Surgical explantation of atrial septal closure devices for refractory nickel allergy symptoms

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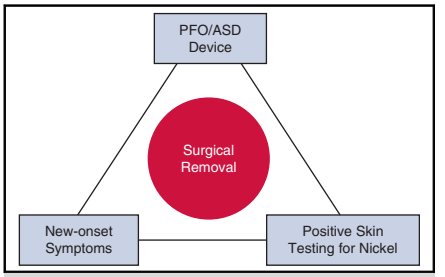
ABSTRACT

Objectives: Systemic allergic reactions to nickel alloys in percutaneous atrial septal defect occlusion devices have a poorly defined natural history. We describe our experience of surgical removal of the offending device in a series of patients with nickel allergy and refractory symptoms.

Methods: Patients with atrial septal defect device explants for nickel allergy were reviewed. Administered questionnaires focused on symptoms, quality of life, and satisfaction along with the 36-Item Short Form Health Survey to measure physical and mental health postsurgery.

Results: Atrial septal defect devices were removed for nickel allergy in 58 patients during the past 10 years. The median age was 42 years (range, 24-71 years) and 95% were women. Explantation occurred at a median of 8 years (range, 6 months-18 years) after insertion. Symptoms included fatigue (82%), chest pain (78%), headache (73%), and palpitation (58%). Surveys were available for 45 patients: 58% rated their quality of life as poor and 69% were not at all satisfied with their device. Postexplant, all patients reported improvement in their symptoms, with 18 patients (42%) noting complete resolution. In 12 patients prospectively studied, the preoperative scores in physical and mental health domains were lower than the validation group, indicating significant disability. Similarly, there was marked improvement in each domain postremoval.

Conclusions: Patients with nickel allergy and severe refractory symptoms after atrial septal defect device implantation experience profound resolution of symptoms and improved quality of life after removal. Nickel allergy should be considered before device insertion, and a low threshold should exist for surgical removal for refractory symptoms. (J Thorac Cardiovasc Surg 2020;160:502-9)



Current approach to management of patients with symptoms of PFO/ASD device hypersensitivity.

CENTRAL MESSAGE

Systemic hypersensitivity after implantation of ASD devices in patients with documented nickel allergy are debilitating. Surgical removal resolves symptoms and marked enhances quality of life.

PERSPECTIVE

Systemic hypersensitivity after placement of nitinol-based ASD/PFO septal occluders has been described, yet no consensus recommendation for preimplant allergy testing or for management of postimplant hypersensitivity exist. We report the largest series of patients with device removal for refractory symptoms, and provide diagnostic and quality of life perspective for these challenging patients.

See Commentaries on pages 510 and 512.

Percutaneous closure of atrial septal defect (ASD)/patent foramen ovale (PFO) is a common interventional cardiac catheterization procedure performed in patients with appropriate anatomy. Between 1988 and 2005, the Nationwide Inpatient Sample demonstrated a 139% increase in ASD and PFO closures.[1] In addition to indications for

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Supported by the Division of Cardiothoracic Surgery, University of Utah, Salt Lake City, Utah.

Read at the 99th Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, May 4-7, 2019.

Received for publication May 10, 2019; revisions received Oct 20, 2019; accepted for publication Oct 27, 2019; available ahead of print Nov 21, 2019.

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0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2019.10.177

Abbreviations and Acronyms
ASD = atrial septal defect
ASO = Amplatzer septal occluder
FDA = Food and Drug Administration
HSO = Helex septal occluder
PFO = patent foramen of ovale
SF-36 = 36-Item Short Form Health Survey

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true ASDs, device closure has been utilized for a number of conditions associated with PFO, including migraine headaches, decompression sickness, platypnea-orthodeoxia, exacerbation of right–left shunting with obstructive sleep apnea, and myocardial infarction due to paradoxical embolism to the coronary arteries. PFO prevalence in patients who experienced cryptogenic stroke is greater (about 40%) than in the general population, and even higher in patients younger than age 55 years (about 55%).[2] Indeed, indications for device closure have been expanded and approved by the Food and Drug Administration (FDA) for patients who have experienced cryptogenic stroke.[3,4] Although device closure is a safe and effective alternative to surgical closure, a number of adverse issues have been reported, including device migration, erosion, and concerns for hypersensitivity reactions.[5-7]

