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Tips, Quips, and Pearls

## Metal allergy and the use of custom implants in primary total ankle replacement



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## ABSTRACT

**Purpose:** Patients with metal allergy often go undiagnosed prior to surgery. This can lead to a high rate of complications, especially with orthopedic implants which can be highly variable in the composition of metals used in their production. The purpose of this technique guide is to highlight the use of pre-operative allergy testing in patients with known history of metal allergy, emphasize the proper steps in identifying a potential metal sensitivity reaction, and to report in literature the success of primary custom printed total ankle arthroplasty implants manufactured without the use of traditional metal compositions.

**Technique guide:** Patients often have undergone treatment in the past, but nevertheless, discussion about all treatment options, both conservative and surgical should be addressed. The author's preference is to maintain motion in the ankle joint if safe and reasonable. Often times patients will be unaware of metal allergy unless they have had prior reaction, usually from a previous orthopedic surgery. In the cases where the patient does report previous hypersensitivity reaction to metals, referral should then be made to an Allergist for comprehensive metal patch testing or lymphocyte transformation testing. Once the metal limitations are identified, orthopedic industry partner with custom printing capabilities is then contacted. Working with engineers, ankle implants free of offending metals are able to be manufactured.

**Analysis & discussion:** To the author's knowledge, very few cases of metal sensitivity to total ankle replacement exist in the literature. The author's experience to date has shown favorable results when metal allergy is identified, particularly in patients with known history of metal allergy. With proper pre-operative planning and industry partner, good outcomes can be achieved in patients with metal allergy undergoing primary total ankle arthroplasty.

## Introduction

Patients with metal allergy often go undiagnosed prior to surgery.<sup>1-3</sup> This can lead to a high rate of complications, especially with orthopedic implants which can be variable in the composition of metals used in their production. Cobalt, chromium, nickel, and titanium have been reported as some of the more utilized metals in orthopedic implant manufacturing.<sup>1,4-7</sup>

There are traditionally two methods to test metal sensitivity, patch testing and lymphocyte transformation testing.<sup>1</sup> The former is considered the gold standard for several reasons. Patch testing is readily available through Immunologist and Allergist specialties. It also has relatively quick turnaround time with observation for potential reaction performed at 48 h, and between 72 and 96 h. Patch testing is also a lower cost option. Conversely, lymphocyte transformation testing (LTT) is high cost and currently has limited availability. This method measures the change of lymphocytes in the peripheral blood over a 7-day span following allergen exposure. LTT does have utility in patients with

indeterminate results to patch testing, or patients with negative patch test but reported history or high index of suspicion for metal allergy.

Liden et al.<sup>4</sup> in 2016 specifically looked at the metal concentrations used in early metal sensitivity patch testing and found that the previously used standard of 0.5% concentration of cobalt led to high rate of false negatives compared to use of 1% concentration. This study also found that patients with confirmed cobalt allergy had high incidence of sensitivity to nickel and chromium.

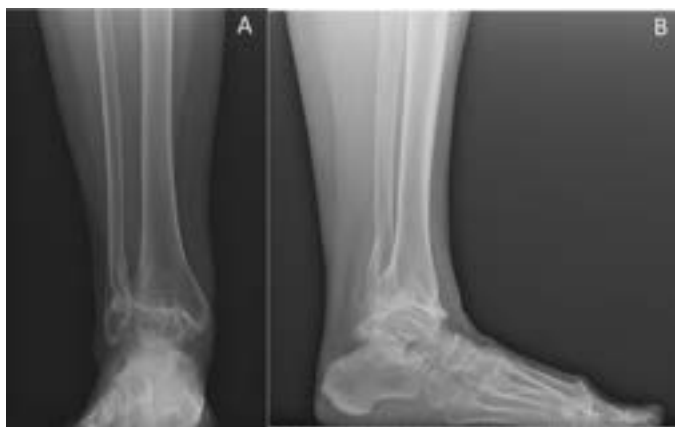
## Technique guide

Encounters begin in typical fashion with patient history and physical examination. In patients with end stage ankle arthritis, there is often long-standing soft tissue edema, complaints of increased pain with increased activity. Radiographs are standard for all patients (Fig. 1). Early identification of any history or signs for metal sensitivity is key to success. An example case of a patient who successfully underwent a

