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Review Article

The Role of Allergies in Outcomes Following Shoulder, Knee, and Hip Arthroplasty: A Review

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Introduction

The incidence of joint arthroplasty continues to rise globally with an aging population. There have been significant improvements in clinical outcomes and survivorship for shoulder, knee, and hip arthroplasty over the last few decades. Given the increasing incidence, significant emphasis has been placed on optimizing complication and revision rates after surgery. Allergies have become a recent area of focus in understanding patient risks for negative outcomes following arthroplasty.

Methods

A PubMed and Google Scholar search was performed to identify articles pertinent to the article topic. The keywords covered a comprehensive range of topics such as metal,

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antibiotic, and food allergies in addition to surgical interventions such as anatomic, reverse, and hemiarthroplasty. The literature review was performed independently by two authors and organized into an outline by a third author. Information relating to clinical outcomes, complication rates, and revision rates were extracted from the relevant articles.

Results

Preliminary research has been mixed; some studies suggest there is no significant disparity in outcomes based on number and type of allergies. However, other studies suggest there are higher rates of complications and worse clinical outcomes in patients with allergies. A key area of interest is the role that allergies may play in increasing the risk of postoperative infections in arthroplasty patients. Allergies remains an area of focus among shoulder, hip, and knee arthroplasty surgeons as they continue to optimize outcomes for patients.

Conclusions

Further research needs to be performed to better understand the relationship between allergies and outcomes following arthroplasty. While current research is mixed, there is enough literature suggestive of a relationship that this area merits an increased focus. An improvement in the understanding between allergies and postoperative outcomes will help improve patient satisfaction following arthroplasty.

1. INTRODUCTION

Joint arthroplasty has witnessed significant growth due to advancements in implant technology and surgical techniques, rendering it a safer and more effective intervention (Galakatos 2018; Jacofsky and Allen 2016; Soeters et al. 2018; Sobieraj and Marwin 2018). This surgical approach aims to improve quality of life, mobility, and alleviate pain - an increasingly critical need as human life expectancy continues to rise, resulting in a projected exponential growth in the prevalence of arthroplasties (Puzzitiello et al. 2020; Canovas and Dagneaux 2018; Fisher et al. 2022). Based on data from the National Inpatient Sample (NIS), total shoulder arthroplasty (TSA) is expected to increase 349% from 2016 to 2025, total hip arthroplasty (THA) by 92%, and total knee arthroplasty (TKA) by 36% (Farley et al. 2019). Given the increasing incidence of joint arthroplasty and necessity to optimize patient outcomes, recent attention has shifted towards understanding how patient-specific factors, such as allergies, may influence surgical outcomes. Allergies to metals, antibiotics, and other substances are being investigated for their potential role in post-operative complications and revision rates. This narrative review aims to focus on one such risk factor, allergies, and seeks to assess the influence of allergies on the outcomes of shoulder, hip, and knee arthroplasty.

Currently, there is no cohesive literature discussing the impact of allergies on the outcomes of joint arthroplasties. Examining the impact of allergies on outcomes following TSA reveals some data indicating that patients with allergies may experience poorer patient reported outcomes (PROs) and decreased American Shoulder and Elbow Scores (ASES) postoperatively (Elrick et al. 2021; Forlizzi et al. 2022). At the same time, studies by Kennon et al. and Rosenthal et al. suggested no association between allergies and negative outcomes (Kennon et al. 2020; Rosenthal et al. 2016). This same trend can be seen in both knee and hip arthroplasty literature, where there is no unanimous consensus on how patient allergies impact postoperative outcomes. Nam et al. reported decreased patient satisfaction following TKA in patients with metal allergies, while Fisher et al. found no increase in postoperative joint infections in patients with penicillin allergies following THA (Fisher et al. 2022; Nam et al. 2016).