Nitinol, an alloy of nickel and titanium, is the primary component of the most commonly used ASD/PFO occluder devices: the Amplatzer septal occluder (ASO) (St Jude Medical Corporation, St Paul, Minn) and the Helex septal occluder (HSO) (W. L. Gore & Associates, Inc, Medical Products Division, Flagstaff, Ariz). Within nitinol alloy, nickel is the more allergenic component than titanium. Nickel allergy has a prevalence of up to 30% in the general population, with the highest documented in women younger than age 30 years. Nickel allergy is primarily manifested as a chronic pruritic cutaneous eruption at the site of direct nickel contact.[8,9] The incidence of cutaneous nickel allergy has increased since 2008 likely due to increase in body piercings and lack of US legislative restriction of nickel in clothing, jewelry, toys, and electronic devices.[10,11] Similarly, the increase in implanted metal devices for multiple medical/surgical indications has sparked much interest and debate regarding biocompatibility and the potential for adverse metal reactions.

Although there is a paucity of literature describing the immunologic environment in metal hypersensitivity, it is believed to be a predominantly delayed T-cell type reaction to metal ions.[12] Major diagnostic criteria for metal hypersensitivity reaction include cutaneous eruption overlying implant, positive patch test reaction to a metal used in implant, and complete recovery after removal of offending device. Minor criteria relevant to this population include unexplained pain and/or failure of the offending agent. Specific to ASD/PFO devices, nickel elution with transient elevation of blood nickel levels has been observed and several reports of severe nickel hypersensitivity reactions have been published.[13-16] FDA labeling for both ASO and HSO devices includes warning for potential allergic reaction in patients with known nickel hypersensitivity. However, allergic reactions to these endoprostheses are rare and unpredictable processes that have a poorly defined presentation and natural history. To better understand this patient population, we report our experience of surgical removal of the offending device in a large series of patients with refractory nickel allergy.

METHODS

We performed a database review to identify ASD/PFO device explantation for nickel allergy during the past 10 years at our institution. This study was approved by our institutional review board (#00107344). During the first phase of study (January 2008-April 2018) retrospective data were obtained on demographic and clinical characteristics, including device type and causes for explantation. A provider-designed questionnaire was utilized that focused on symptoms, quality of life, and satisfaction scores before and after surgery (Appendix E1). In addition, a survey to measure physical and mental health postsurgery was administered 1 and 6 months postoperatively. During phase II (April 2018-September 2019), prospective data were collected with the questionnaires administered pre- and postoperatively.

All patients were evaluated in the Contact Dermatitis Clinic in the Department of Dermatology for confirmation of nickel allergy before device removal. Prospective patients were identified as allergic by cutaneous patch and prick testing to nickel sulfate 2.5% and 5.0%. Patch testing for delayed-type hypersensitivity is standard of care for evaluation of implanted metal device reaction. Our center also performs prick testing due to concern for underrecognized metal contact urticaria, and immunoglobulin E-mediated type-1 hypersensitivity reaction.[12,17]

Surgical removal was performed in nearly all patients through a minimally invasive right anterior thoracotomy on the beating heart with peripheral cannulation for cardiopulmonary bypass. After removal of the device, residual septal defects were either directly repaired or patched closed. Median sternotomy was performed in the case that associated procedures were required.