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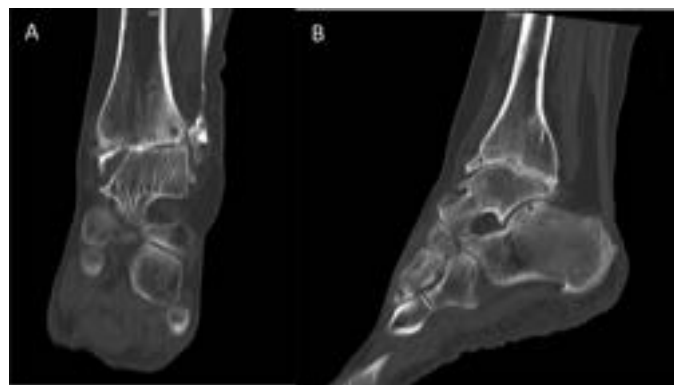
**Fig. 1.** Pre-Operative AP (A) and Lateral (B) radiographs of a patient with end-stage ankle arthritis.

primary total ankle replacement with known history of cobalt allergy is shown in the radiographs as well as advanced imaging (Figs. 2 and 3), which is routinely ordered in the setting of end stage ankle arthritis to assess for periarticular bone quality as well as ligamentous integrity about the ankle joint. After thorough review of all imaging, then a detailed discussion with the patient regarding options is performed at the subsequent visit. Patients often have undergone treatment in the past, but nevertheless, discussion about all treatment options, both conservative and surgical should be addressed. If the patient has not been previously treated, options such as bracing, steroid injections, shock-wave therapy, physical therapy should be attempted. Other, less invasive surgical techniques could also be explored such as ankle arthroscopy and/or regenerative medicine injections. If the patient has exhausted other options and wishes to proceed with definitive surgery, the author's preference is to maintain motion in the ankle joint with replacement if safe and reasonable.

Often times patients will be unaware of metal allergy unless they have had prior reaction, usually from a previous orthopedic implant. In the author's experience, the majority of patients who present with known history of metal allergy had undergone past total knee or hip arthroplasty with post-operative reaction. The signs of metal sensitivity reaction can closely mimic post-operative infection, which must be ruled out first. If metal sensitivity is present, symptoms can begin from weeks to several months after surgery. The patient could present with post-operatively with all or combinations of peri-prosthetic erythema, edema, dermatitis, loosening of hardware, or unexplained pain. Joint aspiration or peri-prosthetic bone biopsy are typically the first step in ruling out infection. If infection is not suspected or ruled out and hardware has failed, removal of metallic implants will likely show resolution of symptoms in setting of metal allergy. In these cases, cement spacer is inserted to maintain alignment and spacing while planning next steps.



**Fig. 2.** Pre-Operative Coronal (A) and Sagittal (B) MRI showing severe tibiotalar joint space narrowing and small peri-articular subchondral cysts.



**Fig. 3.** Pre-Operative Coronal (A) and Sagittal (B) CT showing severe tibiotalar joint space narrowing and small peri-articular subchondral cysts.

In cases of previous reported hypersensitivity reaction to metals whether from previous total joint or other metal implantation, or there is high index of suspicion in a patient without previous reported allergy, prompt referral should be made to an Allergist for comprehensive metal patch testing or lymphocyte transformation testing.

The Allergist will commence patch testing on referral, which involves application of numerous small patches containing metal allergens and/or injection of allergens into the dermis typically placed on the patient's upper back. Signs of dermatitis reaction are observed at 48 h, and after 72 h. Results from patch testing are graded on severity of reaction and are typically shown in table form (Fig. 4). Once the metal limitations are identified, orthopedic implant industry partner with custom printing capabilities is then contacted.

Initially, the surgeon's orthopedic industry partner will request information regarding restrictions of available metals. Common metals used in 3D printed ankle implants include cobalt, chromium, nickel, titanium, copper, and tungsten.<sup>1,4-7</sup> Radiographs and CT with 3D reconstruction of the affected ankle are also needed. In cases of bony collapse or previous surgery to the ankle a contralateral CT may be indicated. Next, a conference call will be scheduled to discuss the case with engineers regarding the initial goals and surgical planning. At this point the engineers will use 3D software to display bony anatomy and possible placement of different implants and sizes of implants. After initial discussion, surgical planning guide is created (Fig. 5) for review. At this time, the surgeon can alter the design of the implant as he/she deems necessary. Once approved by the surgeon, production of the custom implants begins. Ultimately, ankle implants free of offending metals are able to be manufactured without compromise of structural integrity (Fig. 6). Patient specific guides are common to most industry partners with custom printing capabilities, and typically available prior to surgery to directly visualize anatomy and positioning (Fig. 7). In the author's experience, the timeline between initial conference call with engineers and time of surgery has typically been between 4 and 6 weeks.