Despite recent advances, the influence of allergies on arthroplasty outcomes remains poorly understood. While some studies suggest a potential link between allergies and increased complication rates, the evidence is inconsistent, and the mechanisms underlying these associations remain unclear. This review aims to address this gap by synthesizing current findings on how allergies impact outcomes in shoulder, knee, and hip arthroplasty, with a focus on postoperative complications and revision rates. Furthermore,

this narrative discusses the potential role of preoperative testing and machine learning in predicting outcomes based on allergies.

2. CLINICAL OUTCOMES

2.1. SHOULDER

The effects of allergies on clinical and PROs following TSA remains a topic of debate. Various studies present conflicting findings, with some indicating poorer outcomes in individuals with multiple allergies and others showing equivocal results. Elrick et al. examined 411 shoulders with a mean follow-up of 2 years and found that an increased number of preoperative patient reported allergies is associated with worse PROs following SA (Elrick et al. 2021). Specifically, patients with two or more allergies exhibited higher QuickDash scores compared to those without allergies (11.3 vs. 27.2; p=0.043). Elrick et al. also noted an association between greater number of allergies and a worse ASES and SANE scores, but the results were not statistically significant (Elrick et al. 2021). Similarly, in a series of 338 shoulders, Forlizzi et al. demonstrated that patients with allergies were more likely to have lower postoperative ASES scores (OR: 0.83 \95% CI 0.71-0.97], p=0.02) (Forlizzi et al. 2022). Menendez et al. likewise observed that an increased number of allergies was associated with a higher likelihood of experiencing severe postoperative pain (OR: 1.28 per 1-unit increase in allergy count) (Menendez et al. 2018).

In a novel study of 239 shoulders evaluating clinical improvement against cost, Menendez et al. explored the impact of allergies on the overall value of TSA. This value was calculated by dividing the 2-year postoperative ASES score by hospitalization costs (Menendez et al. 2021). Their results indicated a negative association between the number of allergies and postoperative value. Specifically, for each 1-unit increase in allergy count, there was a corresponding 4-point decrease in TSA value (p=0.029). Their findings suggested that patients with more self-reported allergies experience longer hospital stays and higher pain after surgery.

In contrast, two studies have shown no association between self-reported allergies and inferior outcomes following TSA. Kennon et al. analyzed 52 SA patients with allergies to metals (e.g. nickel, cobalt, chromium) over a mean follow up of 5 years (Kennon et al. 2020). While there was no comparison to a control group, all patients showed significant postoperative improvements in range of motion and pain scores after surgery. Rosenthal et al. evaluated 98 SA patients (no allergies, n=51; single allergy, n=21; multiple allergies, n=26) from a single surgeon between 2009 and 2014, with an average follow up of 1.5 ± 0.79 years (Rosenthal et al. 2016). No difference was noted between cohorts concerning SST scores, VAS scores, or forward flexion both preoperatively and postoperatively. Additionally, there was no difference in postoperative patient satisfaction.

2.2. HIP

Studies investigating THA outcomes have suggested worse outcomes in those with allergies, although conflicting evidence exists. Fisher et al. found significantly higher Hip Dysfunction and Osteoarthritis Outcome Score for Joint Replacement (HOOS JR) score in those without allergies compared to those with allergies at both 12 weeks (78.26 ± 14.71, n=1000 vs 76.54 ± 15.31, n=1398; p=.005) and 1 year (84.60 ± 15.93, n=912 vs 81.32 ± 17.54, n=1263; p<.001) (Fisher et al. 2022). There was also a significant increase in HOOS JR score improvements from preoperative scores in those without allergies at both 12 weeks (28.90 ± 9.26 vs 27.42 ± 9.61; p<.001) and 1 year (35.24 ± 9.73 vs 32.20 ± 10.58; p<.001). Nam et. examined 906 patients with primary THA and identified a significantly lower and decreased improvement in SF-12 Mental Component Score in those with metal allergies (p<0.001) compared to the non-metal cohort (p=0.001) (Nam et al. 2016).

