

Patch Testing for the Evaluation of Metal Hypersensitivity in the Nuss Procedure

Annika Selvick, BS, and Rita Lloyd, MD

The Nuss procedure has become the predominant reason for the use of metal implants by pediatric general and thoracic surgeons. Current guidelines recommend preimplant testing for all patients undergoing the Nuss procedure, which differs from the guidelines for all other orthopedic procedures. This review was done to further evaluate this discrepancy.

The Nuss procedure has become the predominant reason for the use of metal implants by pediatric general and thoracic surgeons.¹ The procedure involves substernal placement of 1 or more metal bars custom fitted to a patient's chest. The bars are secured and left in place for a minimum of 2 years, after which they are removed.¹ The procedure is recommended for patients with severe pectus excavatum deformity and symptoms of shortness of breath, chest pain, and exercise intolerance and to improve body image.² In the recently released American Contact Dermatitis Society guidelines, they recommend preimplant testing for all patients undergoing the Nuss procedure.³ This differs from the guidelines for all other orthopedic procedures, which state to consider performing preoperative patch testing only in patients with a clear history of a metal allergy.³ This review was done to assess the data supporting this updated guideline and to review all current studies related to the evaluation of metal hypersensitivity in the Nuss procedure.

EPIDEMIOLOGY

In 2007, a study was done to determine the incidence of metal allergy in patients undergoing pectus excavatum repair at Eastern Virginia Medical School.⁴ The study is a retrospective review of 862 patients who underwent the Nuss procedure. The method of allergy diagnosis included patch testing with both the thin-layer rapid use epicutaneous (TRUE) patch test and the metal sensitivity disc. Of the 862 patients, 19 had suspected nickel allergy on preoperative screening with the TRUE test or metal sensitivity disc or postoperatively based on their clinical presentation. The authors define a postoperative allergic reaction as symptoms of a fever, rash, erythema, effusion, and

granuloma formation without obtainable evidence of infection or positive cultures. The article summarizes these results as a cumulative 2.2% incidence of metal allergy in their population.⁴ In addition, because atopic dermatitis has been shown to be a risk factor for nickel allergy in previous studies, data regarding the patient's history of atopy (eczema, rhinitis, or asthma) were recorded.^{5,6} A history of atopy was present in 56% of patients ($P = 0.001$).⁴ This differs from several other studies, which show a positive correlation between atopic dermatitis and nickel allergy.^{5,6} The 2.2% incidence of metal allergy found in this article is less than the 13% traditionally reported in orthopedic literature and 18.5% in dermatologic literature.^{7–10} Therefore, another study was conducted between 2004 and 2010 to reassess the rate of nickel allergy in patients undergoing the Nuss procedure at Children's Hospital of the King's Daughters in Norfolk, VA. The study is a retrospective review that assessed 639 patients who underwent the Nuss procedure. The study found that 26 patients had a preoperative positive patch test, 10 patients had a postoperative positive patch test, 4 had unknown postoperative patch test results with a positive clinical diagnosis, and 1 patient had a negative preoperative patch test with a subsequent positive postoperative patch testing reading. The study concludes that this incidence (6.4%) is almost 3 times the incidence of the previous study in 2007.¹ However, there are several limitations related to the design of both of these studies, which will be highlighted throughout this article because it addresses important issues in standardizing research studies related to patch testing before and after metal implants.

PREIMPLANT PATCH TESTING

It is crucial for patch testing to be done in the correct manner to have meaningful results that guide our clinical practice. There are several limitations in the cited studies assessing the incidence of metal hypersensitivity in the Nuss procedure. In 1 study, the method of allergy diagnosis included the TRUE test (Allerderm Laboratories, Petaluma, CA) and the metal sensitivity disc (Biomet Microfixation, Warsaw, IN), the latter of which has been proven to be an insensitive method of diagnosing a metal allergy.^{1,11,12} In addition, the study

From the University of Wisconsin Madison School of Medicine and Public Health.

