

Do Self-Reported Drug Allergies Influence Clinically Significant Outcome Improvement Following Osteochondral Allograft Transplantation? A Nested Cohort Study

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Abstract

Objective. To compare clinical outcomes for patients who underwent osteochondral allograft transplantation (OCA) based on the presence or absence of one or more self-reported drug allergies. **Design.** Prospective data were collected from 245 consecutive patients after OCA of the knee from one large academic institution. Patient-reported allergies were obtained via chart review. Patient-reported outcome measures, including activities of daily living of the Knee Outcome Survey (KOS-ADL), Marx Activity Scale, International Knee Documentation Committee (IKDC), and visual analogue scale (VAS) pain were all collected. The minimal clinically important difference (MCID) for each outcome was quantified using a distribution-based method. Independent *t* tests were used to compare patient-reported outcome measures between those with and without self-reported allergies, while chi-square analysis of association was used to compare rates of MCID achievement. **Results.** Of 245 patients included, 83 (33.9%) reported having at least one drug allergy at the time of OCA. There were no statistically significant differences with regard to patient demographics, including age, body mass index, gender, or sports participation between those with and without a reported allergy. Similarly, there were no significant differences found between baseline preoperative patient-reported outcomes. Overall, both cohorts demonstrated a significant improvement from baseline scores at 2 years postoperatively. There were no differences found between any patient-reported outcome at 2 years postoperatively. The presence of at least one self-reported drug allergy was not a significant risk factor for failing to achieve the MCID in any specific outcome measure. **Conclusions.** The presence of one or more drug allergy was not associated with worse patient-reported outcomes or lower rates of clinically significant outcome improvement after OCA.

Keywords

cartilage, allergies, osteochondral allograft, patient-reported allergies

Introduction

Cartilage restoration procedures of the knee have increased roughly 5% annually as they have been demonstrated to reduce pain, improve function, and delay or prevent the need for arthroplasty.^{1,2} Early literature has focused on procedural efficacy and survivorship of OCA. However, as clinicians increasingly perform these procedures and OCA becomes a well-accepted approach to chondral defects of the knee, it is important to establish prognostic, patient-specific information and identify which patients may be at risk for having poor postoperative outcomes.

A specific subset of patients that have been shown to have poor outcomes are patients who self-report one or more drug allergies.³ Patients who report one or more drug allergies have been shown to consistently experience poor outcomes

following total knee arthroplasty when compared with their counterparts,^{3–6} and this finding has also been found after total hip arthroplasty.^{4,6} Outside of the realm of total joint arthroplasty, patient-reported allergies have been reported to correlate with lower subjective improvements in disability and pain in spine patients⁷ and have been associated with

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increased postoperative opioid use following hand surgery.⁸ Although the mechanism remains poorly defined, these findings suggest a consistent association between self-reported allergies and poor outcomes after orthopaedic surgical procedures. However, whether these associations are present for patients undergoing knee preservation procedures such as OCA is not well understood.

The purpose of the current study was to compare clinical outcomes for patients who underwent osteochondral allograft transplantation (OCA) based on the presence or absence of one or more self-reported drug allergies. The authors hypothesized that patients with at least one self-reported allergy would have worse patient-reported outcomes following OCA compared with patients who did not report having an allergy.

Methods

Patient Selection

This study received institutional board approval to collect and analyze the outcomes of patients who underwent OCA. All patient information was obtained from a large prospective institutional knee preservation registry. Patient demographic data, including age, sex, and body mass index (BMI) were obtained. Preoperative, intraoperative, and postoperative data were collected for all patients. Postoperative complications, reoperations, and patient-reported outcomes at a minimum of 2 years were recorded for all patients.