On the other hand, Otero et. all conducted a retrospective analysis on individuals undergoing both THA and TKA (Otero et al. 2016). They found a significantly lower SF-36 physical component score after surgery in those with one or more allergies compared to those without allergies (49.46 vs 51.30; p=.01). However, there was no difference in the change in the physical compartment score (15.72 vs 16.73; p=.2818), change in mental component score (6.79 vs 5.09; p=.1065), or post Western Ontario and McMaster Universities Osteoarthritis Index (94.44 vs 95.12; p=.4479) between individuals with allergies and those without.

2.3. KNEE

Current literature investigating the impact of allergies on outcomes in TKA is also mixed. Two studies have demonstrated a possible link between metal allergies and inferior postoperative outcomes after TKA. A retrospective study by Nam et al. examined 589 patients that received TKA at a single institution, 37 of which had a self-reported metal allergy (Nam et al. 2016). After a 2 year follow up, there was no difference in UCLA Activity Score, Short Form 12 Mental Component Score (SF-12 MCS), or SF-12 Physical Component Score (PCS). However, patients with metal allergies demonstrated a significantly lower postoperative Knee Society Score (KSS) Function subdomain (49.8 ± 17.5 vs 66.8 ± 23, p<0.001). Additionally, patients with allergies had lower KSS Symptoms (p=0.02), satisfaction (p=0.01), and patient expectation (0.004) subdomains, indicating decreased satisfaction after TKA. Desai et al. conducted a case series with 233 patients having a minimum duration of 3 months post TKA (Desai et al. 2019). Utilizing a skin patch test (SPT), they identified 37 patients with a metal allergy. Analysis revealed that patients with a positive SPT (SPT+) were more likely to endorse dissatisfaction (13.51% vs 1.02%, p=0.01) and loss of function (13.51% vs 3.57%, p=0.03) than those with a negative SPT (SPT-)

Conversely, other studies have had equivocal findings. Bravo et al. examined 161 TKAs performed at a single institution, focusing on metal allergies. Of these, 56/161 (35%) were SPT+ and 65% were SPT- (Bravo et al. 2016). At a me-

Table 1. Shoulder

Author (year)	Study design	Allergen	How allergies were determined	Sample size	Follow up length	Outcomes
Elrick et al. (2021)	Retrospective	Drug and Latex allergies	Patient reported	411	1.9 ± 1.2 years	Increased allergies were associated with statistically significant worsening of QuickDash score. Other PROs demonstrated a similar pattern, but was not statistically significant.
Menendez et al. (2018)	Retrospective	All types	Patient reported	415	Minimum of 2 years	Patients with allergies were more likely to experience severe postoperative pain.
Menendez et al. (2021)	Retrospective	All types	Patient reported	239	Minimum of 2 years	Increased allergies were associated with decreased postoperative value, defined as ASES score divided by hospitalization costs. Specifically, each 1-unit increase in allergy count, demonstrated a 4-point decrease in postoperative value.
Kennon et al. (2020)	Retrospective	Metal allergies	Patient reported	43	5.4 years average	Patients with allergies demonstrated significant postoperative improvements in range of motion and pain scores.
Rosenthal et al. (2016)	Retrospective	Drug allergies	Patient reported	98	1.5 ± 0.79 years	The presence of drug allergies was not associated with worse SST score, VAS pain score, or forward flexion.
Forlizzi et al. (2022)	Retrospective	All types	Patient reported	338	2.3 years average	The presence of patient reported allergies was associated with worse postoperative outcomes as measured by ASES scores.

