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Antimicrobial Barrier Dressing versus Closed-incision Negative Pressure Therapy in the Obese Primary Total Joint Arthroplasty

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I. PURPOSE OF THE STUDY AND BACKGROUND

Purpose of the study: To determine whether an occlusive antimicrobial barrier dressing or portable negative pressure wound dressing is superior in preventing wound complications and infection rates in obese patients undergoing total joint arthroplasty (TJA).

Background:

Total joint arthroplasty has been reported as the most effective treatment for end-stage osteoarthritis [Zhang]. In obese patients, a higher body mass index results in elevated articular cartilage loading forces, which may accelerate tissue damage, and obesity leads to a higher rate of osteoarthritis [Pottie]. The risk of developing knee and hip osteoarthritis is nearly four-fold for obese men and five-fold for obese women [Anderson]. Current literature reports an increased risk of perioperative complications associated with total joint arthroplasty for obese patients [workforce], with wound complications and infections among the most concerning for surgeons. Not only has obesity has been associated with higher risks of wound complications following TKA [Springer 2013, Meller 2016], but subcutaneous fat thickness has also been shown to be an independent risk factor for early reoperation for wound complications and infection [Taunton 2016]. In a large study of 7181 primary hip and knee replacements, Jamsen et al reported an increased infection rate from 0.37% in patients with a normal BMI to 4.66% in the morbidly obese group [Jamsen]. Malinzak et al showed patients undergoing total joint arthroplasty with BMI over 50 had an odds ratio of infection of 21.3 compared to non-obese counterparts [Malinzak]. Aside from the detrimental physical, emotional, and psychological impacts on the patient, the economic burden of a periprosthetic infection is substantial. Previous studies estimate the cost of medical and surgical treatment to range between $30,000-50,000 per case [Darouiche, Hebert]. It is therefore of utmost importance to take all measures possible to reduce infection and wound complications in TJA.

There are several dressing choices available to use in the immediate postoperative period following TJA. Both silver impregnated dressings and negative pressure wound therapy (NPWT) dressings have been associated with reductions in infection and wound healing complications after total joint arthroplasty [Cooper, Karlakki, Sharkey]. Currently, both of these modalities are being used by all orthopedic surgeons at NYULMC, but it is primarily a case by case surgeon-specific decision. However, to our knowledge, no prospective study has been performed comparing the efficacy of these dressings in the obese population. This study will therefore evaluate the outcomes associated with these two dressings in treating this subset of patients and analyze the cost benefit of each.

Study Outcomes:

Primary outcome measure:

1) persistent wound drainage (strikethrough leading to saturation in antimicrobial dressing group versus number of canisters filled with fluid in NPWT group)
2) wound dehiscence as evaluated at the first routine postoperative visit to the surgeon.

Secondary outcome measures include:

1) number of dressing changes (in hospital postoperatively, by visiting RN at home, by physician in office)
2) readmission for wound-related issues
3) presence of surgical site infection (i.e. cellulitis requiring antibiotics by mouth)
4) periprosthetic joint infection requiring further surgical treatment
5) patient satisfaction survey with dressing and appearance of wound, which will be administered at first postoperative visit with surgeon.

Study Design: Prospective, non-blinded randomized control trial.

II. CHARACTERISTICS OF THE RESEARCH POPULATION

Number of subjects: Approximately 240 subjects (120 for total knee arthroplasty, 120 for total hip arthroplasty).

Gender of Subjects: There will be no gender-based enrollment restrictions.

Age of Subjects: All over 18

Racial and Ethnic Origin: There will be no racial or ethnically based enrollment restrictions.

Inclusion Criteria: Those identified at pre-operative testing to have an elevated BMI (> 35)

Exclusion Criteria: Active infection, previous scar or wound healing complication, post traumatic DJD with hardware, revision surgery, vulnerable populations, inflammatory arthritis, anticoagulation outside of the standard of care, or patients deemed inappropriate by the attending physician.

