NCT03061903

STUDY TITLE
Closed Incision Negative Pressure Therapy vs. Standard of Care for Surgical Incision Management in High-Risk Patients following Total Hip Arthroplasty: A Randomized Controlled Trial

DOCUMENT DATE: 10/22/2012

RESEARCH PROTOCOL

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INTRODUCTION
Direct anterior approach (DAA) for total hip arthroplasty (THA) is becoming increasingly popular, with an estimated 25% of all procedures being performed through this approach in the United States. However complications have been reported such as an increased risk of wound complications and surgical site infections. Jewett et al[1] cited having a 4.6% wound complication rate with this approach. Christensen et al[2] also reported 1.4% of their direct anterior approach total hips replacements required reoperation for wound complications versus 0.2% of their posterior approach hips. Using stricter criteria to define wound complications, we have recently published a retrospective analysis of 651 consecutive DAA hips,[3] identifying an 11.5% wound complication rate and a 1.9% reoperation rate for these wound complications.

Risk factors for surgical site infections and prosthetic joint infections have been studied in the arthroplasty population. Many have been identified and include morbid obesity and increased comorbidities such as diabetes. [4,5,6] In our retrospective study,[3] we have specifically identified BMI > 30 kg/m^2, the presence of diabetes, active smoking status, and previous hip surgery as risk factors for wound complications and reoperation. Based on preliminary data, we documented a 31% wound complication rate in this "high-risk" subset of patients using standard-of-care dressings and incision management. This rate is unacceptably high for a common elective operation, prompting the desire to investigate alternative therapies.

Closed incision negative pressure therapy (ciNPT) has been used for the treatment and prevention of incisional complications. More recently, studies have reported results of ciNPT over the closed incision for prevention of postoperative wound complications. Karlakki et al[7] reviewed the literature regarding this application in orthopaedic surgery and showed reports of decreases in wound hematoma, drainage, and infection. Most of these reports were of patients that sustained high-energy traumatic injuries. Other studies also show similar support of ciNPT for closed cardiothoracic, abdominal, plastic, and vascular incisions. We have recently published results of a retrospective investigation examining 138 patients undergoing revision hip and knee arthroplasty procedures. In this study, we found significant decreases in wound complications (7% vs. 27%) and surgical site infections (3% vs. 19%) with ciNPT.[8] Based on this study, many surgeons in the US have adopted ciNPT as their standard of care in revision arthroplasty procedures. To our knowledge, few additional studies have examined ciNPT application in the arthroplasty population and none have focused its use in prevention of wound complications in the primary total hip arthroplasty population undergoing surgery through the DAA.

We propose a prospective, randomized controlled trial to examine the utility of ciNPT for incision management in the at-risk patient population following THA performed through the direct anterior approach.

OBJECTIVE(S)/SPECIFIC AIMS AND HYPOTHESES

1) To evaluate the potential effects of ciNPT on reduction of overall wound complications following DAA THA in high-risk patients.

2) To evaluate the potential effects of ciNPT on reduction of reoperation following DAA THA in high-risk patients.

Null hypotheses:

- In the at-risk patient population, there is no difference in 1) the overall wound complication rate, and 2) the rate of reoperation for wound complications, between the standard incision management group and the group where ciNPT is used to aid incision management.

EXPERIMENTAL DESIGN

The goal of this study is to determine the efficacy of ciNPT for prevention of wound complications and return to the operating room for wound complications in patients with pre-determined risk factors that affect wound healing (BMI > 30kg/m^2, diabetes mellitus, smoking, history of prior hip surgery). This is will be a prospective, randomized, controlled trial. Inclusion criteria will be patients undergoing DAA THA by the investigating surgeons that have at least one risk factor for complicated wound healing as described above, based on previous retrospective data. Subjects will be randomly assigned to either the ciNPT intervention group or the control group using computer-generated, randomized envelopes with equal numbers in each treatment arm. Both dressings will be applied under sterile conditions at the end of the DAA THA surgery, while still in the operating room, and then removed after 7 days.

Patients randomized to the control group will receive a conformable, water resistant, silver-impregnated, antimicrobial hydrofiber dressing (AQUACEL® Ag, Convatec) which is currently the standard of care at our institution for postoperative wound dressing. This dressing is left in place for 7 days and then removed by the patient or visiting nurse at home. Patients randomized to the study group will receive an incisional ciNPT device, which is currently being used selectively in high-risk patients at our institution (Prevena™, KCI). Both wound dressings are FDA-approved devices. Due to the obvious difference in appearance of the two dressings, neither patients nor treating surgeons can be blinded to treatment arm.

Wounds will be assessed postoperatively at regular intervals until wound healing is achieved. This will occur at least 2 and 6 weeks after surgery, which are standard intervals in our current postoperative protocol. No additional office visits will be needed for patients in the control or treatment arms. Photodocumentation of the wounds will occur at two and six weeks postoperatively. Primary outcome measure will be uneventful wound healing (requiring no intervention) versus the occurrence of wound complications (wound drainage, breakdown, necrosis, dehiscence, superficial or deep infection) requiring additional intervention. Intervention will be defined as any attempt of the surgeon to improve wound healing (in-office debridement, topical ointment, aspiration, antibiotic therapy, or return to the OR for the wound). Secondary outcome measures will include duration of wound healing delay, length of hospital stay, number of days of antibiotic therapy, and direct and estimated indirect costs. Statistical analysis will be performed to detect differences in the treatment groups