dian follow up of 5.3 years, there was no statistically significant difference in pain between the two groups. Specifically, 86% of SPT+ patients reported none to mild pain, compared to 91% of SPT- patients reporting none to mild pain (p=0.37). In a prospective study by Zeng et al., VAS pain scores and SPT for metal allergies were documented 3 days prior to patients undergoing TKA. The study had a cohort of 25 patients, 11 being SPT+ (Zeng et al. 2014) Pain scores were recorded again 3 months after the surgery, showing no significant difference in preoperative VAS scores (5.00 ± 0.45 vs 4.71 ± 2.02; p>0.05), postoperative VAS scores (0.90 ± 0.54 vs 0.86 ± 0.66; p>0.05) or mean difference (4.09 ± 0.70 vs 3.86 ± 1.83; p>0.05) between the two cohorts. Fisher et al. identified patients who received TKA over a 10-year period (2011-2021) at a single academic institution (Fisher et al. 2022). Their investigation showed that patients with drug allergies compared to patients without allergies demonstrated no significant difference in Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS JR) scores at 12 weeks (62.90 ± 14.19, n=954 vs 63.35 ± 12.68, n=618; p=0.520) or 1 year postoperatively (70.31 ± 16.06, n=863 vs 69.63 ± 17.76, n=56; p=0.467).

3. ADVERSE OUTCOMES: COMPLICATIONS AND REVISIONS

3.1. SHOULDER

In terms of objective sequelae following TSA, such as revision surgery, infection, and other medical complications, prior studies seem to indicate that patient reported allergies can be implicated in suboptimal postoperative courses. Patel et al., using the PearlDiver database, identified 154,478 patients who underwent TSA, categorized into groups based on self-reported allergies (drug, food, antibiotic, and miscellaneous) and no allergies (Patel, Stevens, Shahzad, et al. 2023). Patients with allergies had a significantly increased risk of revision surgery at all postoperative intervals up to 10 years (p<0.001) and a higher risk of complications such as stiffness, wound and implant issues, and infections at 30 and 90 days postoperatively. Furthermore, patients with allergies were also found to have significantly increased risk of developing sepsis at 30 and 90 days postoperatively (p<0.001) (Patel, Stevens, Shahzad, et al. 2023).

Table 3. Hip

Author (year)	Study design	Allergen	How allergies were determined	Sample size	Follow up length	Outcomes
Morwood & Garrigues (2015)	Review	Metal allergies	Patient Reported, Outcomes of studies	n/a	n/a	Orthos and Derms maintain that titanium is best for hypoallergenic rn. Potential growth into industrial coatings pending material science 1° history and patch at surgeon discretion, revision history and recommended patch
Kennon et al. (2020)	Retrospective	Metal allergies	Patient reported	43	5.4 years average	Patients with self-reported allergies demonstrated significant postoperative improvements in range of motion and pain scores.
Menendez et al. (2021)	Retrospective	All types	Patient reported	239	Minimum of 2 years	Increased allergies were associated with decreased postoperative value, defined as ASES score divided by hospitalization costs. Specifically, each 1-unit increase in allergy count, demonstrated a 4-point decrease in postoperative value.
Menendez et al. (2018)	Retrospective	All types	Patient reported	415	Minimum of 2 years	Patients with allergies were more likely to experience severe postoperative pain.
McLaughlin et al. (2018)	Prospective	None	Patient reported	150	Short term hospital stay	Allergy only mentioned as contraindication to multimodal pain control. MMPC shown to be as effective as opioids
Menendez et al. (2019)	Retrospective	All types	Patient reported	415	Minimum of 2 years	Patients with allergies were more likely to experience prolonged hospital stay.
Rosenthal et al. (2016)	Retrospective	Drug allergies	Patient reported	98	1.5 ± 0.79 years	The presence of drug allergies was not associated with worse SST score, VAS pain score, or forward flexion.
Elrick et al. (2021)	Retrospective	Drug and Latex allergies	Patient reported	411	1.9 ± 1.2 years	The most important finding of this investigation is that the number of Patient Reported Allergies was associated with higher postoperative disability and lower

						patient satisfaction. The number of PRAs was the most influential predictor of patient satisfaction, suggesting that PRA is a significant prognostic factor that should be considered in future shoulder arthroplasty outcome predictive modeling
Burrus et al. (2023)	Review Article	Metal Allergy	n/a	n/a	n/a	
Bragg et al. (2023)	Break Even Analysis	B-lactam (penicillin and cephalosporins)	n/a	n/a	n/a	Preoperative allergy testing is considered economically justified if it prevents at least 1 infection out of 223 shoulder arthroplasties (ARR = 0.45%)
Karimi et al. (2023)	Systematic Review	Patient reported Allergies (all)	n/a	n/a	n/a	Allergies are associated with increased risk of PJI, several studies found an association with increased pain, length of stay, and poorer PROs. May be a screener
Somerson et al. (2018)	Retrospective	Failure of TSA	N/A	4063	n/a	Allergies only mentioned in the aTSA failure for 3 cases (0.2%) of 1673 a TSA