Vulnerable Subjects: No vulnerable subjects will be included within this study.

III. METHODS AND PROCEDURES

Sample Size Analysis

The study sample will include all cases that meet inclusion and exclusion criteria that are treated by Ran Schwarzkopf, MD (PI) and all co-investigators. Presume a 5 percent reduction in wound healing complication rates with VAC sponge, using wound complication rates from previous studies--the sample size will be approximately 240 patients.

Methods and Procedures

Identification of eligible patients will be done by reviewing surgical schedules for the following week. Patients meeting enrollment criteria above will be flagged and patients will be approached by the attending surgeon and research staff on the morning of surgery. Study analysis will not breach subjects' privacy as only relevant clinical data without the inclusion of

personal information will be included. Only the principal investigator and the designated research staff will have access to the data.

Prospective, non-blinded, randomized control trial – patient's will be computer randomized on an alternating method to postoperative wound dressing with either anti-microbial dressing or portable NPWT device placed in the operating room from surgery to postoperative day 7. Both of these wound dressing modalities are FDA approved and part of standard care at this institution. This will be a multi-surgeon standard of care study with similar surgical protocols – TKA done under tourniquet, administration of tranexamic acid, deflation of tourniquet after wound is fully dressed, skin closure with 2-0 vicryl suture and staples with no dermabond, enoxaparin with sequential compression device for VTE prophylaxis postoperatively. All patients will have the same postoperative physical therapy protocol in the hospital. Patients will all be expected to be discharged to home with visiting nurse services after clearing physical therapy. The visiting nurse will evaluate the dressing and contact the physician if there is any concern. This is considered standard of care and the patient will not incur any additional costs. The nurse will not be expected to remove the dressing during the first 7 days after surgery. On post-operative day 8, when the dressing is removed, research personnel at NYULMC will call the patient and administer a questionnaire regarding the status of the incision. Questionnaires include the VAS pain score, HWES wound evaluation scale, and satisfaction with their post-operative wound healing. Patients will be followed up with for a year to assess for any wound-related complications such as skin reactions, infections, hematoma developments, or consistent drainage.

Data Analysis

Data on patient baseline characteristics, procedural characteristics, perioperative outcomes, functional outcomes, and costs will be collected. Single variable and multivariate statistical analysis will be performed to assess the aforementioned data points. Dichotomous data outcomes will be analyzed using odd ratios and chi-squared tests while continuous data points will be analyzed using Student t-tests. Each complication will be documented for every patient. The rates of complication will be analyzed individually for each technique, and risk ratios will be conducted between techniques to determine which technique has the lowest risk of developing a complication. Complications include infection, abscess formation, dehiscence, prolonged drainage, allergic reactions, among others. Cost effectiveness will be determined by the differences in quality metrics such as LOS, readmissions, cost of supplies, and differences in wound closure time between the different wound closure techniques. Each of these variables will be calculated based on the estimated hospital costs and analyzed to determine the most cost effective wound closure technique

Data Storage and Confidentiality:

While PHI will temporarily be seen, none will be collected, stored, or recorded for this study. All de-identified data will be stored securely in a password protected excel spreadsheet on a computer in a locked office managed by NYU MCIT. The excel database will be only accessible to those individuals granted access to it by the research staff. No other individuals beyond those identified within the IRB study protocol will be permitted to view, handle, or possess the data.

The research data will be de-identified to protect confidentiality. No PHI will be recorded.Data will not be shared with other individuals or institutions.

IV. RISK/BENEFIT ASSESSMENT

Risks

There are low associated risks with the two wound dressing applications. Commonly documented complications associated with all wound dressings include skin discoloration or staining, skin irritation, pain, susceptibility to infection, delayed wound healing, and allergic reactions. These risks are minimal overall with minimal risk differences between each technique. Thus, at worst, there will be minimal change in risks whether patients are randomized or have the option to choose a specific technique.

