

Does Metal Hypersensitivity Have Relevance in Patients Undergoing TMJ Prosthetic Replacement?

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Purpose: Although concerns regarding implant-related metal hypersensitivity exist, no guidelines have been accepted for screening or treatment of patients with metal sensitivity before temporomandibular joint replacement (TMJR). The present study aimed to determine the trends in TMJR metal sensitivity screening and the effect of positive test results on patient treatment.

Materials and Methods: A questionnaire was distributed to members of the American Society of Temporomandibular Joint Surgeons and the European Society of Temporomandibular Joint Surgeons using a web-based data collection and analysis tool. The questions aimed to establish the screening methods used to establish a diagnosis of metal hypersensitivity and any changes in management when metal hypersensitivity had been documented.

Results: A total of 72 responses (32.43%) were collected through the survey, with respondents primarily practicing in the United States (47.22%). Of the participants, 75% believed that metal hypersensitivity occurs with TMJR and only 2.77% did not. Most agreed that patients should be questioned about any metal sensitivities before consideration for TMJR (91.66%), and 80.55% routinely asked their patients if they had a previous sensitivity to any metals. Nickel was the most commonly encountered metal allergen (64.28%). If a metal allergy were reported, 44.28% of surgeons would refer the patient to determine the specific metal allergen. The diagnosis for metal allergy was based primarily on patient signs and symptoms (52.85%) and an allergist or dermatologist consultation (44.28%). The lymphocyte transformation test was the test most used by respondents to confirm the diagnosis. Of the surgeons, 41.42% would choose to observe/monitor as their first choice for patients testing positive for metal hypersensitivity. In the case of a “mild” reaction to metal hypersensitivity testing, 54.28% would alter their implant choice to a nonreactive metal component. For “severe” reactions to preoperative metal hypersensitivity testing, 62.85% would alter their implant choice to a nonreactive metal component, and 22.85% would choose not to perform TMJR.

Conclusions: The results from the present study have demonstrated that respondent TMJ surgeons agree that metal hypersensitivity occurs with TMJR. However, their approaches to screening and managing metal hypersensitivity vary. Further research of this topic is required to eventually develop specific management pre- and postoperative guidelines for the treatment of patients with metal sensitivities.

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J Oral Maxillofac Surg ■:1-8, 2020

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Conflict of Interest Disclosures: Dr Mercuri is a clinical consultant and minority shareholder with TMJ Concepts, Ventura, CA. Dr Miloro is a consultant for AxoGen, Inc, Alachua, FL. None of the remaining authors have any relevant financial relationship(s) with a commercial interest.

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Received December 14 2019

Accepted January 14 2020

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0278-2391/20/30091-4

<https://doi.org/10.1016/j.joms.2020.01.020>

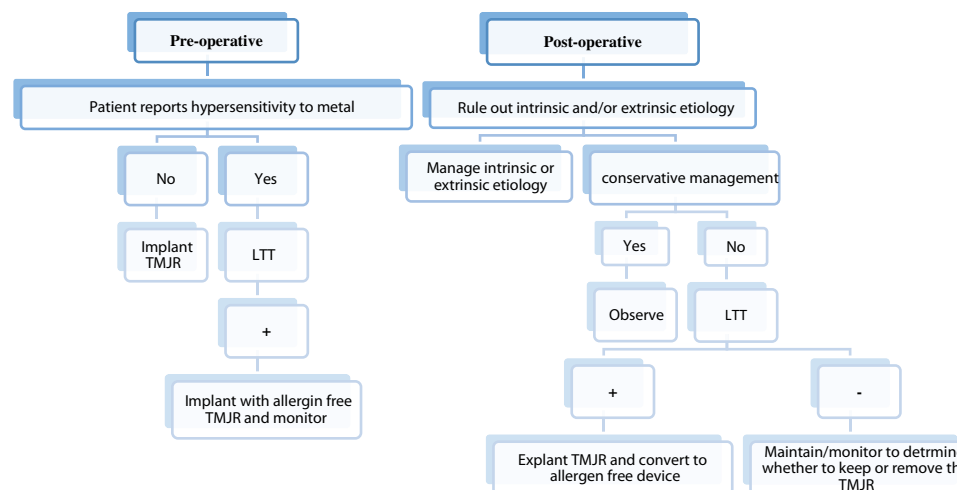


FIGURE 1. Pre- and postoperative temporomandibular joint replacement (TMJR) hypersensitivity testing algorithms. LTT, lymphocyte transformation test. Adapted, with permission, from Mercuri and Caicedo.⁸