Note: Some studies are listed across multiple tables. However, only information pertinent to the relevant joint has been included in each table.

Bahoravitch et al. conducted a retrospective analysis of over 85,000 patients using national databases, categorizing them based on reported antibiotic allergies and a control cohort without reported allergies (Bahoravitch et al. 2022). Patients with reported antibiotic allergies, particularly those with a specified penicillin allergy, faced a significantly increased risk of requiring revision surgery due to prosthetic joint infection at multiple intervals - 30 days, 90 days, 1 year, and 2 years (Bahoravitch et al. 2022). In a retrospective study, Wu et al. analyzed prosthetic joint infection occurrence following TSA, TKA, and THA in over 78,000 patients with self-reported penicillin allergies in[22] While accounting for confounding variables such as BMI, anxiety, and depression, patients with self-reported penicillin allergies displayed increased odds of prosthetic joint infection 1 year after surgery when compared to patients without reported penicillin allergies ($p<0.01$) (Wu et al. 2020).

Contrary to this trend, Kennon et al. reported on adverse outcomes in 52 TSAs with patient self-reported metal allergies (Kennon et al. 2020). They observed a reoperation rate of 3.8% (2/52) and an overall complication rate of 9.6% (5/52) (Kennon et al. 2020). Both reoperations were salvage procedures with poor glenoid stock and progression to hemiarthroplasties due to glenoid failure (Kennon et al. 2020). Otherwise, most patients (n=43) showed significant improvement postoperatively in forward elevation, external rotation, and internal rotation (Kennon et al. 2020).

Results generally seem to indicate that there is a negative impact of patient-reported allergies on pain and satisfaction following TSA. Menendez et al. found patient self-reported allergies as the primary contributor to postoperative pain (Menendez et al. 2018) and identified a 20% increased risk of extended hospital stay following total TSA for each reported allergy in another study (Menendez et al. 2019). Elrick et al. examined outcomes on 411 shoulders and compared clinical outcomes following TSA based on the number of patient reported allergies (Elrick et al. 2021). Patients were separated into groups of zero allergies, one allergy, or at least two allergies (Elrick et al. 2021). While results were not statistically significant, patients with more allergies did report lower ASES and SANE scores. However, an increased number of reported allergies noted a significant increase in postoperative QuickDASH scores, making allergies the fourth most influential predictor ($p=0.043$) (Elrick et al. 2021). Indeed, Elrick et al. also detail that their allergy group was the sole significant independent predictor ($p=0.016$) of postoperative satisfaction when adjusting for other patient variables, such as age, sex,

Table 2. Knee

Author (year)	Study design	Allergen	How allergies were determined	Sample size	Follow up length	Outcomes
Bravo et al. (2016)	Retrospective	Metal allergies	Skin patch testing	161	5.3 years	The presence of SPT+ was not associated with increased postoperative pain.
Nam et al. (2016)	Retrospective	Metal allergies	Patient reported	589	2 years	The presence of patient reported allergies was not associated with differences in UCLA Activity Score, Short Form 12 Mental Component or Physical Component Scores. However, patients with allergies had significantly lower Knee Society Scores for the Function, Symptoms, Satisfaction, and Expectation subdomains.
Desai et al. (2019)	Case series	Metal allergies	Skin patch testing	233	3 months minimum	Patients with allergies were more likely to endorse dissatisfaction and loss of function after TKA than those with a negative skin test.
Zeng et al. (2014)	Case series	Metal allergies	Skin patch testing	25	3 months	The presence of allergies was not associated with a difference in VAS pain scores.
Fisher et al. (2022)	Retrospective	Drug allergies	Patient reported	14,811	12 weeks, 1 year	The presence of drug allergies was not associated with inferior PROs at 12 weeks or 1 years, as measured by KOOS JR score.

arthroplasty type, and mental health scores (Elrick et al. 2021).