Clinical and Functional Outcomes

All patients completed the Knee Outcome Score (KOS)—activities of daily living (ADL), Marx Activity Scale, International Knee Documentation Committee (IKDC) subjective knee form, and visual analogue scale (VAS) for pain and overall health state both preoperatively and a minimum of 2 years postoperatively. The minimal clinically important difference (MCID) was also calculated for these outcomes using the distribution-based method where the MCID threshold for each outcome was equal to one-half the standard deviation of the mean change in outcome scores between 2-year postoperative and preoperative time points.⁹ Following this calculation, the MCID thresholds for our specific patient population were determined to be a change of 8.4 points for the KOS-ADL, 3 points for the Marx Activity Scale, 10.12 points for the IKDC subjective knee form, 1.6 points for the VAS pain score, and 1.8 points for the VAS overall health score.

Statistical Analysis

Prior to analysis, data were explored for normality using the Shapiro-Wilks test. Subsequently, all data was analyzed

using parametric methods. Baseline demographic data were described using means with standard deviations and frequencies with percentages where appropriate. Independent *t* tests and chi-square analyses of association were performed to compare baseline demographics, patient-reported outcomes, and rates of clinically significant outcome improvement between the 2 cohorts. Multivariate logistic regression analyses controlling for age, BMI, and sex were performed to determine the influence of cumulative number of allergies on clinically significant outcome improvement. All statistical analyses were performed using Stata version 16.1 (StataCorp, College Station, TX, USA). Statistical significance was considered to be $P < 0.05$ for all analyses.

Results

Study Population Characteristics

A total of 245 patients were included in the final analysis, having at least 2 years follow-up with all questionnaires completed. The mean age and BMI were 41.4 ± 12.6 years and 26.3 ± 4.6 kg/m², respectively. Of these patients, a total of 164 (66.9%) were male and a total of 148 (60.4%) participated in sports activities. Patients on average demonstrated statistically significant improvements in the KOS-ADL (65.6 ± 16.4 vs. 82.5 ± 13.5 , $P < 0.001$), the Marx Activity Scale (3.9 ± 5.5 vs. 5.8 ± 5.4 , $P = 0.0008$), IKDC subjective knee form (47.9 ± 15.8 vs. 69.6 ± 19.3 , $P < 0.001$), VAS pain (6.6 ± 2.4 vs. 4.5 ± 2.4 , $P < 0.001$), and VAS for subjective health state (4.7 ± 1.7 vs. 7.1 ± 1.9 , $P < 0.001$).

Self-Reported Allergy Stratification

All 245 patients were stratified based on the presence or absence of self-reported allergies recorded at initial clinic visits. A total of 162 (66.1%) patients did not report a history of an allergy, while the remaining 83 (33.9%) patients reported a having a minimum of one allergy (**Table 1**). At baseline, no statistically significant differences were observed in demographic factors, including age, BMI, gender, or sports participation.

Clinical and Functional Outcome Analysis

At baseline, no statistically significant differences were observed in the preoperative KOS-ADL (65.7 ± 17.0 vs. 65.5 ± 16.6 , $P = 0.93$), preoperative Marx Activity Scale (6.8 ± 6.5 vs. 7.2 ± 6.2 , $P = 0.67$), preoperative IKDC subjective knee form (47.9 ± 15.4 vs. 47.3 ± 15.6 , $P = 0.81$), preoperative VAS pain (4.8 ± 2.3 vs. 4.5 ± 2.2 , $P = 0.42$), and VAS for subjective health state (4.6 ± 4.3 vs. 4.4 ± 2.0 , $P = 0.38$) between those reporting history

Table 1. Baseline Characteristics of Cohorts Stratified by Presence or Absence of Self-Reported Allergies.^a

Characteristic	No Allergies (n = 162)	Allergies (n = 83)	All (n = 245)	P
Age, years	40.9 ± 12.8	42.3 ± 12.4	41.4 ± 12.6	0.43
Body mass index, kg/m ²	26.5 ± 4.8	26.0 ± 4.3	26.3 ± 4.6	0.47
Male sex	112 (69.1%)	52 (62.7%)	164 (66.9%)	0.31
Sports participation	94 (58.0%)	54 (65.1%)	148 (60.4%)	0.34

^aIndependent t tests and chi-square analysis of associations performed for baseline comparisons based on parametric data distribution. Continuous data listed as means ± standard deviations, while categorical data listed as frequencies (percentages).

