is made to proceed with skin closure AND they continue to be eligible.

Recruitment: We will offer the trial to all pregnant subjects admitted to L&D and who meet our eligibility criteria. Whenever practical and feasible, information about our research project will be made available to subjects prior to labor. We will not consent subjects who appear not to be able to evaluate their options (such as recent intravenous narcotics). This strategy is currently followed in other approved OB/GYN studies with similar recruitment timing, and has been well received among participants without concerns or complaints. Subjects will be enrolled at the time of admission to labor and delivery (L&D) for delivery or thereafter. Once the inclusion criteria for our study are met, the clinical team will inform the subject about the study and ask her authorization to contact one of the study personnel.

Consenting process: Written consent will be obtained by direct person-to-person contact. The research staff will be responsible for the informed consent. For non-English speaking subjects, informed consent will be provided in their primary language. The research data collected will not be used for clinical diagnosis or treatment purposes. Subjects will be reassured that participation in the study is voluntary and will not interfere with diagnose or treatment of her condition. The subjects will receive the same care and expertise as any other patient treated in our unit.

4.2 Randomization

A confidential computer-generated simple randomization scheme will be prepared and provided on an ongoing basis to our research staff. A randomization log with group assignment, patient name and medical record number will be used to track the randomization process.

4.3. Study visits/Follow-up

A single maternal follow-up study visit will be scheduled to ascertain/confirm outcomes at the same time as the routine clinical visit (~7 days postoperative). This visit is the standard postpartum visit at UTMB for a wound check. The standard procedure in our postpartum care unit is that the providers will schedule the postpartum visit before the patient leaves the hospital. Our research staff will document the time and date of the postpartum appointment in the datasheet, in order to ascertain follow up. The subject will be informed of the appointment and will be given a phone number for any questions and concerns regarding the study (contact information will be in the consents). We will also collect a provider satisfaction

questionnaire (Appendix A) from the provider/clinical staff that took care of the subject during her hospital stay. Subject's participation will end 30 days after delivery.

At the visit, the research staff or trained provider will give the quality of life (QoL) and satisfaction survey to the patient (Appendix B). We will also review the electronic medical record for the relevant outcomes. We will have research staff at every obstetrical clinic available during regular hours. If the subject does not present at this visit, or the survey was not completed during the visit, every effort will be made to contact her by phone and outcomes further ascertained. If greater than 30 post-operative days have passed and the subject could not be reached, she will be designated as "lost to follow-up."