3.2. HIP

Multiple studies have found a relation between patient-reported drug allergies and adverse outcomes following THA (Fisher et al. 2022; Otero et al. 2016). A study by Fisher et al. conducted a retrospective review of 31,109 patients who underwent THA or TKA at a single-institution over a 10-year period, revealing a 111% higher prosthetic joint infection (PJI) rate in patients with self-reported allergies, without affecting functional scores at 3 month and 12 month follow-ups ($p<0.0001$) (Fisher et al. 2022). Graves et al. evaluated 459 patients undergoing THA or TKA, finding that patients with 4 or more self-reported allergies had lower scores on the SF-36 survey than patients with 3 or less allergies ($p=0.0002$) (Graves et al. 2014).

Furthermore, careful consideration of patient reported allergies in THA is emerging as a pivotal factor influencing prophylactic antibiotic regimens (Stevoska et al. 2022). Adequate antibiotic coverage is crucial to avoid serious side effects, such as PJI. While PJI is well-documented, current literature is limited when considering patients with allergies undergoing THA (Thyssen et al. 2009). In a study of 16 patients undergoing THA revision, Thomas et al. proposes a link between failed metal-on-metal THA and allergic hyper-reactivity (P. Thomas et al. 2009). Using patch testing and lymphocyte transformation testing, 13 of the 16 patients (81%) were found to have systemic metal hypersensitivity despite a low incidence of metal implant allergy. Similarly, Haddad et al. considered the relation of allergic contact dermatitis to N-N-dimethylparatoluidine (DMT), an accelerator used in bone cement, to aseptic loosening of total hip replacements (Haddad et al. 1996). Of the 70 patients considered, 7 were SPT+ and all experienced rapid onset of aseptic loosening. Their results suggest the use of patch testing in high-risk cases of THA, specifically in patients who have prior exposure to DMT by dental or occupational exposure.

In a retrospective review of 3411 arthroplasties in 2576 patients undergoing preoperative antibiotic allergy testing, Wyles et al. proposed that there was an increased rate of postoperative PJI secondary to the use of second-line antibiotics, such as vancomycin or clindamycin, emphasizing the need for preoperative antibiotic allergy testing (Wu et al. 2020; Wyles et al. 2019). Wu et al. used a database of 122 million patients from 2010 to 2017 to explore the incidence of PJI within one year of THA, TKA, and TSA (Wu et al. 2020). However, there was no relation found between use of second-line antibiotics and rates of PJI among patients undergoing THA (Wu et al. 2020). Both Wyles et al. and Wu et al. suggest preoperative allergy testing in patients with self-reported antibiotic allergies, given the low rate of true penicillin allergy positivity (Wu et al. 2020; Wyles et al. 2019). In contrast, Stevoska et al. found that there was no difference in PJI rates among patients using second-line antibiotics when compared to use of first-line antibiotics

when analyzing 3419 THAs and 2666 TKAs (Stevoska et al. 2022).

3.3. KNEE

Like THA, patient-reported allergies have been found to impact the postoperative course of TKA. Fisher et al. considered patient-reported drug allergies in THA and TKA patients (Fisher et al. 2022). When analyzing patients who underwent revision surgery, a significantly higher rate of patient-reported allergies was observed ($p<0.0005$). Thomas et al. followed 15 TKA patients with proven gentamicin hypersensitivities, noting pain, limited mobility, swelling, and/or effusions postoperatively (B. Thomas et al. 2020). Of these, 9 elected for TKA revision with cementless implants or gentamicin-free cement, reporting significantly improved Knee Injury and Osteoarthritis Outcome Scores ($p=0.028$) as compared to the six patients not receiving TKA revision ($p=0.14$) (B. Thomas et al. 2020). Wu et al. considered patients stratified by having a self-reported penicillin allergy, and those without a patient-reported penicillin allergy (Wu et al. 2020). After using multiple logistic regression and controlling for confounding variables such as alcohol use, smoking, and comorbid conditions, patient-reported penicillin allergies were associated with increased likelihood of PJI after TKA ($p<0.01$).