Table 2. Comparison of Postoperative Patient-Reported Outcome Measures Between Patient Cohorts with and without a History of Self-Reported Allergies.

Postoperative Outcome	No Allergies (n = 162)	Allergies (n = 83)	All (n = 245)	P
KOS-ADL	81.7 ± 14.0	84.5 ± 11.5	82.5 ± 13.5	0.25
Marx	6.6 ± 5.8	5.5 ± 5.2	5.8 ± 5.4	0.26
IKDC	69.6 ± 19.2	69.4 ± 19.8	69.6 ± 19.3	0.95
VAS pain	4.6 ± 2.3	4.3 ± 2.5	4.5 ± 2.4	0.42
VAS SHS	7.1 ± 1.9	7.1 ± 2.0	7.1 ± 1.9	0.87

KOS-ADL = Knee Outcome Score—activities of daily living; IKDC = International Knee Documentation Committee; VAS = visual analogue scale; SHS = self-reported health state.

Table 3. Comparison of Rates of Clinically Significant Outcome Improvement at 2 Years Following Osteochondral Allograft Transplantation Between Patient Cohorts with and without a History of Self-Reported Allergies.

MCID	No Allergies (n = 162), %	Allergies (n = 83), %	All (n = 245), %	P
KOS-ADL	65.6	79.5	69.8	0.11
Marx	18.6	12.2	16.3	0.36
IKDC	76.4	69.1	73.9	0.37
VAS pain	16.4	17.7	17.1	0.88
VAS SHS	73.1	70.7	72.7	0.91

MCID = minimal clinically important difference; KOS-ADL = Knee Outcome Score—activities of daily living; IKDC = International Knee Documentation Committee; VAS = visual analogue scale; SHS = self-reported health state.

of an allergy and those that did not. Minimum 2-year postoperative outcomes are depicted in **Table 2**. At this time point, no statistically significant differences were observed in clinical or functional outcomes based on the presence or absence of self-reported allergies. A total of 10 (12.1%) of patients with allergies underwent a concomitant procedure, while a total of 16 (9.9%) of patients without allergies underwent a concomitant procedure, which did not represent a statistically significant difference ($P = 0.60$).

Clinically Significant Outcome Improvement

The propensity for clinically significant outcome improvement as determined by the rate of achieving the MCID at a minimum of 2 years after OCA was quantified and compared. Stratification-based quantitative comparisons of the MCID are displayed in Table 3. Results from this analysis

indicated that the presence of self-reported drug allergies was not a significant risk factor for failing to achieve clinically significant outcome improvement in any of the outcome measures for this specific population.

Subsequently, the influence of the cumulative number of total self-reported allergies on clinically significant outcome improvement was explored while adjusting for age, BMI, and sex. These analyses revealed that there were no statistically significant associations between cumulative number of self-reported allergies and clinically significant outcome improvement for the IKDC subjective knee form (odds ratio [OR] 0.78, $P = 0.27$), Marx Activity Scale (OR 0.91, $P = 0.75$), VAS pain (OR 1.3, $P = 0.38$), and VAS for subjective health state (OR 1.2, $P = 0.71$). Furthermore, no statistically significant associations were observed between the MCID for the KOS-ADL and cumulative number of self-reported allergies, though this relationship trended toward significance (OR 2.0, $P = 0.056$).

Discussion

The main findings of the current study are as follows: (1) there were no significant differences in rates of clinically significant outcome improvement between patients with and without self-reported allergies and (2) increasing number of self-reported allergies did not correlate with outcome scores.