Address reprint requests to Annika Selvick, BS, 2258 N 72nd St, Wauwatosa, WI 53213. E-mail: aselvick@wisc.edu.

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reveals no details regarding which TRUE test antigens were used for patch testing, which providers applied and interpreted the patch tests, the degree of reactivity, or the time at which the patch tests were read.⁴ Another study conducts preoperative patch testing variously applied by nurses in the surgical clinic, the patient's primary care doctor, or, in some cases, a dermatologist or an allergist, with the overwhelming majority of the interpretations done by someone other than dermatology or allergy specialists.¹ Final readings were done at 72 hours to be classified as either positive or negative, and data were not recorded regarding the degree of positivity or the time course of reaction to the metal.¹ There was no delayed reading at 96 hours or more, which is important for metal allergy testing.

In addition, there is a lack of standardization regarding which allergens to include in the preoperative patch test.^{1,13} The Nuss bar is composed of more than 10 elements, including carbon, manganese, phosphorus, sulfur, silicon, chromium, nickel, molybdenum, nitrogen, copper, and iron.¹³ We argue that, if preimplant testing is done, all potentially allergenic components should be included in the preoperative patch test, including nickel, chromates, manganese, and molybdenum. If a patient is found to be positive to any of these metals, most surgeons use a titanium bar instead of the standard stainless-steel bar. Titanium is a biocompatible metal, and thus it provokes few allergic reactions. However, titanium bars are actually made of titanium alloy, which contains a small amount of other metals, such as aluminum and vanadium.¹⁴ Therefore, there is still a potential risk of developing a metal allergy to the titanium bar. This phenomenon is documented in a case report by Sakamoto et al¹⁴ involving a 17-year-old boy who underwent the Nuss procedure with 2 titanium bars. The patient subsequently developed a postoperative metal hypersensitivity reaction and was placed on a maintenance dose of oral prednisone until bars were removed 2 years later.

The decision whether to perform preoperative patch testing is further complicated by the fact that screening questions have proven to be unreliable in several studies.^{15,16} A study by Kieffer¹⁵ found that 13 of 28 persons with a self-reported history of metal contact dermatitis had negative patch test reactions to nickel; 8 of 23 persons with positive patch test reactions to nickel had never experienced skin reaction from metal contacts. Another study by Josefson et al¹⁶ screened 369 women, aged 30 to 40 years, with a questionnaire involving 2 questions: "Are you sensitive/hypersensitive/allergic to nickel?" and "Do you get a rash from metal buttons, jewelry, or other metal items that come in contact with your skin?" Results showed nickel-positive reactions in 30% of the subjects. Self-reported prevalence of nickel allergy as indicated by the 2 respective questions was 40% and 35%, with a positive predictive value of 59% and 60%.¹⁶ The American Contact Dermatitis Society guidelines acknowledge this challenge and state that, although patient history is not completely trustworthy, listening to concerns about a metal allergy is reasonable. In patients who strongly believe that they are metal allergic, evaluation through patch testing is prudent.³

Furthermore, it is important to note that the preoperative predictive value of a positive patch test is not optimal. The immune

environment around an implanted metal device is complex, and the patch test does not completely evaluate all mechanisms of hypersensitivity.³ However, the epicutaneous patch test appears to still be the best test for the evaluation of potential metal reactions, both before and after implantation.³