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Temporomandibular joint (TMJ) replacement (TMJR) using alloplastic implants is a common procedure performed in increasing numbers worldwide.¹ It has been projected that by 2,030, a 58% increase in the demand for TMJR surgeries in the United States will have occurred.² The goals of treatment with alloplastic TMJR include improvement in function, reduction in pain and disability, and prevention of further morbidity.³ Many studies have demonstrated alloplastic TMJR is a safe and effective management option for patients with end-stage TMJ pathologic features, while providing substantial quality-of-life improvement.⁴⁻⁷

Despite documented successful outcomes, as with any surgical intervention, some patients will experience complications requiring further treatment. Although a variety of causes exist for these unplanned events, such as periprosthetic joint infections, heterotopic ossification, nerve injuries, and implantation errors, during the past decade, concerns regarding implant-related metal hypersensitivity have increased.⁸

Currently, the only Food and Drug Administration-approved TMJR implants are the Zimmer Biomet (Jacksonville, FL) and TMJ Concepts (Ventura, CA) total TMJR systems.⁹ The Zimmer Biomet system uses a stock prosthesis available in different standard sizes. The ramal component is composed of a cast cobalt-chromium-molybdenum alloy, which also contains limited amounts of nickel (<0.5 to 1%). Although the fossa component is made solely of ultra-high-molecular-weight polyethylene (UHMWPE).^{7,9,10} In contrast, the TMJ Concepts System is a custom-made, patient-fitted, computer-aided design/computer-aided manufacturing prosthesis, with the fossa composed of an UHMWPE articulating surface backed by commercially pure titanium mesh. The ramal

component is composed of forged computer numerical control milled titanium-aluminum-vanadium alloy (Ti-6Al-4V), which can potentially contain a maximum of 0.3% nickel. Both systems use Ti-6Al-4V screws for fixation.^{9,11}

In the general population, the prevalence of hypersensitivity to metals has been estimated to be 10 to 17%.¹² One study estimated that 17% of women and 3% of men were sensitive to nickel, with 1 to 3% sensitive to cobalt and chromium.¹³ Intolerance to metal implants can manifest as cutaneous skin reactions (eg, dermatitis, eczema), joint effusions, persistent pain, psychiatric or mental status changes, and/or loosening of the prosthesis.^{8,14,15} Therefore, the role of metal hypersensitivity relative to alloplastic implants has been a topic of great interest and research in the orthopedic literature. Some investigators have hypothesized that intolerance to metal alloys could be attributable to hypersensitivity reactions to the implanted metals,^{15,16} although others do not share that point of view.^{17,18}

In a report by Mercuri and Caicedo,⁸ a management algorithm for metal hypersensitivity in patients with TMJR was proposed (Fig 1). However, no guidelines have been generally accepted nor a consensus reached among oral and maxillofacial surgeons (OMSS) regarding how to screen patients for metal sensitivity before TMJR or which specific alterations in TMJR planning and overall management should be implemented if metal hypersensitivity has been identified either pre- or postoperatively.

The present study aimed to gain insight into the experience and opinions of TMJ surgeons relating to TMJR and metal hypersensitivity, examine the trends in TMJR screening, and determine how positive test results influence patient treatment.