#### *Surgical technique*

Surgical approach does not differ greatly in the technique when dealing with custom implants or patients with known metal sensitivity. There are a few additional important factors to consider. Once initial dissection is completed and the surgeon is ready to begin with bony work, either the jig is applied, or the custom patient specific instrumentation (PSI) guide is press fit to the anterior ankle and pinned in anatomic alignment under fluoroscopic guidance (Fig. 8). Most of the orthopedic implant industry partners currently producing custom ankle implants have the option of utilizing PSI guides. Prior to surgery the surgeon should ensure that the guides are manufactured in the same manner as the final implants, free of any offending metals. In the author's practice, prophylactic fixation of the tibia is also performed using one or two

METALS				#1	#2	#3	#4
#	ARTICLE	VEH/CDNE	DESCRIPTION				
1	N-002A	5.0 pet	Nickel sulfate hexahydrate	1+	3+	3+	
2	C-017A	1.0 pet	Cobalt(II) chloride hexahydrate	1+	3+	3+	
3	M-031	2.0 pet	MANGANESE CHLORIDE	FA	-	-	
4	C-021	5.0 pet	Copper(I)oxide	-	-	-	
5	V-003	1.0 pet	Vanadium(III)chloride	-	-	1R	
6	M-038	0.5% pet	Molybdenum(V)chloride	-	-	-	
7	T-042	10.0 pet	Titanium	-	-	-	
8	A-038	10.0% pet	ALUMINUM HYDROXIDE	-	-	-	
9	T-047	1.0% pet	Tantalum	-	-	-	
10	Z-009	0.1% pet	ZIRCONIUM DIOXIDE	-	-	-	
11	N-008	0.2% pet	Niobium(V)chloride	-	-	-	
12	P-001	2.0 pet	Palladium(II)chloride	1R	3+	3+	
13	S-017	3.0 pet	Sodium tetrachloropalladate(II) hydrate	1+	3+	3+	
14	C-022	2.0 pet	Copper(II)sulfate pentahydrate	-	-	-	
15	A-022	2.0 pet	Aluminium(III)chloride hexahydrate	-	-	-	
16	T-008	50.0 pet	Tin	-	-	-	
17	M-005	0.5 pet	Mercury	-	-	-	
18	Z-001	2.5 pet	Zinc	-	-	-	
19	G-005B	2.0 pet	Gold(I)sodium thiosulfate dihydrate	-	-	-	
20	I-014	1.0 pet	Iridium	-	-	-	
21	C-040	10 pet	Calcium titanate	-	-	-	

Fig. 4. Pre-Operative metal patch test results showing strong positive to Cobalt, Nickel, Palladium.

medial malleolus screws to help prevent stress fracture. The surgeon must also ensure prior to surgery that all ancillary implants/hardware such as screws and anchors are free of offending metals as well. Final fluoroscopic images (Fig. 9) are shown for the afore mentioned patient who underwent primary total ankle replacement in the setting of cobalt allergy.

Recovery does not differ from traditional total ankle arthroplasty. In the author’s practice, the patient is kept in posterior splint or cast with instruction to remain non-weight bearing until week 3 post-operatively. At week 3 when all incisions have typically healed, and the patient is placed in a short leg fiberglass cast and weight-bearing begins. At week 4 transition is made to tall walking boot and formal physical therapy commences. At week 6 the patient is placed in an ankle brace and allowed to resume normal activities while continuing physical therapy.

Radiographs are taken at regular intervals throughout the recovery process (Fig. 10) to monitor maintenance of stable alignment of the implants. Careful attention to the soft tissues is recommended post-operatively for the afore mentioned signs of skin reaction which could be indicative of metal sensitivity.

