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Does Metal Allergy to Total Knee Arthroplasty Components Exist?

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Does Metal Allergy to Total Knee Arthroplasty Components Exist?

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. Other allergies, including acrylic bone cement and its polymerization additives, may also be considered, although not well understood. 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.

Expert Vote: Agree 75.2%, Disagree 16.2%, and Abstain 8.6%.

Rationale

Implant-related metal hypersensitivity reactions have been reported in various case reports and cohort studies. Type IV or delayed type hypersensitivity is 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 from 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

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arthroplasties indicated a prevalence of 25% [4–12]. The nine studies had high heterogeneity ($I^2 = 91\%$, $P < 0.01$).

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

There were five studies that 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%. A study by Nam et al. demonstrated that the use of a specific question about the presence of metal allergy before the surgery could find more patients susceptible to metal allergies [18]. However, there is no evidence to support further allergy studies in these patients.

A 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% [9,10,15,19–21]. The six studies included in this analysis demonstrated high heterogeneity ($I^2 = 94\%$, $P < 0.01$) and reported prevalence was within the range of 13 to 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 arthroplasties [22].

In studies evaluating the cause of revision cases of total joint arthroplasties, it was found that metal allergy accounted for around 0.6 to 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 affects 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 who had positive and 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].

CRediT authorship contribution statement

Seyed Mohammad Javad Mortazavi: Writing – review & editing, Writing – original draft, Supervision, Project administration. **Valentin Antoci:** Writing – review & editing, Writing – original draft, Validation, Supervision, Investigation. **Pooya Hosseini-Monfared:** Writing – original draft, Validation, Investigation, Formal analysis, Data curation. **Mohammadreza Razzaghof:** Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation. **Eleftherios Tsiridis:** Writing – review & editing, Validation, Supervision. **Samih Tarabichi:** Validation. **Shang-Wen Tsai:** Validation. **Alfredas Smailys:** Validation. **Nelson Enrique Medina Socorro:** Validation, Supervision. **Ismet Gavrankapetanovic:** Validation, Writing – review & editing.

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:e0251885. https://doi.org/10.1371/journal.pone.0251885.

[2] Uyesugi BA, Sheehan MP. Patch testing pearls. Clin Rev Allergy Immunol 2019;56:110–8. https://doi.org/10.1007/s12016-018-8715-y.

[3] Thyssen JP, Linneberg A, Menne T, Johansen JD. The epidemiology of contact allergy in the general population–prevalence and main findings. Contact Dermatitis 2007;57:287–99. https://doi.org/10.1111/j.1600-0536.2007.01220.x.

[4] Desai MM, Shah KA, Mohapatra A, Patel DC. Prevalence of metal hypersensitivity in total knee replacement. J Orthop 2019;16:468–72. 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;64:273–9. 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;29:1494–500. https://doi.org/10.1016/j.biomaterials.2007.11.038.

[7] Niki Y, Matsumoto H, Otani T, Yatabe T, Kondo M, Yoshimine F, et al. Screening for symptomatic metal sensitivity: a prospective study of 92 patients undergoing total knee arthroplasty. Biomaterials 2005;26:1019–26. 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 J Dermatol Venereol Leprol 2021;87:826–30. 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. Front Immunol 2022;13:1050315. 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. Semin Arthroplasty 2013;24:261–4. 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 (Baltimore) 2019;98: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. Int Orthop 2014;38:2231–6. https://doi.org/10.1007/s00264-014-2367-1.

[13] Brozovich A, Clyburn T, Park K, Harper KD, Sullivan T, Incavo S, et al. Evaluation of local tissue peri-implant reaction in total knee arthroplasty failure cases. Ther Adv Musculoskelet Dis 2022;14:1759720X221092263. https://doi.org/10.1177/1759720X221092263.

[14] Munch HJ, Jacobsen SS, Olesen JT, Menne T, Soballe K, Johansen JD, et al. The association between metal allergy, total knee arthroplasty, and revision: study based on the Danish knee arthroplasty register. Acta Orthop 2015;86:378–83. 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;86:531–8. 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. Arthroplast 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;73:343–9. 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? J Arthroplasty 2016;31:1910–5. 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 (Am Soc Test Mater) Spec Tech Publ 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. J Bone Joint Surg Am 2017;99:621–8. 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. J Knee Surg 2021;34:233–41. 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;94:1126–34. https://doi.org/10.1302/0301-620X.94B8.28135.

[23] Agarwal S, Kabariti R, Kakar R, Lopez D, Morgan-Jones R. Why are revision knee replacements failing? Knee 2019;26:774–8. 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;34:29. 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. J Arthroplasty 2016;31:1717–21. 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 Surg Sports Traumatol Arthrosc 2013;21:636–40. https://doi.org/10.1007/s00167-012-2000-z.