Table 1. RESPONDENT DEMOGRAPHICS*

Variable	Respondents (n; %)
Gender	
Male	68 (94.44)
Female	4 (5.55)
Age group (yr)	
<30	1 (1.38)
30-39	12 (16.66)
40-49	16 (22.22)
50-59	17 (23.61)
≥60	26 (36.11)
Practice location	
North America	51 (70.83)
United States	34 (66.66; 47.22 overall)
Canada	5 (9.8; 6.94 overall)
Unspecified	12 (23.52; 16.66 overall)
Europe	12 (16.66)
United Kingdom	4 (33.33; 5.55 overall)
Italy	2 (16.66; 2.77 overall)
Spain	2 (16.66; 2.77 overall)
Germany	1 (8.33; 1.38 overall)
Sweden	1 (8.33; 1.38 overall)
Unspecified	2 (16.66; 2.77 overall)
Other	9 (12.5)
South America	3 (33.33; 4.16 overall)
Brazil	2 (22.22; 2.77 overall)
Unspecified	1 (11.11; 1.38 overall)
Australia	4 (44.44; 5.55 overall)
New Zealand	1 (11.11; 1.38 overall)
India	1 (11.11; 1.38 overall)

* Average years of experience, 23.58 (1,698 years total for 72 respondents).

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Materials and Methods

An anonymous, 18-question survey was developed to ascertain the experiences and opinions of TMJ surgeons relative to TMJR metal hypersensitivity. The questions were aimed to establish which screening methods were used to diagnose metal hypersensitivity and which changes in patient treatment the surgeons would make when they had documented a metal hypersensitivity.

The American Society of Temporomandibular Joint Surgeons (ASTMJS) and the European Society of Temporomandibular Joint Surgeons (ESTMJS) have online membership listings with preferred e-mail contact information. An e-mail with a short description of the study purpose and a request to complete an online questionnaire was sent to the members of the ASTMJS and ESTMJS. Surgeons who agreed to participate were directed via a web-link to a commercially available, web-based data collection and analysis tool (SurveyMonkey, San Mateo, CA) to complete the

questionnaire. As follow-up, 4 reminders were sent during the 8-week period in which the survey remained open. The responses were subsequently cataloged into an Excel spreadsheet (Microsoft, Redmond, WA), and the totals and means for each response were calculated. The data were analyzed using charts and graphs rendered by SurveyMonkey. The University of Illinois at Chicago institutional review board approved the present study (protocol no. 2019-1,313).

Results

A total of 222 invitations were sent, with 84 responses collected during the 8-week period in which the survey was open. Of the 84 participants, 12 were removed from the study because of incomplete responses, for a total of 72 participants (32.43%).

The demographic data are listed in Table 1. Of the 72 respondents, 94.44% were men and 5.55% were women. Most survey participants (81.94%) were older than 40 years of age, with 36.11% older than 60 years. Of the 72 respondents, 78.83% practiced in North America, with 66.66% practicing in the United States (47.22% of total participants). The average number of years of clinical experience of the respondents was 23.58 years.

Of the 72 participants, 54 (75%) reported that metal hypersensitivity can occur with TMJR and only 2 (2.77%) did not; 16 were unsure (22.22%). Most agreed that patients should be questioned about any metal sensitivities before consideration for TMJR (91.66%). Also, 80.55% routinely asked their patients if they were sensitive to any metals and 16.66% did not. Of the 70 positive responses (2 participants skipped this question), only 17 (24.28%) had patients who developed sensitivity to a TMJR metal, 40 (57.14%) reported that none of their patients experienced a hypersensitivity reaction to a metal in a TMJR, and 13 (18.57%) were unsure.

The respondents were asked to list the signs and symptoms recorded from patients presenting with a suspected metal hypersensitivity reaction. In descending order, these included swelling, cutaneous manifestations, pain, loss of mandibular function, osteolysis around the TMJR implant, and other (eg, chronic fatigue, heat, metallosis, facial nerve weakness; Fig 2). When asked with which metal they had seen a sensitivity reaction, 70 of the 72 participants (64.28%) replied that nickel was the most commonly reported metal and aluminum was the least commonly reported hypersensitive metal (2.86%; Fig 3).