BIOMET MICROFIXATION METAL DISC FOR PREOPERATIVE EVALUATION

Studies conducted assessing the utility of the metal disc offered by Biomet Microfixation for preoperative testing for metal sensitivity conclude that the disc is not accurate in diagnosing a preoperative metal allergy.^{11,12} The first study conducted by Aneja et al¹¹ was conducted over 30 months during which 50 patients underwent the Nuss procedure. The study population was limited to those who developed clinically significant cutaneous reactions postoperatively. The authors found that all 4 patients who developed cutaneous reactions after implantation of the Nuss bar tested negative to the stainless steel disc preoperatively.¹¹ Two of the 4 patients underwent expanded patch testing with an abbreviated screening series and Cleveland Clinic prosthesis series, and 1 patient was confirmed to have metal allergy. Patients 3 and 4 did not undergo further patch testing, so it is not known whether their skin eruptions were caused by metal allergy.¹¹ Another study conducted by Heitmiller et al¹² found similar conclusions. Preliminary preoperative testing of 2 pectus excavatum patients was assessed with both nickel sulfate and the metal disc, revealing inconsistencies between the 2 methods. This prompted the authors to further assess 7 patients without pectus excavatum with both the North American Contact Dermatitis Group series and the metal disc supplied by Biomet Microfixation. Based on patch testing, 5 (71.4%) of the 7 patients exhibited positive reactions to 2.5% nickel sulfate in petrolatum at 72 hours. Of these 5 patients, 4 patients (80%) did not exhibit reactions to the metal disc. The remaining patient showed only a weak positive reaction to the metal disc detected at 72 hours after disc application.¹²

SENSITIZATION

Metal salts, in concentrations routinely used for patch testing by experts, are thought not to be sensitizers.¹⁷ However, the implant itself may be a sensitizer, meaning that a negative preoperative patch test does not ensure a hypersensitivity reaction will not occur. This was addressed in a case report written by Sesia et al¹³ involving a 14-year-old boy who underwent the Nuss procedure after a negative preoperative patch test. The patient returned on postoperative day 47 with bilateral superficial wound erythema and induration. Superficial wound infection was suspected, prompting local wound exploration and cultures, which demonstrated methicillin-resistant *Staphylococcus aureus*. The patient was started on sulfamethoxazole/trimethoprim and had complete healing of both wounds. However, he continued to have a rash on both sides of his chest. A repeat patch test was ordered, which was positive to potassium dichromate, copper sulfate, and molybdenum. Sensitization likely (based on the timing of

TABLE 1. Diagnostic Criteria for a Metal Hypersensitivity Reaction After Implantation

Major Criteria	Minor Criteria
Eruption overlying the metal implant	Unexplained pain and/or failure of the offending implant
Positive patch test reaction to a metal used in the implant	Dermatitis reaction is resistant to therapy
Complete recovery after removal of the offending implant	Morphology consistent with dermatitis (erythema, induration, papules, vesicles)
Chronic dermatitis beginning weeks to months after metallic implantation	Systemic allergic dermatitis reaction
	Histology consistent with allergic contact dermatitis
	Positive in vitro test to metals (Lymphocyte Transformation Testing)

Adapted from Schalock et al.¹⁷

the eruption approximately 6 weeks after surgery) occurred from the implant itself.

POSTIMPLANT PATCH TESTING

In the study conducted by Sesia et al,¹³ all patients with a rash, edema, pain, tenderness, or serous drainage with negative cultures were diagnosed as having a postoperative metal allergy. However, all noninfectious complications are not solely due to a metal allergy. Diagnostic guidelines for postimplant testing have recently been published and reviewed by an international group of patch testing dermatologists.¹⁷ These guidelines should be considered when diagnosing postoperative metal hypersensitivity reactions. A list of the major and minor criteria, highlighted by Schalock et al,¹⁷ is provided in Table 1.

SUMMARY

Current guidelines listed by the American Contact Dermatitis Society recommend preimplantation testing for all patients before the Nuss procedure. Although there are flaws in the current data, the American Contact Dermatitis Society guidelines should remain in place unless more refined studies indicate that the current recommendations are flawed. However uncertain we are about the relevance of a positive patch test in making recommendations about an implant, patch testing in the correct manner is crucial to having useful data. This includes consistently trained applicators and readers of the patch test, performance of a final reading at 96 hours or more, patch testing to all potentially allergenic components of a metal device, and strict criteria to diagnose a postimplant metal hypersensitivity reaction.

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