An *a priori* sample size calculation was performed based on data from our pilot study and from the existing literature. Currently, our retrospective data indicates wound complications should occur in approximately 31% of our “high risk” patients in the control group. We do not have reliable retrospective data for the study ciNPT group, so we are assuming a 4.57 relative risk reduction in wound complications using the ciNPT device based on existing data in the literature.[9] An intention-to-treat analysis will be used. Given the short-term nature of this study, our expected dropout rate is very close to zero (and will in all likelihood be zero). Assuming an ITT analysis, any dropouts should be counted as failures. With an estimated dropout rate of 5%, the incidence of wound complications in the control group would be 34.5% and the incidence of wound complications in the ciNPT group would be 11.5%. Our assumptions include an equality analysis, 2-sided p-value < 0.05, and Fisher’s exact test. Using these baseline assumptions, 116 patients (58 per group) will be required to achieve 80% power.

Based on our pilot study, 37% of our patient population should meet our inclusion criteria. Patients will need to be followed for at least 90 days to assess postoperative wound healing complications.

INCLUSION AND EXCLUSION CRITERIA

Subject Selection

Prospective inclusion criteria:

1. Patients undergoing primary THA through a direct anterior approach by one of the investigating surgeons
2. The presence of one or more of these risk factors for delayed or problematic wound healing:
    a. Diabetes
    b. Obesity (BMI > 30)
    c. Active smoking
    d. Previous Hip Surgery

RECRUITMENT PROCEDURES

Patients will be recruited in the offices of the treating surgeon if they meet subject criteria, based on routine consultation. No active recruitment, such as advertisements, will be made. No compensation will be offered to participants.

DATA COLLECTION

Columbia University Medical Center will be used as a central location for data processing and management. Vanderbilt University, with collaboration from a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the Biostatistics Unit of Columbia University Medical Center. The iterative development and testing process results in a well-planned data collection strategy for individual studies. REDCap servers are housed in a local data center at Columbia and all web-based information transmission is encrypted. REDCap has been disseminated for use locally at other institutions and currently supports 965 active institutional partners and other institutions in 78 countries (www.project-redcap.org).

INFORMED CONSENT

Patients willing to participate in the prospective study will be given written informed consent preoperatively. This will be performed by one of the investigators. Subjects will be informed that this study is being done to evaluate the potential effects of closed incision negative pressure therapy (ciNPT) on reduction of overall wound complications following direct anterior approach (DAA) total hip arthroplasty (THA) in high-risk patients compared to the standard dry dressing. Participating allows the researcher to use data from his/her medical record. No identifying information will be transmitted to other parties. Benefits and risks of participation will also be explained. Patients will also be given the option not to participate and receive routine care. Tests and treatment given will be a part of the standard of care and no extra procedures or treatments will be required for solely research purpose.

DISCOMFORTS AND RISKS

The Prevena Incision Dressing has an acrylic adhesive coating and a skin interface layer with silver, which may present a risk of an adverse reaction (redness, rash, itching, swelling or bruising) in patients who are allergic or hypersensitive to acrylic adhesives or silver. These risks are essentially identical to those seen with the control dressing. Please note that there is no evidence to support the risk of adverse skin reaction will be any higher than that of a traditional postoperative dressing. No additional risks to the standard care are anticipated for this study.

POTENTIAL BENEFITS

This includes improved wound healing from the use of the negative pressure dressing. The goal of this study is to determine if there is advantage of using this dressing on a routine basis compared to the standard dressing.

DEVICE PRECAUTIONS

Participants should contact the investigator in the event of visual or audible alerts as this may signal a leak, full canister, low battery, or device error. Participants need to remove the Prevena device prior to having a magnetic resonance imaging procedure or other diagnostic imaging procedures. The device should not be worn during hyperbaric oxygen therapy. Contact with the device must be avoided in the event of defibrillation or electrocardiograms.

DISCONTINUATION OF STUDY/SUBJECT WITHDRAWAL

If subject wish to be withdrawn from the study at anytime, then they may do so and contact the surgeon investigators with this request. Subjects may also be withdrawn by the investigators for the follow reasons:

- failure to follow instructions,
- failure to show up for study visits,
- it is not in the subject's best interest to continue on this study, or
- the study is stopped.

ADVERSE EVENTS

Adverse events occurring as a result of experimental intervention is not anticipated. However, if such event does arise, this will be documented and written report will be given to the IRB and sponsor.

DATA AND SAFETY MONITORING

The Principal Investigator will be tasked with ensuring the safety of the study. The Principal Investigator will review the aggregate data every 6 months to determine if aspects of the study need to be changed or stopped. In addition, the Principal Investigator will review any and all deviations, adverse events and unanticipated problems that may occur to determine their relatedness to the study, their severity, and whether they require study changes. In addition, any unanticipated problems or instances of non-compliance will be reported to the IRB as per their reporting requirements. If any protocol changes are needed, the investigator will submit a modification request to the IRB. Protocol changes will not be implemented prior to IRB approval unless necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB will be promptly informed of the change following implementation.

CRITERIA FOR EVALUATING RESPONSE/STATISTICAL ANALYSIS

For the randomized control trial, a t-test for independent samples or a nonparametric Mann-Whitney U test will be used for determination of differences of mean values between the two treatment groups. The Kolmogorov-Smirnov test will determine the distribution form. For analysis of categorical data, a Fisher exact test will be used. The level of alpha will be set at $p < 0.05$.

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