When asked what their next step would be if a metal allergy was suspected from the patient's reported history, 44.28% of the surgeons would refer the patient to determine the specific metal allergen,

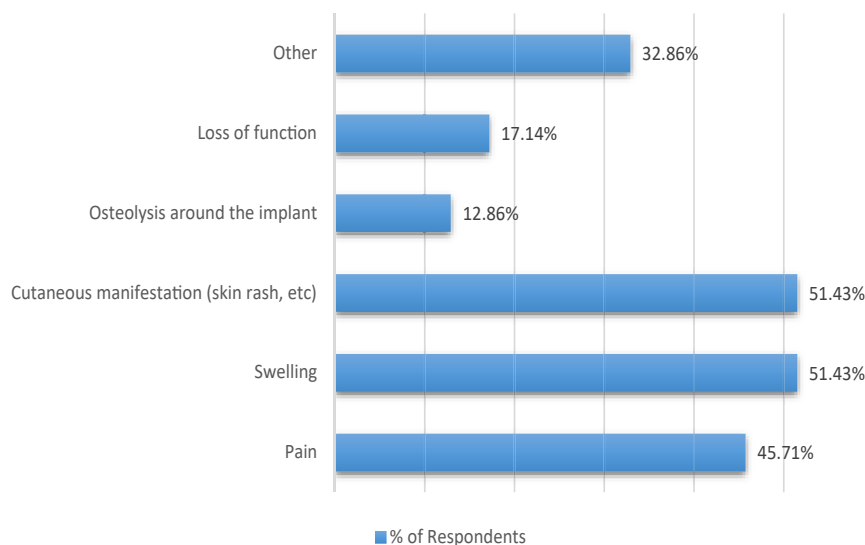


FIGURE 2. Presenting signs and symptoms for suspected metal hypersensitivity reaction (70 of 72 respondents).

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and only 2 of 70 (2.86%) would proceed with the surgery (Fig 4). The responses showed that the surgeons' diagnosis of metal hypersensitivity was mainly based on the patients' signs and symptoms (52.86%) and the findings from an allergist or a dermatologist consultation (44.28%). The lymphocyte transformation test (LTT) was used by 40% of the respondents, and the leukocyte migration inhibition test was the least used method for the diagnosis of a metal allergy (1.43%). Other tests used included serum metal ion concentrations (10%), the skin metal disc test (17.14%), the skin patch test (24.28%), and the memory lymphocyte immunostimulation assay (5.71%; Fig 5).¹⁹⁻²²

The first choice for the treatment of patients testing positive for metal hypersensitivity were recorded as follows: observe/monitor, 41.42%; nonsteroidal anti-inflammatory drugs or steroids, 22.85%; remove or replace implant, 24.28%; other (eg consultation with other clinicians, antibiotics), 15.71%; and referral to another OMS for a second opinion and or treatment, 7.14%.

In the case of a pre-TMJR report of a "mild" reaction to metal hypersensitivity testing, 54.28% would alter their implant choice to a nonreactive metal component. However, for 28.57%, this information would not alter their choice of TMJR prosthesis. For a reported "moderate" reaction to metal allergy testing,

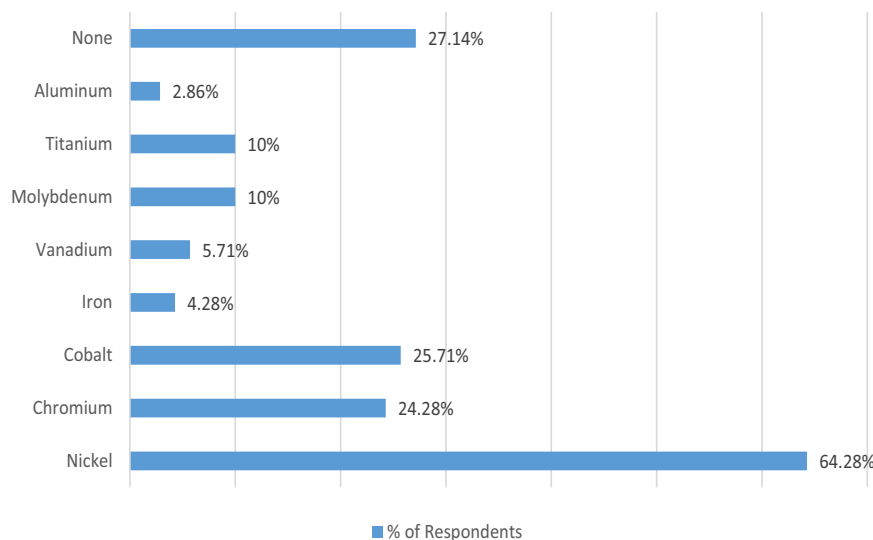


FIGURE 3. Metal allergens encountered by surgeons (70 of 72 respondents).

