Does Metal Allergy to Total Knee Arthroplasty Components Exist?

Mortazavi SMJ, Hosseini-Monfared P, Gavrankapetanovic I, Antoci V, Tarabichi S, Shang-Wen T, Smailys A, Socorro N, Eleftherios T, Razzaghof M

Response/Recommendation:

Metal hypersensitivity around total knee arthroplasty has been documented in various case reports and cohort studies. Most patients reporting metal allergy have well-functioning implants, and failure due to metal allergy is a very rare occurrence. Routine testing for metal allergy is not recommended, and a positive test does not correlate well with implant failure. Considering the available clinical evidence, while hypersensitivity-related complications after total joint arthroplasty likely exist, revision surgery for metal hypersensitivity is not recommended, and should be considered only as the last rule-out diagnosis.

Level of Evidence: Moderate

Rationale:

Implant-related metal hypersensitivity reactions have been reported in various case reports and cohort studies. Type IV or delayed type hypersensitivity is considered to be T-lymphocyte mediated which could lead to complications such as osteolysis and endoprosthetic loosening [1]. The skin patch test (SPT) is considered the gold standard test to evaluate type IV hypersensitivity [2].

The incidence of metal allergy based on positive SPTs was reported to be around 10 to 20% in the general population [3]. The exact extent of the prevalence of metal hypersensitivity to metallic orthopaedic implants is difficult to define given its complicated presentation and diagnosis. Studies evaluating metal hypersensitivity in patients who underwent total joint arthroplasties reported a wide range of prevalence among different populations ranging from 15 to 54% [4-12]. The pooled incidence of positive SPT to metals reported in the nine studies evaluating metal hypersensitivity in patients who underwent total joint arthroplasties indicated a prevalence of 25% **(Figure 1).** The nine studies had high heterogeneity (I^2=91%, p-value<0.01).

It should be considered that metal sensitization is reported in around 20% of the general population and not all the cases with positive SPTs should be attributed to the metal implants used in orthopaedic surgeries.

We performed an extensive literature review and systematic review. Among the studies evaluated, five reported the incidence of metal allergy among those who were suspected of having metal allergy based on previous cutaneous reactions to jewelry or bracelets [13-17]. The pooled incidence of metal allergy was higher in this high-risk group and was found to be around 39 % (**Figure 2**). A study by Nam et. al. demonstrated that the use of a specific question about the presence of metal allergy before the surgery could reveal many patients susceptible to metal allergies [18]. However, there is no evidence to support conducting further allergy testing in these patients.

Meta analysis of the studies that reported the prevalence of metal allergy among patients who were symptomatic after total joint arthroplasties, demonstrated a pooled prevalence of 28% (Figure 3). The six studies included in this analysis demonstrated high heterogeneity (I^2=94%, p-value<0.01) and reported prevalence was within the range of 13-45 % [9, 10, 15, 19-21]. Similarly, in a meta-analysis by Granchi et. al. it was found that the rate of metal hypersensitivity was higher among patients who had failed total joint replacements [22].

In studies evaluating the cause of revision cases of total joint arthroplasties, it was found that metal allergy accounted for around 0.6 – 1 % of the revisions [23, 24]. Also, a study was conducted by Bravo et. al. to evaluate whether the presence of metal allergy and positive SPT affect the failure rate of total joint arthroplasties or the postoperative complications of these surgeries [25]. They found that the revision rate and postoperative complications were not significantly different between the patients with positive or negative SPTs [25].

Although the incidence rate of metal hypersensitivity is higher among the patients who underwent total joint arthroplasties, these allergies are not necessarily associated with implant failure. Since there are reports of patients who tolerated the metal implants regardless of the presence of metal hypersensitivity, a general metal allergy screening is not recommended [26].

