Official Title: Randomized Trial of Dilute Povidone-Iodine Soak and Scrub for Orthopaedic Foot and Ankle Surgery

NCT Number: NCT03926208

Document Date: 4/12/2019

Study Protocol:

Patient enrollment and randomization

Inclusion criteria were (1) age greater than 18 years and (2) undergoing a surgical procedure on the foot or ankle. Exclusion criteria were (1) active infection of the foot or ankle, (2) allergy to any component of chlorhexidine, povidone-iodine, or alcohol, (3) unwilling to participate, (4) incarcerated, incapacitated, or otherwise unable to provide appropriate informed consent, and (5) non-English-speaking.

Eligible patients scheduled for a foot or ankle procedure were approached, invited, and consented preoperatively by a research assistant. A distinct 1:1 block-randomization table with random block sizes of four, six, eight, and ten was created using a computerized number generator and used to randomize subjects to either the intervention or control group. Randomization status was revealed only once the subject was on the operating table and the plastic nonsterile u-drape had been applied. Subjects were completely blinded to their randomization until completion of the study.

Skin preparation and culture technique

Subjects randomized to the control group received a standard two-step skin preparation with alcohol and chlorhexidine. First, 70% isopropyl alcohol was generously applied to the skin

using 4x4 gauze from the toes to the knee. This was done in a nonsterile fashion in that nonsterile gloves were worn and the foot was supported by a nonsterile post. Particular attention was paid to covering the web spaces, nail folds, and subungual regions during this step. Second, a 26 mL ChloraPrep stick (2% w/v chlorhexidine, 70% v/v isopropyl alcohol; CareFusion 213, LLC, El Paso, TX, USA) was used to prep the skin a second time. This was done in a sterile fashion in that sterile gloves and a sterile post were used to elevate and support the foot.

Subjects randomized to the intervention group received a three-minute dilute povidone-iodine soak and scrub followed by the same two-step skin preparation with alcohol and chlorhexidine described above. Specifically, 1,000 mL of normal saline was combined with 118 mL of 7.5% povidone-iodine (Aplicare Products, LLC, Meriden, CT, USA) in a large nonsterile basin.The subject's foot was placed in the nonsterile basin and scrubbed from the plantar aspect of the foot to the malleoli using soft sponge brushes from a wet prep kit for a total of three minutes. This was done in a nonsterile fashion in that nonsterile gloves were used and the foot was allowed to rest on a nonsterile post following prep. After the full three-minutes, the foot was removed from the basin, wiped down, and the standard two-step skin preparation with alcohol and chlorhexidine described above was performed.

For subjects in both groups, routine draping was then performed. After draping and immediately before skin incision, using strict sterile technique, a swab stick was lightly touched to the hallux nail fold. The swab stick was immediately sealed and transported to the in-house microbiology lab for aerobic culture processing. All laboratory staff and technicians were blinded to the randomization of the swabs. The swabs were placed in separate containers with the following growth plate media: Blood agar, Chocolate agar, MacConkey agar, and Columbia

agar. All media is supplied by Thermo Fisher Scientific Remel Products, Lenexa, KS, USA. Plates were incubated for 24 hours and then evaluated by a technician for growth. Plates were held for a total of 72 hours at which time a final report was created.

Statistical Analysis: Statistical analyses were conducted in Stata Version 16.0 ® (College Station, TX, USA). *T*-tests (for continuous variables), Pearson's chi-squared tests (for categorical variables with expected cell counts ≥5), and Fisher's exact tests (for categorical variables with expected cell counts <5) were used to compare baseline characteristics. Growth rates and wound complications were compared using Pearson's chi-squared tests. Growth rates were compared overall and stratified by presentation wearing a splint versus not wearing a splint. The level of significance was set at $p< 0.05$.

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Title of Study: ***Randomized Trial of Dilute Betadine Soak and Scrub for Foot and Ankle Surgery***

Sponsor: *Department of Orthopedics*

RUSH

SUBJECT INFORMATION SHEET AND CONSENT FORM

Introduction

You are being invited to take part in this research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the information in this form carefully, as it may contain words you do not understand. You may wish to discuss it with your doctor, family, and/or friends. If there is anything that you do not understand or you would like more information, please ask questions and the study doctor or study staff will try their best to answer them. Once the study has been explained and you have had all your questions answered to your satisfaction, you will be asked to sign this form if you wish to participate. Before anything is done for this study, you must sign this form. A copy of this signed form will be given to you.

You do not have to take part in this study. You are free to withdraw from this study at any time you choose without giving a reason. This will not affect any future care you will receive. No promises can be made about the outcome of this as far as your current condition, either positive or negative. People who take part in research are called "subjects" instead of "patients".

Why are you being invited to participate in this study?

You are being asked to take part in this study because you have been diagnosed with a disorder of the foot and or ankle that requires operative attention.