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If a metal allergy is suspected based on history in a patient who is about to undergo TMJR, what would be your next step?

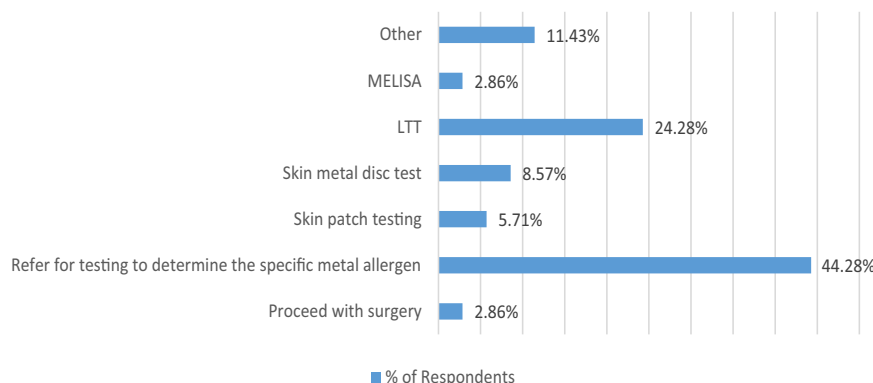


FIGURE 4. Workup of a patient with suspected metal hypersensitivity before temporomandibular joint replacement (TMJR; 70 of 72 respondents). LTT, lymphocyte transformation test; MELISA, memory lymphocyte immunostimulation assay.

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71.42% would alter their implant choice to a nonreactive metal component, and 8.57% would choose not to perform TMJR at all. Finally, for “severe” reactions to preoperative metal hypersensitivity testing, 62.85% would alter their implant choice to a nonreactive metal component, and 22.85% would choose not to perform TMJR. The actual questionnaire is provided in Figure 6.

Discussion

The topic of metal hypersensitivity and its role in alloplastic metal implants has remained a topic of significant debate in the orthopedic literature. Little consensus has been reached on how to screen for

metal hypersensitivity before implant placement or how to treat patients with a metal implant and confirmed metal hypersensitivity.

Scheidt et al¹² were the first to perform a largescale study to survey orthopedic surgeons to assess their attitudes and opinions on metal hypersensitivity, its incidence, diagnosis of and screening for metal hypersensitivity, implant choice changes, and management of metal hypersensitivity in their patients. Their study demonstrated that most respondent orthopedic surgeons (68%) believed that metal hypersensitivities can occur with metal implants. Therefore, most would alter their choice of implant when a metal hypersensitivity has been confirmed by serum testing to an implant containing a nonreactive material. However,

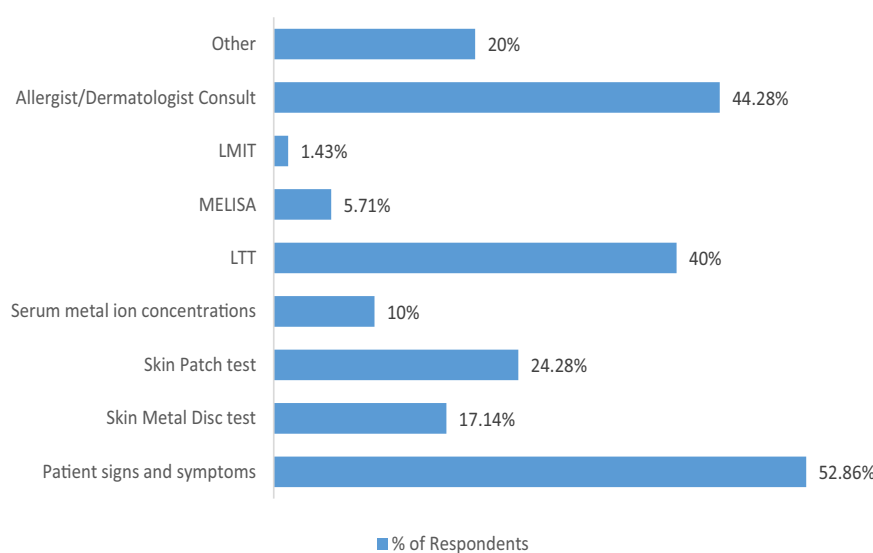


FIGURE 5. Methods used to diagnose metal hypersensitivity. LMIT, leukocyte migration inhibition test; LTT, lymphocyte transformation test; MELISA, memory lymphocyte immunostimulation assay.