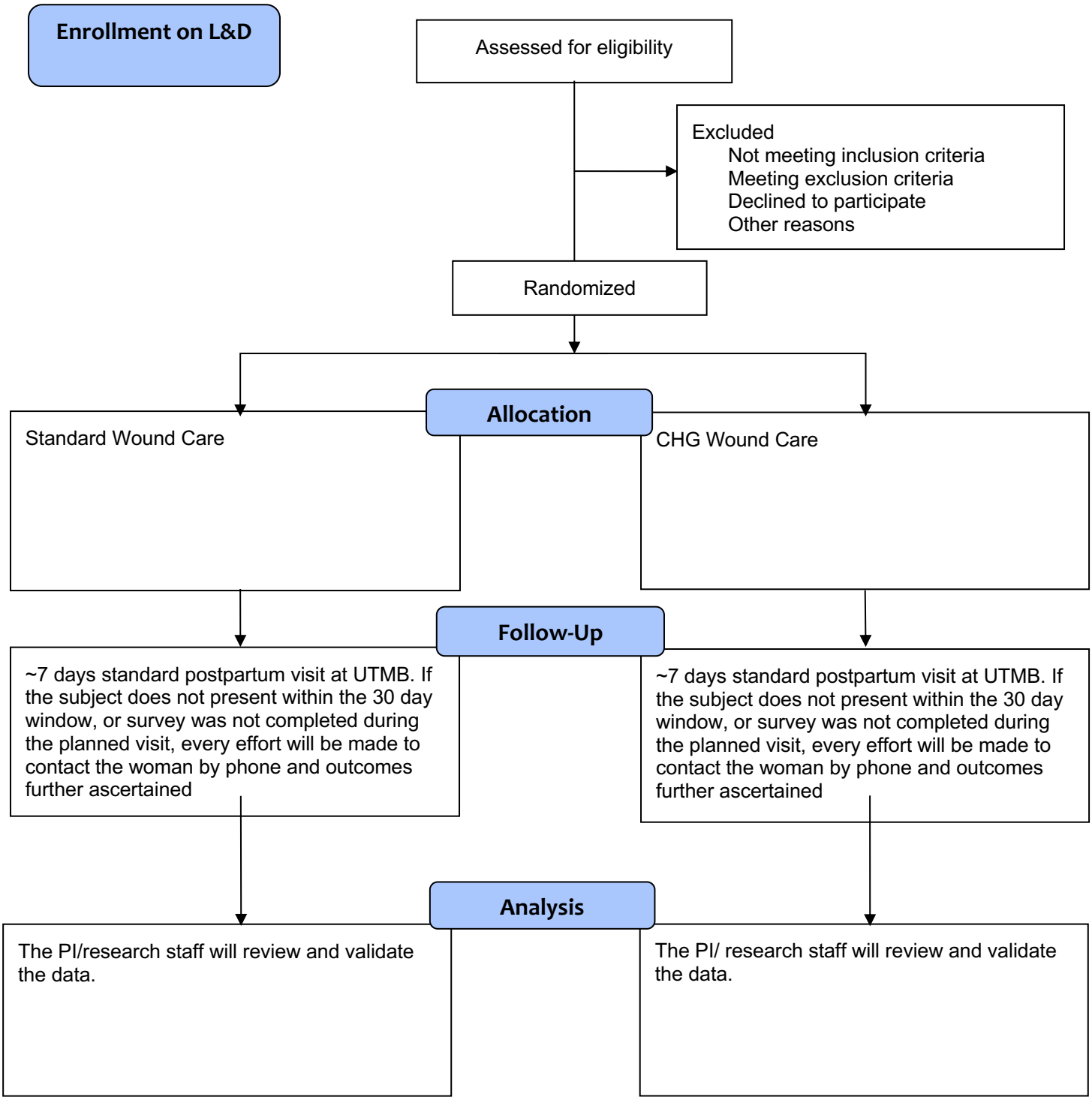
4.4. Baseline Procedures

Routine post-cesarean care will be according to the subjects' clinical providers. Trained and experienced research staff will be responsible for all research data abstraction. The PI will review and validate the data. Data on these forms devoid of personal identifiers will be securely stored in our perinatal research division offices.

4.5. Withdrawals

Subjects who withdraw from the study after randomization will be excluded from further follow-up. Outcomes will be reported by intent to treat fashion. Those who withdraw prior to ascertaining of the primary outcome and refuse further data collection will be accounted for by randomizing an equal number of additional subjects and will not be included in the analysis.

Study Summary Flow Diagram



4.6. Primary Outcome

Satisfaction and QoL questionnaire.

4.7. Secondary Outcomes

- Composite wound complication.
    - Defined as presence of any of the following within 30 days from surgery: **Wound infection**: Presence of either superficial or deep incisional SSI described as cellulitis/erythema and induration around the incision or purulent discharge from the incision site, with or without fever, such as necrotizing fasciitis (diagnosed based on necrotizing wound infection). **Wound hematoma, seroma, or breakdown alone.**
- Endometritis, wound infection (including necrotizing fasciitis), other infections including abscess, septic thrombosis, pneumonia, pyelonephritis and breast infection.
- Maternal Death.
- Puerperal fever: Temperature > 100.4^{o}F after first 24 hours or ≥101^{o}F any time.
- Postpartum antibiotic use.
- Wound hematoma or seroma.
- Wound dehiscence.
- Use of resources: hospital stay, postpartum clinic or emergency room visit within 30 days of delivery, need for imaging or other invasive procedures.
- Adverse events: allergic reactions (anaphylaxis, angioedema, skin rashes including Stevens Johnson and Toxic Epidermal Necrolysis).
- Provider satisfaction survey.