**Analysis and discussion**

End-stage ankle arthritis is a difficult pathology to treat, and limited options are currently available. The most widely utilized definitive surgical treatments include ankle arthrodesis or ankle replacement. Total ankle arthroplasty (TAA) has been gaining popularity recently, with increasing number of cases performed each year.<sup>6</sup> However, patient selection is of greater importance during TAA compared to arthrodesis

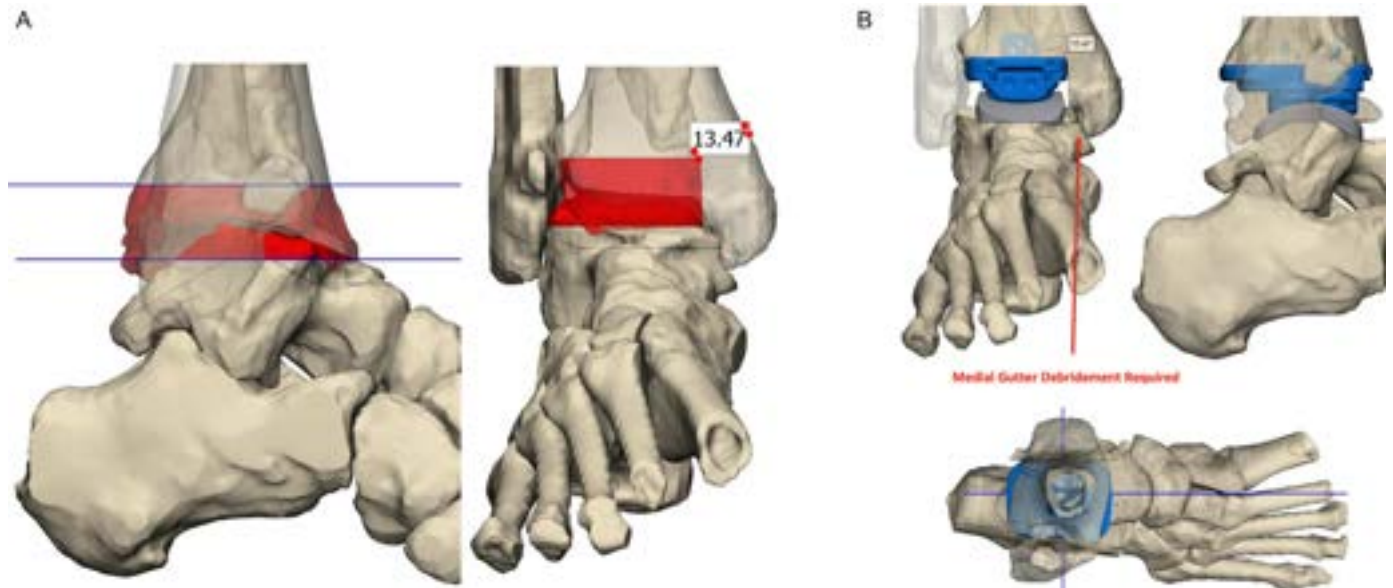


Fig. 5. Pre-Operative surgical planning guide with proposed bone resection (A), and proposed implant positioning (B).



Fig. 6. Cobalt free tibial and talar components.



Fig. 9. Final intra-operative AP (A) and Lateral (B) ankle radiographs.



Fig. 7. (A) Coupled guide and anatomic replica of tibiotalar joint able to be visualized prior to surgery. (B) Coupled and uncoupled guides available to utilize per surgeon's discretion.

due to many factors such as age, comorbidities. When any orthopedic pathology is combined with metal allergy, treatment can become even more challenging.

Anastasio et al.<sup>6</sup> recently published a review article in 2023 which included a case of revision total ankle arthroplasty after confirmed metal allergy. They relate that metal sensitivity in total joint implants is a difficult diagnosis, and alternative etiologies of post-operative pain or



Fig. 8. Intra-operative AP ankle radiograph with coupled cut guide press fit and pinned.



Fig. 10. 6-month post-operative AP (A) and Lateral (B) ankle radiographs.

implant failure must be explored. They also emphasize a team approach when dealing with metal sensitivity to orthopedic implants. Immunologists, radiologists, infectious disease, surgeons, and industry engineers all must work together to ensure the optimal outcome.