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Does Metal Hypersensitivity Have Relevance in Patients Undergoing TMJ Prosthetic Replacement? – Questionnaire

1. Gender?
 - ☐ Male
 - ☐ Female
2. Age?
 - ☐ Less than 30
 - ☐ 30-39
 - ☐ 40-49
 - ☐ 50-59
 - ☐ 60 or older
3. Where do you practice?
 - ☐ North America (Specify: _____)
 - ☐ AAOMS District (Specify: _____)
 - ☐ Europe (Specify: _____)
 - ☐ Other (Specify: _____)
4. How long have you practiced OMFS?
_____ years
5. Do you perform TMJR surgery?
 - ☐ Yes (continue to next question)
 - ☐ No (end of survey)
6. Do you believe metal allergies occur with TMJR implants?
 - ☐ Yes
 - ☐ No
 - ☐ Unsure
7. Every patient should be asked about a history of metal and jewelry allergy prior to placement of TMJR implant?
 - ☐ Agree
 - ☐ Disagree
 - ☐ Unsure
8. Do you routinely ask patients if they are allergic to metals or jewelry prior to TMJR?
 - ☐ Yes
 - ☐ No
9. If a metal allergy is suspected based on history in a patient who is about to undergo TMJR, what would be your next step?
 - ☐ Proceed with surgery
 - ☐ Refer for testing to determine the specific metal allergen
 - ☐ Skin patch testing
 - ☐ Skin metal disc test
 - ☐ Lymphocyte Transformation Test (LTT)
 - ☐ Memory Lymphocyte ImmunoStimulation Assay (MELISA)
 - ☐ Other (Specify: _____)
10. Have you had a patient develop a metal allergy after implanting a TMJR prosthesis?
 - ☐ Yes
 - ☐ No
 - ☐ Unsure

FIGURE 6. Questionnaire. AAOMS, American Association of Oral and Maxillofacial Surgeons; NSAIDs, nonsteroidal anti-inflammatory drugs; OMFS, oral and maxillofacial surgery; TMJ, temporomandibular joint; TMJR, temporomandibular joint replacement. (**Fig 6 continued on next page.**)

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only 41% of the participants had questioned their patients regarding a sensitivity to metals before implanting a metal-containing orthopedic prosthesis.¹² To the best of our knowledge, no studies have been reported on the attitudes and opinions of TMJR surgeons related to metal hypersensitivity in the oral and maxillofacial surgery literature.

Most of the surgeon participants in the present study (75%) reported that metal hypersensitivity can occur with TMJR, 2.77% did not, and 22.22% were unsure. These findings are comparable to the results reported by Scheidt et al.¹² Unlike the results reported by Scheidt et al,¹² most of the respondents to the

present survey agreed that patients should be asked about metal allergy before TMJR (91.66%), and 80.55% routinely asked their patients if they were hypersensitive to metals preoperatively.

If through the patient history, a metal hypersensitivity were suspected by a respondent to the present survey, the diagnosis was determined primarily from the patient's signs and symptoms (52.85%) and an allergist or a dermatologist consultation (44.28%). The LTT was the test most used by the respondents to confirm the diagnosis.