Metal hypersensitivity in TKA has been suggested as an alternative explanation for increased postoperative complications in patients with self-reported allergies (Edwards and Gardiner 2007; Kaplan et al. 2002). Polymethylmethacrylate is a component of bone cement that is often used in TKA. Edwards and Gardiner reported a case where a patient developed a systemic reaction and intractable pain following TKA, with postoperative analysis revealing hypersensitivity to benzoyl peroxide, a bone cement component (Edwards and Gardiner 2007). Another case report by Kaplan et al. demonstrates preoperative identification of an allergy to methyl methacrylate bone cement (Kaplan et al. 2002). Lack of preoperative identification may have led to postoperative complications, as seen in the case report by Edwards and Gardiner. Skin patch testing has been proposed as a preoperative method to identify metal hypersensitivity before undergoing operation. Bravo et al. conducted a study involving 127 patients who underwent 161 TKA operations over 12 years, suggesting that positive skin patch testing to metal did not correlate with higher rates of postoperative complications, revision surgery, or reoperation - challenging the need for routine preoperative testing for metal hypersensitivity (Bravo et al. 2016).

4. FUTURE DIRECTIONS: PREOPERATIVE TESTING AND MACHINE LEARNING

In recent years, there has been rapid expansion of artificial intelligence and the subset of machine learning (ML). ML is a field wherein computers utilize algorithms to identify relationships between variables and outcomes (Sidey-Gibbons and Sidey-Gibbons 2019; Patel, Stevens, Mallory, et al. 2023). This may facilitate pattern recognition in patient management and expectations in the postoperative course as it pertains to patient reported allergies and especially metal hypersensitivity as we progress in our understanding of the complications and outcomes.

4.1. SHOULDER

The effects of allergies on shoulder outcomes following TSA continues to be mixed, as some studies cite that increased numbers of patient reported allergies is associated with increased postoperative pain, or longer hospital stay (Elrick et al. 2021; Menendez et al. 2018, 2021, 2019; Burrus et al. 2023). At the same time, other studies report that the mere presence of drug allergies is not related to poorer PROs or that patients still demonstrate significant postoperative improvement following TSA (Kennon et al. 2020; Rosenthal et al. 2016).

Looking specifically at metal hypersensitivity, a recent study by Morwood and Garrigues posits that surgeons should base implant choice off of patient-reported history for specific metal allergies and that they may utilize patch hypersensitivity testing at their discretion (Morwood and Garrigues 2015). They further advise that patch hypersensitivity testing should be used for revision implant selection due to reported cases linking metal allergy to implant failure. Titanium is suggested as the top hypoallergenic option. While the role in preoperative screening for patients with self-reported metal hypersensitivity remains controversial for primary TSA, ML may be able to elucidate its prognostic value in predicting implant failure or hospital outcomes. Arvind et al. has already shown ML to have efficacy in predicting risk factors for non-home hospital discharges following TSA, this may serve as a starting point for "working forwards" and providing prognostic value (Arvind et al. 2021).