The 36-Item Short Form Health Survey (SF-36) was used as a health-related quality-of-life measure and the scoring was done based on the instructions available at the RAND corporation website.[18,19] Scoring the SF-36 was a 2-step process. First, precoded numeric values were recoded per the scoring key, so that the lowest and highest possible scores were 0 and 100, respectively. All items were scored so that a high score defined a more favorable health state. Scores represented the percentage of total

TABLE 1. Demographic and patient characteristics (N = 58)

Characteristic	Result
Age (y)	42 (24-71)
Female sex	55 (95)
White race	58 (100)
Device type	
Amplatzer*	32 (55)
Helex†	26 (45)
Cardiovascular	
Coronary artery disease	1 (2)
Heart disease, unspecified	2 (3)
Hyperlipidemia	9 (16)
Hypertension	10 (17)
Pulmonary hypertension	1 (2)
Psychiatric	
Attention deficit–hyperactivity disorder	2 (3)
Anxiety	16 (28)
Depression	19 (33)
Panic attacks/panic disorder	3 (5)
Posttraumatic stress disorder	4 (7)
Autoimmune	
Celiac disease	3 (5)
Multiple sclerosis	2 (3)
Rheumatoid arthritis	2 (3)
Hashimoto thyroiditis	1 (2)
Thyroid	
Hypothyroidism	6 (10)
Hyperthyroidism	1 (2)
Hyperparathyroidism	1 (2)
Other	
Chronic fatigue syndrome	3 (5)
Chronic kidney disease	2 (3)
Diabetes mellitus	2 (3)
Type 2 diabetes	1 (2)
Fibromyalgia	5 (9)
Hepatitis/nonalcoholic steatohepatitis	2 (3)
Sleep apnea	4 (7)

Values are presented as median (range) or n (%). *St Jude Medical Corporation, St Paul, Minn. †W. L. Gore & Associates, Inc, Medical Products Division, Flagstaff, Ariz.

possible score achieved. In step 2, items in the same scale were averaged together to create the 8 scale scores.

Patient characteristic data are reported as absolute numbers with percentages. Quantitative assessment of SF-36 numbers in the phase 1 group is only qualitatively related because validation cohort raw data are not available. Prospective SF-36 results compared preimplant and postimplant scores using paired *t* tests with significance set at the 95% confidence interval.

RESULTS

During the study period, 58 consecutive patients underwent ASD/PFO device removal. Baseline characteristics are detailed in Table 1. The median age was 42 years (range, 24-71 years) and the majority were women (n = 55 [95%]). Slightly more patients had the ASO device (n = 32 [55%]) compared with the HSO device (n = 26 [45%]).

All patients had documented positive dermatological testing to nickel. As demonstrated in Figure 1, nearly all patients had patch testing and 72% patients underwent both patch and prick skin testing. Various combinations of positive skin testing resulted in positive studies. Nearly 20% of patients were patch-negative and scratch-positive.

Surgical approach was right minithoracotomy in 54 patients (93%), whereas 4 patients (7%) received sternotomy, with 2 of the latter patients requiring concomitant procedures (coronary unroofing and pericardiectomy). After removal of the device, 53 patients (91%) had primary, direct repair of the residual defect, whereas 5 patients (9%) necessitated patch closure. There were no mortalities. Four patients (7%) had postoperative complications: supraventricular rhythms with prolonged initial hospitalization (n = 2) and refractory serous pericarditis requiring subsequent pericardiectomy (n = 2).

Of 58 surgical patients, 45 patients responded to our provider-generated and SF-36 surveys and submitted responses. The most common indications for device placement were headaches (migraines) and history of stroke or transient ischemic attacks (Table 2). The temporal relationship from device implantation to symptom onset ranged from 1 day to 1 year, with 20 patients (44%) occurring in <48 hours. Despite symptoms occurring relatively early postimplantation, patients were managed medically for a median of 8 years (range, 6 months-18 years) before being assessed for device removal. As depicted in Table 3, a plethora of postimplant symptoms were reported, including fatigue (n = 37 [82%]), chest pain (n = 35 [78%]), migraine/headache (n = 33 [73%]), palpitations (n = 26 [58%]), dyspnea (n = 22 [49%]), and skin rash/arthralgia (n = 21 [47%]).