The following are risks and discomforts that patients may experience during their participating in this research study. The risks that are associated with participating in this randomized control study include exposure of protected health information to those individuals unauthorized to view such data.

Following data collection, all reviewed charts will be assigned a unique study number that cannot be linked to the patient. This study number will be used to code their data throughout the study. All de-identified subject data will be stored in a secured database, located in one of the research drives on the NYULMC server.

All study data will be reviewed directly from the institution's electronic clinical database retrospectively. It is firewall and password protected. All data will be de-identified and subjects will be assigned unique study numbers that do not contain PHI or any portion of a medical record identifier.

Protection against Risks

Strict adherence of all approved study personnel to the protocol and patient data protection measures in order to uphold subject safety, confidentiality, and autonomy.

Potential Benefits to the Subjects

Study Cohort patients will receive no direct potential benefit by participating in this study. The purpose of this study is to determine whether an occlusive antimicrobial barrier dressing or closed-incision negative pressure therapy is superior in preventing wound complications and infection rates in obese patients undergoing TJA. Any benefit generated by this study will be experienced by future patients with similar conditions.

V. INVESTIGATOR'S QUALIFICATIONS AND EXPERIENCE

The CVs are attached for all investigators who are participating in this study.

VI. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT/ASSENT

Process of Consent

A consent form for this study has been included with this IRB submission. Informed consent will be obtained prior to surgery during their pre-admission testing visit by the attending surgeon or by his or her IRB approved research staff. Once consent is obtained, the person obtaining the consent will document appropriately that all of the information on the consent form was explained to the patient and that they understood the implications associated with their participation.

Costs and payments:

Patients will not be financially reimbursed throughout this study. Also, there will be no funding necessary for this study as both wound dressings are currently and regularly in use at the institution and there will be no increased cost to the patient.

Data Safety Monitoring Plan:

The investigator and his or her research team will allocate adequate time to monitor the activities of the study. A copy of their CV along with their credentials is supplied to the IRB. They will ensure that the monitor or other compliance or quality assurance reviewer is given access to all the above noted study-related documents and study related facilities (e.g. pharmacy, diagnostic laboratory, etc.), and has adequate space to conduct the monitoring visit. The Investigator and his research staff is able to stop the study whenever they see fit, specifically if there is conclusive evidence that there is ongoing harm to patients as a result of treatment interventions. However, this is not anticipated as the level of safety associated with the study has minimal to no differences in risk compared to the normal standard of care. Written reports will be submitted to the IRB if any concerns regarding the monitoring plan arise. To further ensure safety, the other study members will monitor the participants on an ongoing basis. Each member will be trained in the definition, monitoring, and reporting of adverse events, as well as both anticipated and unanticipated problems.

Study data and safety monitoring will focus on several areas and will be periodically reviewed to ensure that the study is meeting study expectations. These areas will be reviewed biweekly:
- Safety – to assess the mechanisms used to protect the safety and privacy of the study participants as well as the extent and magnitude of adverse events.
- Performance – to assess performance with respect to participant recruitment, retention, and follow-up, Case Report Form (CRF) tracking, protocol adherence, and quality of data
- Intervention effects – to assess whether the study should continue based on safety and efficacy data (if applicable).

Auditing and Inspecting

The investigator will permit study-related monitoring, audits as frequently as necessary, and inspections by the IRB, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.). Written reports will be submitted to the IRB if any concerns regarding auditing and/or inspection arise. Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

Unanticipated Problems Involving Risk to Subjects or Others:

Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc)
- Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

Adverse Event

An adverse event (AE) is 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

Adverse events are classified as serious or non-serious. A serious adverse event is any AE that is

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as non-serious adverse events.

Adverse Event Reporting Period
The study period during which adverse events must be reported is normally defined as the period from the initiation of any study procedures to the end of the study treatment follow-up. For this study, the study treatment follow-up is defined as 30 days following the last administration of study treatment.

