Prospective Evaluation of Type IV Hypersensitivity Reactions After Aquacel Dressing Application in Partial and Total Joint Arthroplasty Patients

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Prospective Evaluation of Type IV Hypersensitivity Reactions After AQUACEL Ag Dressing Application in Partial and Total Joint Arthroplasty Patients

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Purpose: The aim of this multi-surgeon, single institution study is to prospectively evaluate the incidence of allergic contact dermatitis (ACD) following application of AQUACEL Ag, a silver-containing hydrofiber dressing, in total hip and knee arthroplasty patients. Arthroplasty-naïve patients will be compared to prior total joint arthroplasty patients who received a Aquacel dressing postoperatively.

Hypothesis: We hypothesize that patients who receive a AQUACEL Ag dressing a second time are at an increased risk of developing ACD secondary to a type IV delayed hypersensitivity reaction.

Background:
Total joint arthroplasty remains the standard of care for management of patients with end stage hip and knee osteoarthritis who have exhausted nonoperative management. As more emphasis is placed on value based care and reducing complications, significant effort has been placed on identifying interventions which can mitigate early postoperative complications. One area of focus continues to be on postoperative incisional dressings.

Wound complications can be devastating following total joint arthroplasty, resulting in an increased practice burden in the form of more frequent follow ups, increased clinic visits potential for wound dehiscence, superficial infection and deep infection with possible return to the operating room and revision surgery. Several dressing options are currently on the market designed to minimize wound complications in addition to traditional dressings, including negative pressure dressing, antimicrobial dressing, occlusive dressings, and/or skin adhesives.[1,2]

Aquacel dressing, a silver-containing hydrofiber dressing, has increased in popularity as a dressing option used by joint arthroplasty surgeons. AQUACEL Ag surgical dressings contain a hydrofiber layer with ionic silver that absorbs exudate to create a cohesive gel that provides an antimicrobial layer.[3] Further, AQUACEL Ag dressing is extensible to accommodate skin movement, avoiding blistering seen in traditional surgical dressings. The use of this dressing has been shown to reduce surgical site infections and improve patient satisfaction when compared to traditional surgical dressings.[1,3,4]

There is a well-documented adverse allergic response with these dressings resulting in peri-incisional erythema, urticaria, and/or an eczematous skin reaction.[3,5] Kuo et al reported on 5 patients of 240 (2.1%) developing allergic reactions to AQUACEL Ag dressing following total knee arthroplasty, requiring patients to change to standard dressing.[3] Premkumar et al reviewed 13,271 patients undergoing total joint arthroplasty and found that 0.5% of patients with topical adhesives, such as AQUACEL Ag.[5] In addition to these documented allergic reactions, literature suggests that repeat exposure to AQUACEL Agdressing can result in sensitization through a T-cell mediate process, resulting in ACD upon repeat exposure (Valois).[6] Traditionally, this reaction is treated with systemic corticosteroids and/or antihistamines. However, severe cases can lead to skin breakdown and further wound issues, increasing risk of superficial and deep infection.[7]

To the author's knowledge, there are no present studies that compare rates of ACD in patients who receive an AQUACEL Ag dressing for a second time following total joint arthroplasty to rates of ACD in arthroplasty-naïve patients who receive the AQUACEL Ag dressing. We hypothesize that patients who receive a second AQAUCEL Ag dressing are more likely to have ACD secondary to sensitization through

a Type IV hypersensitivity reaction. The purpose of this study is to evaluate the rates of allergic contact dermatitis and clinical outcomes in these patient populations.

Study Design:

Level I: Prospective Cohort Study

Patients will be recruited into the study after completing a standard questionnaire for pre-operative enrollment. After meeting inclusion criteria and passing the screening process, the patient will be enrolled into the study. Variables of interest related to sociodemographic status, operative details and postoperative outcomes will be taken from the electronic medical records associated with Midwest Orthopedics at Rush and Rush University Medical Center will be performed. This review will comprise patients of Dr. Craig Della Valle. Relevant variables that will be collected include:

Inclusion Criteria:

1. Patients older than 18 years that underwent primary total hip arthroplasty (THA)
2. Patients older than 18 years that underwent primary total or unicompartmental knee arthroplasty (TKA/UKA)

Exclusion Criteria:

1. Revision surgery
2. Prior history of allergic contact dermatitis
3. Prior history of non-TJA or UKA surgery with AQUACEL Ag dressing post-op
4. Occupational exposure to surgical dressings
5. Documented history of silver allergy

Sample Size:

A power analysis to determine how many patients need to be enrolled was performed with a rate of ACD in the AQUACEL Ag naïve group and the AQAUCEL Ag-exposed group of 1% and 2%, respectively. A one-tailed z-test of proportions between the two groups with 80% power, a 5% level of significance, and 1:1 allocation ratio, requires a sample size of 314 (157 per group). To account for 20% attrition rate amongst both cohorts, we plan to enroll 400 patients (200 each group).