According to our provider-generated qualitative survey, 26 patients (58%) viewed their quality of life after device implantation as poor with 31 (69%) expressing dissatisfaction postimplant. Following device removal, all patients reported enhanced satisfaction and improvement in symptoms, with 18 of 44 postoperative patients (42%) noting complete resolution.

To more formally quantify changes in quality of life, 32 accessible patients retrospectively filled out SF-36 surveys after at least 5 postoperative months (Figure 2). The average scores for the 8 domains were similar to the validation cohort. Unfortunately, these data are limited without preoperative scores. Nevertheless, when looking at the question in the SF-36 regarding rating health in general now versus 1 year ago, 21 patients responded "much better," 3 were "somewhat better," 8 were "about the same," 3 were "somewhat worse," and none were "much worse."

To better assess quality of life, a secondary phase was recently initiated that enrolled 12 patients to prospectively

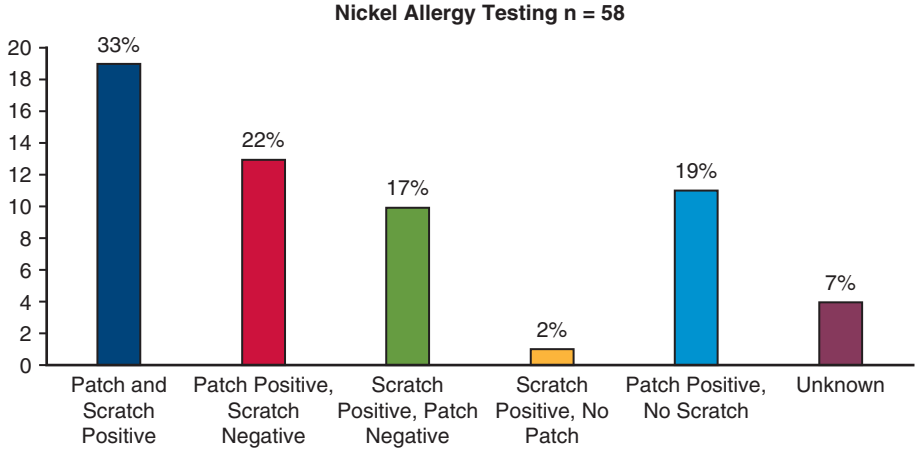

FIGURE 1. Dermatologic assessment of nickel allergy by patch and scratch testing amongst the cohort of 58 patients.

and longitudinally follow their physical and mental health by serially recording SF-36 scores. The preoperative scores in all subgroups were substantially lower than the validation group, indicating significant disability. Following removal of the device, nearly all scores across both domains were improved as early as 1 month and further improved or sustained at 6-month follow-up, with the majority being higher than those of the validation group (Table 4).

DISCUSSION

Metal hypersensitivity reactions to implanted devices are challenging to evaluate and manage. As a result of few large study cohorts, great variation in symptom presentation, and a lack of diagnostic criteria that necessitate the offending object being removed, these patients are often treated conservatively for years. This series represents the largest reported cohort of ASD/PFO device surgical explant patients with documented dermatologic evidence of nickel allergy and severe refractory symptoms suggestive of device syndrome or systemic metal hypersensitivity reaction.

TABLE 2. Indications for device placement (N = 45)

Indication	n
Headaches/migraines	30
History of stroke/transient ischemic attack	14
Asymptomatic	1
Other	17
Vertigo/dizziness	5
White spots on brain magnetic resonance imaging scan	2
Shortness of breath	2
Fainting	2
Weakness	2
Numbness	2
Blood pressures	1
Chest pain	1
Failed 6-min walk test	1
Fatigue	1
Decreased endurance	1
Multiple sclerosis symptoms	1
Significant family history of stroke	1
Vision disturbance	1
Brain tumor resection	1

With the recent completion of 2 randomized controlled trials and subsequent FDA approval of the ASO device for PFO closure for cryptogenic stroke,[4,20] the number of devices being placed is expected to increase. All intracardiac shunt closure devices have nickel as a component. There have been numerous reports of nickel leaching into the bloodstream and device corrosion has been reported that can lead to type-4 hypersensitivity reactions and immune-mediated toxicity resulting in hypersensitivity reactions.[21,22] The scope of the problem is immense and understanding the population at risk, symptomatology, and management is important.