References

[1] Samelko L, Caicedo M, McAllister K, Jacobs J, Hallab NJ. Metal-induced delayed type hypersensitivity responses potentiate particle induced osteolysis in a sex and age dependent manner. PLoS One 2021;16:5:e0251885 https://doi.org/10.1371/journal.pone.0251885.
[2] Uyesugi BA, Sheehan MP. Patch testing pearls. Clin Rev Allergy Immunol 2019;56:1:110-8 https://doi.org/10.1007/s12016-018-8715-y.
[3] Thyssen JP, Linneberg A, Menné T, Johansen JD. The epidemiology of contact allergy in the general population–prevalence and main findings. Contact dermatitis 2007;57:5:287-99.
[4] Desai MM, Shah KA, Mohapatra A, Patel DC. Prevalence of metal hypersensitivity in total knee replacement. Journal of Orthopaedics 2019;16:6:468-72 https://doi.org/10.1016/j.jor.2019.05.005.
[5] Frigerio E, Pigatto PD, Guzzi G, Altomare G. Metal sensitivity in patients with orthopaedic implants: A prospective study. Contact Dermatitis 2011;64:5:273-9 https://doi.org/10.1111/j.1600-0536.2011.01886.x.
[6] Granchi D, Cenni E, Tigani D, Trisolino G, Baldini N, Giunti A. Sensitivity to implant materials in patients with total knee arthroplasties. Biomaterials 2008;29:10:1494-500 https://doi.org/10.1016/j.biomaterials.2007.11.038.
[7] Niki Y, Matsumoto H, Otani T, Yatabe T, Kondo M, Yoshimine F, Toyama Y. Screening for symptomatic metal sensitivity: A prospective study of 92 patients undergoing total knee arthroplasty. Biomaterials 2005;26:9:1019-26 https://doi.org/10.1016/j.biomaterials.2004.03.038.
[8] Shanmugham HA, Handa S, De D, Dhillon MS, Aggarwal S. An observational study to determine the sensitizing potential of orthopedic implants. Indian Journal of Dermatology, Venereology and Leprology 2021;87:6:826-30 https://doi.org/10.4103/ijdvl.IJDVL_789_18.
[9] Summer B, Lill D, Remmel K, Schraml A, Schopf C, Banke IJ et al. An interleukin-1 polymorphism additionally intensified by atopy as prognostic factor for aseptic non-mechanical complications in metal knee and hip arthroplasty. Frontiers in Immunology 2022;13 https://doi.org/10.3389/fimmu.2022.1050315.
[10] Thomas P, Ständer S, Stauner K, Schraml A, Banke IJ, Gollwitzer H et al. Arthroplasty patients and nickel sensitization: What do patch test and lymphocyte transformation test tell us. Seminars in Arthroplasty JSES 2013;24:4:261-4 https://doi.org/10.1053/j.sart.2014.01.012.
[11] Wu PY, Muo CH, Tsai CH. Increased risk of eczema after joint replacement: A population-based retrospective cohort study. Medicine 2019;98:45:e17914 https://doi.org/10.1097/MD.0000000000017914.
[12] Zeng Y, Feng W, Li J, Lu L, Ma C, Zeng J et al. A prospective study concerning the relationship between metal allergy and post-operative pain following total hip and knee arthroplasty. International Orthopaedics 2014;38:11:2231-6 https://doi.org/10.1007/s00264-014-2367-1.
[13] Brozovich A, Clyburn T, Park K, Harper KD, Sullivan T, Incavo S, Taraballi F. Evaluation of local tissue peri-implant reaction in total knee arthroplasty failure cases. Therapeutic Advances in Musculoskeletal Disease 2022;14 https://doi.org/10.1177/1759720X221092263.
[14] Münch HJ, Jacobsen SS, Olesen JT, Menné T, Soballe K, Johansen JD, Thyssen JP. The association between metal allergy, total knee arthroplasty, and revision study based on the danish knee arthroplasty register. Acta Orthopaedica 2015;86:3:378-83 https://doi.org/10.3109/17453674.2014.999614.
[15] Oppel E, Kapp F, Bohm AS, Pohl R, Thomas P, Summer B. Contact sensitization to iron: A potentially underestimated metal allergen and elicitor of complications in patients with metal implants. Contact Dermatitis 2022;86:6:531-8 https://doi.org/10.1111/cod.14074.
[16] Sato E, Maeyama A, Yamasaki Y, Yamamoto T, Imafuku S. Impact of preoperative metal patch testing on surgery using metal implants. Arthroplasty Today 2022;14:170-4 https://doi.org/10.1016/j.artd.2022.02.014.
[17] Thomas B, Kulichova D, Wolf R, Summer B, Mahler V, Thomas P. High frequency of contact allergy to implant and bone cement components, in particular gentamicin, in cemented arthroplasty with