While OCA typically results in reliable improvements in knee pain and function, approximately 11% of patients are not satisfied with their outcomes.^{10,11} Identifying risk factors for poor results after OCA is important for refining patient selection and may have implications for reimbursements as health care continues to shift toward value-based models. A number of authors have observed that patients with multiple self-reported allergies tend to be more clinically challenging and may be less satisfied with the results of their surgery.⁶ Awareness of patients' allergies is crucial for safe perioperative care; however, many patient-reported allergies are in fact adverse drug reactions rather than true IgE-mediated histamine response. For example, approximately 10% of patients self-report a penicillin allergy, whereas only 1% show a true allergy on confirmatory testing.¹² Some authors have proposed that multiple self-reported allergies may suggest underlying psychiatric pathology or negative outlooks in a proportion of patients and risk for poor perceived outcomes.^{6,13}

However, the results of this study suggest that presence of a self-reported allergy is not associated with compromised outcomes following OCA. Both absolute scores on patient-reported outcome measures and rates of MCID achievement were comparable between those with and without self-reported allergies. The association of self-reported allergies with outcome measures has been variable in the orthopedic literature. Graves *et al.*⁶ evaluated 459 patients undergoing total hip arthroplasty or total knee arthroplasty and found that patients with 4 or more self-reported allergies had less improvement on Short Form-36 Physical Component Scores (SF-36 PCS) and Western Ontario and McMaster Universities Arthritis Index (WOMAC) Functional scores. In contrast, Coxe *et al.*⁸ studied a cohort of patients who underwent various ambulatory hand procedures and reported that presence of a self-reported allergy did not affect postoperative pain levels or satisfaction. Similarly, Nixon *et al.*¹⁴ found no differences in PROMIS (Patient Reported Outcome Measurement Information System) preoperative or postoperative physical function, pain, or depression based on self-reported allergies in patients undergoing foot and ankle surgery. A lack of association between patient-reported drug allergies and satisfaction was demonstrated following shoulder arthroplasty as well.¹⁵ It is unclear why significant differences in outcomes were seen in patients undergoing total hip and knee arthroplasty and not several other orthopedic procedures. In contrast to the current study, the sample of patients in the

report by Graves *et al.*⁶ was predominantly female and approximately 10 years older. These factors were not included in a multivariate analysis and may influence their results. In addition, while statistical differences in outcome scores between the groups were reported, the magnitude of the effect sizes did not exceed previously established MCID thresholds for SF-36 PCS or WOMAC scores and cloud the clinical implication of their results.^{16,17}

Results of the current study also indicate that cumulative number of patient-reported drug allergies was not associated with worse functional outcomes when controlling for age, gender, and BMI. In contrast, McLawhorn *et al.*⁵ studied a cohort of 274 patients undergoing total hip and total knee arthroplasty and reported that each additional patient-reported allergy was associated with an approximately 50% increased odds for poorer ratings on quality-of-life scales. Similar trends were seen regarding WOMAC pain, stiffness, and function subscales. However, these differences also did not exceed clinically significant score thresholds, and the authors cautioned that clinically significant effects on WOMAC scores would only be expected in patients with an exceedingly high number of self-reported allergies (approximately 6 to 27). Taken with these previous findings, the current study provides additional evidence that self-reported drug allergies may not be a poor prognostic indicator and should not bias patient selection or counseling regarding postoperative expectations following OCA.

This study has a number of limitations. The data reflected in this study were collected prospectively but were analyzed retrospectively. Patient-reported allergy information was obtained via chart review and may reflect an underrepresentation of the true number of patient-perceived allergies. The data obtained from the institutional registry feature functional outcome measures and do not capture adverse events. Finally, while the registry data are robust with both demographic information and patient-reported outcome measures, they do not capture many psychosocial factors which have been implicated in relation to self-reported allergies, including anxiety and depression.¹³

Conclusion

The presence of one or more drug allergy was not associated with worse patient-reported outcomes or lower rates of clinically significant outcome improvement after OCA.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

This study received institutional board approval to collect and analyze the outcomes of patients who underwent osteochondral allograft transplantation.

Informed Consent

Written informed consent was obtained from all subjects before the study.

Trial Registration

Not applicable.

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