As the documentation of a hypersensitivity reaction's severity increased, more TMJR surgeons

11. To which of these metals have you seen a hypersensitivity reaction? (You may choose more than one if indicated)
 - ☐ Aluminum
 - ☐ Chromium
 - ☐ Cobalt
 - ☐ Iron
 - ☐ Molybdenum
 - ☐ Nickel
 - ☐ Titanium
 - ☐ Vanadium
 - ☐ Other (Specify: _____)
12. What were the signs and symptoms? (Check all that apply)
 - ☐ Pain
 - ☐ Swelling
 - ☐ Cutaneous manifestation (skin rash, etc.)
 - ☐ Osteolysis around implant
 - ☐ Loss of function
 - ☐ Other (Specify: _____)
13. How did/would you make the diagnosis of metal hypersensitivity to a TMJR implant? (Check all that apply):
 - ☐ Patient signs and symptoms
 - ☐ Skin Metal Disc test
 - ☐ Skin Patch test
 - ☐ Serum metal ion concentrations
 - ☐ Lymphocyte Transformation Test (LTT)
 - ☐ Memory Lymphocyte ImmunoStimulation Assay (MELISA)
 - ☐ Leukocyte Migration Inhibition Test (LMIT)
 - ☐ Allergist/Dermatologist Consult
 - ☐ Other (Specify: _____)
14. How did/would you treat the allergic response to the implant? (Rank from most likely [5] to least likely [1])
 - ☐ Observe/monitor _____
 - ☐ NSAIDs/Steroids _____
 - ☐ Remove/Replace implant _____
 - ☐ Referral to another OMFS _____
 - ☐ Other (Specify: _____)
15. How would a mild reaction on allergy testing influence your management?
 - ☐ Does not alter my management choice
 - ☐ Alters implant choice to non-reacting metal component (e.g. Titanium only)
 - ☐ Choose not to perform the TMJR procedure
 - ☐ Obtain second opinion or refer to another physician
 - ☐ Other (Specify: _____)
16. How would a moderate reaction on allergy testing influence your management?
 - ☐ Does not alter my management choice
 - ☐ Alters implant choice to non-reacting metal component (e.g. Titanium only)
 - ☐ Choose not to perform the TMJR procedure
 - ☐ Obtain second opinion or refer to another physician
 - ☐ Other (Specify: _____)
17. How would a severe reaction on allergy testing influence your management?
 - ☐ Does not alter my management choice
 - ☐ Alters implant choice to non-reacting metal component (e.g. Titanium only)
 - ☐ Choose not to perform the TMJR procedure
 - ☐ Obtain second opinion or refer to another physician
 - ☐ Other (Specify: _____)
18. Please provide any additional information on how you manage metal hypersensitivity.

FIGURE 6 (cont'd).

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responded that they would be willing to alter their management plans. For a mild reaction to metal allergy testing, only one half of the participants would alter their implant choice to nonreactive metal components (eg, titanium alloy). For severe reactions, 62.85% would alter their TMJR choice to nonreactive metal components; however, 22.85% responded that they would choose not to perform TMJR at all.

When metal hypersensitivity is suspected postoperatively, most participants in the present study chose to remain rather conservative in their treatment, with

41.42% choosing only observation or continued monitoring without intervention. However, 24.28% responded that they would choose to remove and replace the implant with nonreactive metal components.

Regarding the strengths and limitations of the present study, to the best of our knowledge, the present study is the first to examine the attitudes and opinions of TMJR surgeons regarding metal hypersensitivity. Also, the present study surveyed a wide range of experienced TMJ surgeons from around the globe with

varied TMJR experience. However, the results were based on a 32.43% response rate (72 of 222). Although the survey was sent to members of the 2 largest societies of TMJ surgeons, the small response rate might have resulted in a bias of the opinions of only those respondents who participated in the study or simply reflects the number of TMJ surgeons in those societies who perform TMJR.

In conclusion, the results from the present study have demonstrated that respondent TMJ surgeons agree that metal hypersensitivity occurs in TMJR. However, their approaches to screening and managing metal hypersensitivity varied. These results should provoke further research to investigate the prevalence and possible role of metal hypersensitivity in TMJR device failure, to assess whether TMJR long-term outcomes are affected by the use of nonreactive metals in patients with documented preoperative metal hypersensitivity, and/or lead to the development of TMJR devices using new nonreactive materials. In addition, investigation is required to determine whether a specific management algorithm could be adopted for treatment of patients who have developed a metal sensitivity after TMJR implantation.

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