5. Inclusion Criteria:

- 18-50 years of age.
- Women ≥ 24 weeks' viable gestation.
- To undergo cesarean delivery.
- Admission BMI ≥ 35.

6. Exclusion Criteria:

- Patient unwilling or unable to provide consent.
- No prenatal care or a non-resident patient who is unlikely to be followed-up after delivery.

- Immunosuppressed subjects: i.e., taking systemic immunosuppressant or steroids (e.g. transplant subjects; not including steroids for lung maturity), HIV with CD4 <200, or other.
- Decision not to have skin closure (e.g. secondary wound closure, mesh closure).
- Current skin infection.
- Coagulopathy.
- High likelihood of additional surgical procedure beyond cesarean (e.g. scheduled hysterectomy, bowel or adnexal surgery).
- Known allergy to CHG.
- Incarcerated individuals.
- Chorioamnionitis.

7. Sources of Research Material: Electronic Medical chart/records; questionnaires.

8. Potential Risks:

8.1. Randomization risk

Since wound dressing care will be randomized, it is possible that the patient may be in a group with higher adverse outcomes.

8.2. Loss of Confidentiality

Any time information is collected, there is a potential risk for loss of confidentiality. Every effort will be made to keep patient's information confidential; however, this cannot be guaranteed.

8.3. Allergic reaction to CHG (Very rare, unreported but possible)

Subjects receiving a CHG wound dressing may have the following bad effects: Allergic reaction.

9. Subject Safety and Data Monitoring

The PI and research staff will be responsible for monitoring the safety of this study. A report to the IRB will be submitted according to its policy if adverse events (AEs) or serious adverse events (SAEs) occur, and any changes in the protocol as a result of these events. No interim analysis will be planned and there will be no study-specific criteria to halt the study. Since, CHG Wound dressings are deemed safe and available for use according to the FDA, there are no safety and minimal toxicity concerns for patient withdrawal.

The research staff will ensure all aspects of **data quality** including monitoring for adherence to consent procedures, inclusion and exclusion criteria, valid abstraction, correct entry, timeliness and responsiveness to data queries.

Data collection will take the form of excel data entry and will be identified with a participant ID number. Data will be collected and stored with the participant ID code only. The master enrollment log linking patient identifiers with study ID numbers will be kept in a password-protected database on the Ob/Gyn Department's internal server separate from the data. Several data collection forms will be used. Data on these forms devoid of personal identifiers will be securely stored at our perinatal research division. The research staff will be available to monitor the data and correct any discrepancies based on source documents if needed.

10. Procedures to Maintain Confidentiality

Each patient will be assigned a study number with personal identifiable information deleted or removed. Subjects' information will be de-identified and tagged with a number. Data will be collected and stored on a UTMB password-protected computer in a locked room.

11. Potential Benefits

A potential benefit is that the CHG impregnated dressing leads to better patient satisfaction and quality of life. We also hope that this dressing will ultimately reduce SSI rates and maternal health costs.

12. Statistical Approach

In preparation for sample size calculation, and following IRB exemption, ~20 patients with standard wound care filled the satisfaction and QoL surveys. The total mean score was 46 with a standard deviation of 9.1. Using effect sizes of 10%, power of 90% and 2-sided alpha of 0.05, we estimate that we will need 144 with complete ascertainment. Assuming a 10% loss to follow, we propose to enroll a total of 160 patients. Analyses will be performed by intent to treat. We will be using STATA 15 (Dallas, TX) for statistical computations. We will be also doing an analysis of the questionnaire using the Cochran-Armitage test for trend. $P<0.05$ was considered significant.This trial will be registered with Clinical Trials Register (Clinicaltrials.gov), before recruitment is initiated and after IRB approval.

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