complications: Usefulness of late patch test reading. Contact Dermatitis 2015;73:6:343-9 https://doi.org/10.1111/cod.12465.
[18] Nam D, Li K, Riegler V, Barrack RL. Patient-reported metal allergy: A risk factor for poor outcomes after total joint arthroplasty? Journal of Arthroplasty 2016;31:9:1910-5 https://doi.org/10.1016/j.arth.2016.02.016.
[19] Caicedo MS, Samelko L, Hallab NJ. Lymphocyte reactivity to nickel correlates with reported high-pain levels in patients with total joint arthroplasties: Implications for pain-related hypersensitivity responses. ASTM Special Technical Publication 2013;1560 STP:99-112 https://doi.org/10.1520/STP156020120025.
[20] Caicedo MS, Solver E, Coleman L, Jacobs JJ, Hallab NJ. Females with unexplained joint pain following total joint arthroplasty exhibit a higher rate and severity of hypersensitivity to implant metals compared with males: Implications of sex-based bioreactivity differences. Journal of Bone and Joint Surgery - American Volume 2017;99:8:621-8 https://doi.org/10.2106/JBJS.16.00720.
[21] Sasseville D, Alfalah K, Savin E. Patch test results and outcome in patients with complications from total knee arthroplasty: A consecutive case series. Journal of Knee Surgery 2021;34:3:233-41 https://doi.org/10.1055/s-0039-1694984.
[22] Granchi D, Cenni E, Giunti A, Baldini N. Metal hypersensitivity testing in patients undergoing joint replacement: A systematic review. J Bone Joint Surg Br 2012;94:8:1126-34 https://doi.org/10.1302/0301-620x.94b8.28135.
[23] Agarwal S, Kabariti R, Kakar R, Lopez DJ, Morgan-Jones R. Why are revision knee replacements failing? Knee 2019;26:3:774-8 https://doi.org/10.1016/j.knee.2019.04.012.
[24] Roof MA, Kreinces JB, Schwarzkopf R, Rozell JC, Aggarwal VK. Are there avoidable causes of early revision total knee arthroplasty? Knee Surg Relat Res 2022;34:1:29 https://doi.org/10.1186/s43019-022-00157-z.
[25] Bravo D, Wagner ER, Larson DR, Davis MP, Pagnano MW, Sierra RJ. No increased risk of knee arthroplasty failure in patients with positive skin patch testing for metal hypersensitivity: A matched cohort study. Journal of Arthroplasty 2016;31:8:1717-21 https://doi.org/10.1016/j.arth.2016.01.024.
[26] Thienpont E, Berger Y. No allergic reaction after tka in a chrome-cobalt-nickel-sensitive patient: Case report and review of the literature. Knee Surgery, Sports Traumatology, Arthroscopy 2013;21:3:636-40 https://doi.org/10.1007/s00167-012-2000-z.

Figures

Figure 1 Prevalence of Metal Allergy Among Patients Who Underwent Total Joint Arthroplasty

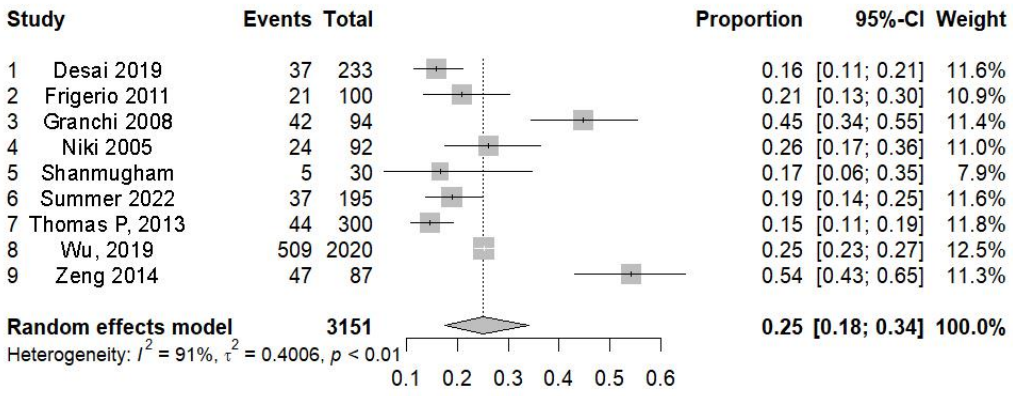

Figure 2 Prevalence of Metal Allergy Among Patients Who Were suspected to have metal allergy and Underwent Total Joint Arthroplasty

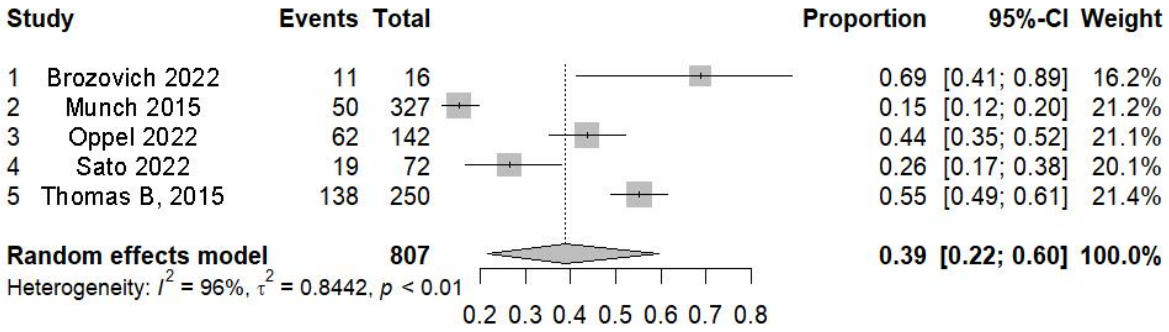

Figure 3 Prevalence of Metal Allergy Among Patients Who Were Symptomatic after Total Joint Arthroplasty