One of the few cases found in the literature of metal allergy to total ankle implants was reported by Gaston et al.<sup>8</sup> in 2020. Their patient developed a diffuse skin rash approximately 7 weeks after implantation without any other apparent cause. Infectious cause was explored and excluded. The patient eventually went on to conversion to ankle

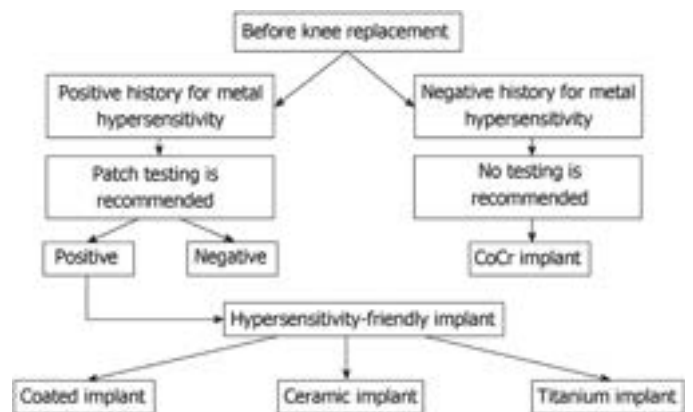


Fig. 11. Pre-operative algorithm for diagnosis of metal sensitivity and selection of appropriate implants (Saccomanno).

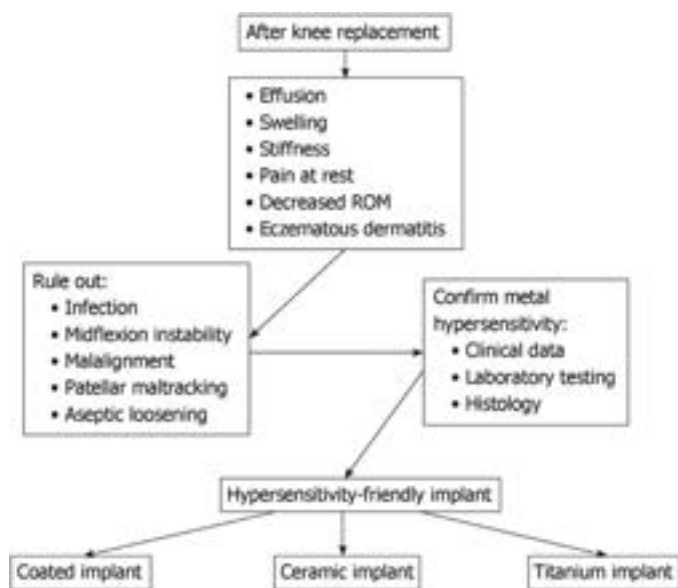


Fig. 12. Post-operative algorithm for treatment of adverse reactions caused by metal sensitivity (Saccamanno).

arthrodesis. They stress evaluation of both articulating and non-articulating surfaces of the implants.

Kresciz et al.<sup>5</sup> performed a prospective study in 2012 investigating the allergenic properties of metal knee and hip implants up to 24 months post-operation as well as relation between confirmed metal allergy and implant failure. They included 2 separate stages in the study, with stage 1 involving patch testing for several metals prior to surgery. Stage 2 performed the same patch testing but occurred after surgery. They found interesting results, with stage 1 subjects having a 21.7% rate of metal dermatitis. It is also noteworthy that 27.9% of females were found to have metal dermatitis compared to only 5.9% of males. Nickel, palladium, cobalt, and chromium were the most common metals found to cause a reaction. Stage 2 did find a 10.4% rate of positive patch test results. Overall, the authors strongly recommended pre-operative patch

testing in patients with reported history of metal sensitivity, and custom implants free of the offending metals.

Saccamanno et al.<sup>9</sup> 2019 developed a pre-operative (Fig. 11) and post-operative (Fig. 12) algorithm, and post-operative criteria (Fig. 13) for testing and implant selection pertaining to metal allergy. His study specifically investigated total knee arthroplasty; however, his work can be beneficial to surgeons when attempting to diagnose and treat a potential metal allergy after any joint replacement surgery.