What is the purpose of this study?

The purpose of this study is to determine whether a standard chlorhexidine preparation can be made more effective by adding a soak & scrub technique using dilute betadine to reduce the rate of positive cultures from the hallux nail fold.

How many study subjects are expected to take part in the study?

This study is open to both male and female subjects, 18 years old and older who are diagnosed with any disorder of the foot and or ankle that requires operative attention. If you agree to

participate in this study, you will be one of approximately 242 research subjects enrolled at Rush University Medical Center.

What will you be asked to do?

If you decide to be a part of this research study you will be randomly assigned (like the flip of a coin) to receive either a standard chlorhexidine preparation (cleanse) prior to surgery [control group] or an alternative version that includes a soak and scrub technique using dilute betadine in addition to the standard chlorhexidine preparation [experimental group]. After the preparation technique has been applied a culture will be taken from the hallux nail fold via a cotton swab to test for presence of any organisms. In addition, you will be asked to follow-up as normal after routine ankle surgery at 2 weeks, 4 weeks, 8 weeks, 6 months, and 1-year.
Additional information will be collected from you or your medical chart including your diagnosis, bone disease and injury and related past medical history, and any follow up information related to your orthopedic injury.

How long will you be in the study?

You will be in the study for 52 weeks after your initial outpatient visit.
You may be removed from this study without your consent. Possible reasons may be that the study doctor decides that continued participation in the study will be harmful to you or the study is canceled.

What are the possible risks of the study?

There is no risk associated with the culture of the nail with a swab.
The study involves collecting information from your medical records and surveys. The only risk is the release of confidential personal health information. We will take every precaution to protect your information. All data collected will be protected on a password protected encrypted computer. Information identifying subjects will not be released to the public. Once all data is collected and analyzed we will remove all identifying data.

Are there benefits to taking part in the study?

There may be no direct benefit to you for participating in this study. Subjects in the experimental group will be receiving the operative preparation that is the standard of care at our institution in addition to an extra cleansing step that we hope may decrease infection risk.

What other options are there?

The only alternative to participating in this study is not to participate. If you decide not to participate in this study you will then receive the standard of care sterilization technique currently in use at Rush Medical Center prior to your orthopedic surgery.

What about confidentiality of your information?

Records of participation in this research study will be maintained and kept confidential as required by law. If you withdraw from this study, the data already collected from may not be removed from the study records. The study doctor and/or study team may ask you whether they

can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Confidentiality and disclosure of your personal information is further described in the attachment to this form. The attachment is titled HIPAA Authorization to Share Personal Health Information in Research (2 pages).

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human subjects.

What are the costs of your participation in this study?

All costs that are part of your usual medical care, such as clinical visits, surgery and any tests associated with these visits will be charged to you or your insurance company. You will be responsible for all costs that are not paid by your insurance company. You should check with your insurance company before you enroll in this research study.

What happens if you experience a research related injury?

If you experience any injury or illness as a direct result of your participation in this research study, immediate treatment will be provided. However, the cost of that treatment will be billed to you or your insurance company. Please check with your insurance company regarding coverage.

If you have any medical problems during the study, please contact the study doctor. He or she will explain your treatment options to you and/or help you find a place to get treatment.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

What happens if you need emergency care?

If you need emergency care while you are participating in this study, it is important that you tell emergency personnel of your participation in this study and notify the study doctor as soon as possible.

Whom do you call if you have questions or problems?

Questions are encouraged. If there are any questions about this research study or if you experience a research related injury, please contact: **Kamran Hamid, MD at (312) 243-4244.** Questions about the rights of research subjects may be addressed to the Rush Research & Clinical Trials Administration Office at 1-800-876-0772.

By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions,

which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent form.

SIGNATURE BY THE SUBJECT

Name of Subject _____

Signature of Subject_____

Date of Signature_____

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the subject. I further attest that all questions asked by the subject were answered to the best of my knowledge.

_____ _____
Signature of Individual Obtaining Consent Date of Signature

☐ *Check here if the Individual Obtaining Consent observed the signing of this consent document and can attest, to the best of their knowledge, the person signing the consent form is the subject and the person signing the form has done so voluntarily. By checking this box, the Individual Obtaining Consent does not need to sign on the Witness signature line (below).*

SIGNATURE BY WITNESS/TRANSLATOR
(for use if this consent is being used as a written summary of the research along with a short form consent OR when the person obtaining consent is not the witness):

I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the subject and the person signing the form has done so voluntarily.

_____ _____
Signature of Witness/Translator Date of Signature

☐ Check here if a separate witness signature is not necessary.

SIGNATURE OF THE PRINCIPAL INVESTIGATOR
I attest that I am aware of the enrollment of this subject in the study discussed in this consent document.

_____ _____
Signature of the Principal Investigator Date of Signature a separate signature is not

☐ required.

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