Demographic/Patient Specific Data Collected:
Age, Sex, Body Mass Index (BMI), Allergy History, Past Surgical History, Prior exposure to surgical dressing (Either occupational (i.e. healthcare worker) or as a patient), Number of prior arthroplasty surgeries with AQUACEL Ag dressing (i.e. 0, 1, 2, 3), Past adverse reaction to AQUACEL Ag dressing, Any Adverse Skin Reactions with any past adhesive exposure

Operative details:
Surgical date, Operation/Laterality (THA/TKA/UKA, Left/Right), Length of incision, Patient reported skin check at 1 week (via picture from patient if wound issue/skin reaction present), Size of Rash if present, Provider skin Check at 1st post-operative appointment (2-4 weeks post-op), Any Wound Complications

Primary Outcome Measure:
The primary outcome is the rate of contact allergic dermatitis or adverse skin reaction at 1 week post op and 1st post operative visit (2-3 weeks after surgery). We will also quantify time from surgery to reaction

onset (Days). We will measure the size of the rash at post-operative follow up as well as classify the rash according to the classification system used in prior studies examining ACD.[7]

Classification of AQUACEL Ag Reactions[8]	
Mild	Erythema, infiltration, possible papules
Moderate	Erythema, infiltration, papules and vesicles
Severe	Spreading reaction (outside area of application), bullous reaction, extreme pruritus

Secondary Outcome Measures

1. Wound complications
2. Any workup for PJI (Serologic labs (ESR/CRP), arthrocentesis)
3. Any administration of post-operative antibiotics outside of normal protocol
4. Return to Operating Room for debridement, manipulation, other surgical interventions
5. Surgical Site Infection (SSI)
6. Confirmed Periprosthetic Joint Infection (PJI)
7. Stiffness requiring Manipulation Under Anesthesia (MUA)

Risks and Benefits: Given that this study is prospective in nature, there is a minimal risk to patients. Risks include the development of adverse skin reactions, wound complication, surgical site infection, periprosthetic joint injection, or complication requiring further surgery. This risk will be further minimized with thorough chart review of patient past medical, surgical and allergy history and with continued follow up throughout the duration of this study. This study will be of great benefit to both patients and orthopedic surgeons. Adverse skin reactions can be a debilitating and frustrating complication of total joint arthroplasty. The authors of this study believe that this study can help inform a clinician's decision-making process in regards to which dressing option would be most beneficial to patients in the perioperative & post-operative period. A risk inherent to every study is the potential for breach of confidentiality and/or privacy. Below is a description of the procedure for maintaining confidentiality

Procedures for Maintaining Confidentiality: A breach of confidentiality and/or privacy is a risk of this study. To prevent this, all collected data will be stored electronically in password-protected files to protect patient identity and information. All information will be collected and reviewed by the research team only. Data will be maintained on a password-protected computer connected to the Rush network that will be accessible only to the study team. No patient identifiers will be maintained in the dataset.

References

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Statistical plan

An a priori power analysis was performed based on reported allergic contact dermatitis/adverse skin reaction rates of 1% in patients naïve to AQUACEL Ag exposure and 2% in patients with prior AQUACEL Ag exposure. Using a one-tailed z-test of proportions, 80% power, alpha of 0.05, and a 1:1 allocation ratio, a total sample size of 314 patients was required. To account for approximately 20% attrition, the planned enrollment was 400 patients, with 200 patients per cohort.

Patients will be analyzed according to exposure cohort: AQUACEL Ag naïve versus prior AQUACEL Ag exposed. Descriptive statistics will be used to summarize baseline demographics, comorbidities, operative characteristics, and postoperative outcomes. Continuous variables will be reported as means with standard deviations or medians with interquartile ranges, as appropriate. Categorical variables will be reported as frequencies and percentages.

The primary outcome is the rate of allergic contact dermatitis or adverse skin reaction at 1 week postoperatively and/or at the first postoperative visit, approximately 2 to 3 weeks after surgery. The primary outcome will be compared between exposure cohorts using a Chi-square test of independence. Fisher's exact test will be used when expected cell counts are less than five.

Continuous variables will be compared using independent-samples t-tests when normally distributed. If normality assumptions are not met, nonparametric rank-sum testing will be used. Categorical variables will be compared using Chi-square tests or Fisher's exact tests, as appropriate.

Multivariable logistic regression will be performed to evaluate whether prior silver-impregnated dressing exposure is independently associated with allergic contact dermatitis or adverse skin reaction. Covariates will include age at surgery, sex, Charlson Comorbidity Index, body mass index, procedure type, and prior dressing exposure. Robust standard errors will be used to account for potential model misspecification and heteroskedasticity.

Subgroup analyses may be performed to evaluate allergic contact dermatitis or adverse skin reaction rates among patients who received topical liquid adhesive. These analyses will be considered exploratory.

Missing data will be assessed for frequency and pattern. Analyses will be performed using available data. No formal imputation is planned unless the extent of missing data warrants sensitivity analysis.

All statistical tests will be conducted with statistical significance set at $p < 0.05$. Analyses will be performed using Stata Standard Edition, version 19.5, and Microsoft Excel.