4.2. HIP

Like the shoulder, evidence on the impact of allergies in THA is controversial. While one study states that metal release from implants may trigger hypersensitivity reactions impacting aseptic loosening in THA (Christiansen et al. 2019), another reports that an elevated number of patient-reported allergies appears to be associated with an increased risk of prosthetic joint infection (Fisher et al. 2022). While the relationship between allergies and THA may indeed require further investigation, there may be a role for ML to aid in that research of prognostication based on allergies. In a recent study by Abraham et al. ML has shown efficacy in using both qualitative and quantitative inputs to predict 30-day mortality in revision THA and TKA (Abraham et al. 2022). Their findings indicated that hematocrit levels below 36% were associated with increased risk of mortality, that the risk increased as the hematocrit decreased below this level, and that ML was accurately able to predict patients at risk. With this demonstrated efficacy, future investigation may be able to extrapolate this algorithm to both characterize and quantify the risk for mortality, or morbidity for THA based on allergy type, severity, and quantity.

4.3. KNEE

Currently, literature suggests that patients who report allergies of any type have less favorable outcomes after TKA (Nam et al. 2016; Otero et al. 2016; Wu et al. 2020; Stathopoulos et al. 2017; Norvell et al. 2023). Yet, there are not any clear guidelines or initiatives that address these differences. A few studies have proposed a systematic approach to evaluating for metal hypersensitivity testing. One study proposed an evaluation based on medical history, patch testing, and laboratory assays which included lymphocytic transformation testing, ELISA and confocal microscopy (Innocenti et al. 2014). However, a review examining the approach to patients with a metal hypersensitivity suggests that there is not enough evidence to warrant detailed hypersensitivity testing for metals and that there is no predictive value of patch testing patients before routine TKAs. It also suggests that patients who have a medical history of an allergic reaction after contact with metal may be offered an alternative alloy, a recommendation made from anecdotal evidence (Lachiewicz, Watters, and Jacobs 2016). Furthermore, another study demonstrated that there was not a difference in outcomes between groups who received a standard metal implant compared to those who received a nickel-free implant among patients who self-reported metal allergies (Schmidt et al. 2019). While the predictive utility of allergy testing for metal hypersensitivity remains unclear, various studies have shown that patients who self-reported metal allergies and received an alternative implant achieved good to excellent clinical outcomes (Bulaïd et al. 2022; Walker et al. 2019). The existing literature lacks a definitive link between self-reported metal hypersensitivity and adverse effects following TKA. Nevertheless, given the potential for adverse effects in metal-hypersensitive patients and evidence supporting alternative implants, routine screening via medical history, patch testing, and laboratory values is recommended to mitigate worse outcomes among those with self-reported metal allergies.

With respect to patients who report penicillin allergies, literature demonstrates that preoperative allergy testing for antibiotics has a positive impact. In a recent study, 97% of 2493 patients cleared for cephalosporins had a significantly higher infection-free survival rate with cefazolin compared to non-cefazolin antibiotics (Wyles et al. 2019). Furthermore, a study found that a simple screening protocol safely cleared two-thirds of patients who self-reported a penicillin allergy to receive a cephalosporin preoperatively without the need for formal allergy testing (Goh, Shohat, and Austin 2021). Current literature greatly suggests that patients who are given a second line antibiotic rather than a cephalosporin are at an increased risk of infection. To mitigate infection risk in patients with self-reported penicillin allergy, routine allergy testing or pre-approved screening protocols for antibiotic hypersensitivity are recommended.

5. CONCLUSION

This comprehensive review examines the intricate relationship between allergies and outcomes following shoulder, hip, and knee arthroplasty. As joint arthroplasty procedures become increasingly more common, understanding the potential impact of allergies on postoperative outcomes becomes more crucial than ever. The existing literature on this topic presents conflicting findings, with some studies indicating poorer outcomes for patients with multiple allergies while others have insignificant evidence. The exploration of adverse outcomes, including complications and revisions, suggests potential associations between allergies and increased risks of prosthetic joint infections, highlighting the importance of careful consideration in patient management. Due to the mixed effects observed and an unclear association of causation, further investigation is likely necessary to determine the true impact of allergies on patients following joint arthroplasty.

Looking ahead, preoperative allergy testing and machine learning in predicting outcomes is emerging. As the field advances, the integration of artificial intelligence may provide valuable insights into patient management and postoperative expectations.

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