Preexisting Condition
A preexisting condition is one that is present at the start of the study. A preexisting condition should be recorded as an adverse event if the frequency, intensity, or the character of the condition worsens during the study period.

General Physical Examination Findings
At screening, any clinically significant abnormality should be recorded as a preexisting condition. At the end of the study, any new clinically significant findings/abnormalities that meet the definition of an adverse event must also be recorded and documented as an adverse event.

Post-study Adverse Event
All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study. The sponsor should also be notified if the investigator should become aware of the development of cancer or of a congenital anomaly in a subsequently conceived offspring of a subject that has participated in this study.

References:

1. Zhang, W., et al., OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage, 2008. **16**(2): p. 137-62

2. Pottie P, Presle N, Terlain B, et al. Obesity and osteoarthritis: more complex than predicted! Ann Rheum Dis 2006;65(11):1403.

3. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. Am J Epidemiol 1988;128(1):179.

4. Jämsen E, Nevalainen P, Eskelinen A, et al. Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection: a single-center analysis of 7181 primary hip and knee replacements for osteoarthritis. J Bone Joint Surg Am 2012;94(14):e101. 24.

5. Malinzak RA, Ritter MA, Berend ME, et al. Morbidly obese, diabetic, younger, and unilateral joint arthroplasty patients have elevated total joint arthroplasty infection rates. J Arthroplasty 2009;24(6 Suppl):84.

6. Springer BD, Beaver WB, Griffin WL, Mason JB, Odum SM, Role of Surgical Dressings in Total Joint Arthroplasty: A Randomized Controlled Trial. Am J Orthop. 2015 September;44(9):415-420.

7. Meller MM, Toossi N, Johanson NA, Gonzalez MH, Son MS, Lau EC. Risk and Cost of 90-Day Complications in Morbidly and Superobese Patients After Total Knee Arthroplasty. J Arthroplasty. 2016 Oct;31(10):2091-8.

8. Darouiche RO. Treatment of infections associated with surgical implants. N Engl J Med. 2004;350(14):1422-9. 3. Hebert CK, Williams RE, Levy RS, Barrack RL. Cost of treating an infected total knee replacement. Clin Orthop Relat Res. 1996;(331):140-5.

9. Grosso MJ, Berg A, LaRussa S, Murtaugh T, Trofa DP, Geller JA. Silver-Impregnated Occlusive Dressing Reduces Rates of Acute Periprosthetic Joint Infection After Total Joint Arthroplasty. J Arthroplasty. 2016 Sep 28. pii: S0883-5403(16)30648-9.

10. Watts CD, Houdek MT, Wagner ER, Taunton MJ. Subcutaneous Fat Thickness Is Associated With Early Reoperation and Infection After Total Knee Arthroplasty in Morbidly Obese Patients. J Arthroplasty. 2016 Aug;31(8):1788-91.

11. Cai J, Karam JA, Parvizi J, Smith EB, Sharkey PF. Aquacel surgical dressing reduces the rate of acute PJI following total joint arthroplasty: a case-control study. J Arthroplasty. 2014 Jun;29(6):1098-100.

12. Cooper HJ, Bas MA. Closed-Incision Negative-Pressure Therapy Versus Antimicrobial Dressings After Revision Hip and Knee Surgery: A Comparative Study. J Arthroplasty. 2016 May;31(5):1047-52.

13. Karlakki SL, Hamad AK, Whittall C, Graham NM, Banerjee RD, Kuiper JH. Incisional negative pressure wound therapy dressings (iNPWTd) in routine primary hip and knee arthroplasties: A randomised controlled trial. Bone Joint Res. 2016 Aug;5(8):328-37.

14. Workgroup of the American Association of Hip and Knee Surgeons Evidence Based Committee. Obesity and total joint arthroplasty: a literature based review. J Arthroplasty. 2013 May;28(5):714-21.