Recent literature has been growing in support for patch testing and/or lymphocyte transformation testing in cases of chronic pain/inflammation after total joint arthroplasties in cases where infection is excluded.<sup>1,10,11</sup> Although it is still highly debated whether pre-operative allergy testing should be performed even if history suggests allergy. Overall, a 3.9% post-operative rate of metal sensitivity related pathology has been reported.<sup>10</sup>

It is still unclear whether a complication following total joint replacement can be attributed to the metal allergy alone. The large majority of evidence currently available is with respect to total knee and total hip arthroplasty. It also seems that metal sensitivity may be more common in females.<sup>5</sup>

**Conclusions**

To the author’s knowledge, very few cases of metal sensitivity to total ankle replacement exist in the literature. The author’s experience to date has shown favorable results when metal allergy is identified, particularly in patients with known history of metal allergy undergoing primary procedure. With proper pre-operative planning and industry partner, good outcomes can be achieved in patients with metal allergy undergoing primary total ankle arthroplasty.

**Financial Disclosures**

None.

**Informed Patient Consent**

Complete informed consent was obtained from the patient for the publication of this study and accompanying images.

Table 1 Diagnostic criteria for post-implantation metal hypersensitivity <sup>12-1</sup>	
<b>Major criteria</b>	
Eruption overlying the metal implant	
Positive patch test reaction to a metal used in the implant	
Complete recovery after removal of the offending implant	
Chronic dermatitis beginning weeks to months after metallic implantation	
<b>Minor criteria</b>	
Unexplained pain and/or failure of the offending implant	
Dermatitis reaction is resistant to therapy	
Morphology consistent with dermatitis (erythema, induration, papules, vesicles)	
Systemic allergic dermatitis reaction	
Histology consistent with allergic contact dermatitis	
Positive <i>in vitro</i> test to metals (e.g., lymphocytes transformation test)	

Fig. 13. Post-operative criteria for metal sensitivity after total joint surgery (Saccamanno).

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.fastrc.2023.100285](https://doi.org/10.1016/j.fastrc.2023.100285).

## References

- Richards LJ, Streifel A, Rodrigues JM. Utility of patch testing and lymphocyte transformation testing in the evaluation of metal allergy in patients with orthopedic implants. *Cureus*. 2019;11(9):e5761.
- Amini M, Mayes WH, Tzeng A, Tzeng TH, Saleh KJ, Mihalko WM. Evaluation and management of metal hypersensitivity in total joint arthroplasty: a systematic review. *J Long Term Eff Med Implants*. 2014;24(1):25–36.
- Battaglia AG, Ali-Zade C, Monti L, Al Khawashki H, Winkler H, Del Sel H, Mavrogenis AF, Benzakour T, Drago L, Romano CL. Metal hypersensitivity or missed periprosthetic joint infection? A critical review. *Orthopedics*. 2022;45(2):e73–e78.
- Lidén C, Andersson N, Julander A, Matura M. Cobalt allergy: suitable test concentration, and concomitant reactivity to nickel and chromium. *Contact Dermatitis*. 2016;74(6):360–367.
- Kręcisz B, Kieć-Świerczyńska M, Chomiczewska-Skóra D. Allergy to orthopedic metal implants - a prospective study. *Int J Occup Med Environ Health*. 2012;25(4):463–469.
- Anastasio ATMD, Johnson LGMBA, Willhite JPMD, Mousallem TMD, Hendershot EFMD, Parekh SGMD. Team approach: metal hypersensitivity in total joint arthroplasty. *JBJS Rev*. 2023;11(1):e22.
- Pinson ML, Coop CA, Webb CN. Metal hypersensitivity in total joint arthroplasty. *Ann Allergy Asthma Immunol*. 2014;113(2):131–136.
- Gaston TE, Kwan S, Skibicki HE, Cheesman QT, Daniel JN. Morbidity after metal allergy to a total ankle implant. *Foot Ankle Spec*. 2020;13(6):502–507.
- Sacomanno MF, Sircana G, Masci G, Cazzato G, Florio M, Capasso L, Passiatore M, Autore G, Maccauro G, Pola E. Allergy in total knee replacement surgery: is it a real problem? *World J Orthop*. 2019;10(2):63–70.
- Toro G, De Cicco A, Braile A, Landi G, Schiavone Panni A. New insights on metal allergy in total joint arthroplasty. *J Biol Regul Homeost Agents*. 2020;34(5 Suppl. 1):125–130.
- Bao W, He Y, Fan Y, Liao Y. Metal allergy in total-joint arthroplasty: case report and literature review. *Medicine (Baltimore)*. 2018;97(38):e12475.