Why does it appear that there is an epidemic of this problem in the Intermountain West? This is, in part, related to a disproportionately large per capita number of implants in Utah.[6] In particular, there was a single cardiologist who historically placed >300 devices per year for more than 10 years. As such, Utah (and the Salt Lake Valley) have a very concentrated population of young women with PFO who had these devices placed. Furthermore, the University of Utah has a particularly robust Allergy-Immunology Clinic that has opened its doors to patients who had often been shuffled for years through the health care system.

As demonstrated in this series, the management conundrum is manifest by a large temporal range between initial implant and removal as well as the diverse spectrum of debilitating symptoms. Whereas many had chest pain,

TABLE 3. Symptoms after device placement (N = 45)

Symptom	n
Pain	
Chest pain	35
Headaches/migraines	33
Arthritis/joint pain	9
Muscle/body aches	6
Pain, unspecified	2
Fibromyalgia	1
Bladder pain	1
Stomach pain	1
Neurologic	
Dizziness/vertigo	6
Blurred vision	2
Numbness	3
Tremors	2
Hemiplegic migraines	2
Aura	1
Balance	1
Brain fog	1
Double vision	1
Neuropathy	1
Ocular migraines	1
Memory issues	1
Burning sensation	1
Vision issues, unspecified	1
Weakness	1
Gastrointestinal	
Gastrointestinal, unspecified	9
Gallbladder problems/removal	5
Nausea	4
Vomiting	4
Diarrhea	3
Dermatologic	
Skin rash	21
Itching	2
Cardiovascular	
Palpitations	26
Breathlessness on exertion	22
Tachycardia	4
Hypertension	2
Fainting	2
Arrhythmia	2
Fluctuating blood pressure	1
Stenosis in carotid artery	1
Bubbles still present on study	1
Varicose veins	1
Pericarditis	1
Pleurisy	1
Cold hands and feet	1
Increased oxygen requirements	1
Abnormal echocardiogram	1
Systemic	
Fatigue	37
Paleness	1
Fever	1
Other	
Depression	2
Insomnia	2
Fluid in bones	1
Food allergies	1
Interstitial cystitis	1
Loss of appetite	1
Open sores	1
Reynaud syndrome	1
Sinus infections	1
Gastric sleeve placed	1
Kidney stones	1
Kidney problems, unspecified	1
Liver problems, unspecified	1
Appendix removed	1
Hot flashes	1
Dry skin	1
Eye swelling	1

fatigue, and headaches, others experienced arthralgias and gastrointestinal symptoms—with several of the latter patients undergoing cholecystectomy for ill-defined biliary colic. Fewer than one third of patients had skin rashes as a presenting symptom. The onset of symptoms can be from few days to months, if not years, after device placement. The nonspecific symptoms and varied natural history contribute to the delay in diagnosis and alternative medical management with trials of anti-inflammatory, antiplatelet, steroids, and antianxiety medications. Many patients had seen a variety of specialists, including cardiology, rheumatology, psychiatry, gastroenterology, and endocrinology before seeing a dermatologist or cardiac surgeon.

The surgical approach through right minithoracotomy was utilized for the majority of patients. This access defused some of the anxiety that many patients had related to undergoing heart surgery and reduced the potential use of sternal wires that also contain nickel. Visualization was adequate and devices could be safely removed and defects closed with no evidence of residual shunting and low morbidity. The 2 cases of refractory pericarditis requiring pericardiectomy were out of proportion to our experience with other procedures performed through similar access (ie, minimally invasive mitral, tricuspid, and aortic valve interventions). One could speculate that this patient population has a predilection for hyperinflammatory responses that could fuel pericarditis.

Given the paucity of robust evidence with which to guide practice, our series provides reasonable evidence for clinicians with patients with metal hypersensitivity concerns after ASD/PFO closure. Patch testing still remains the

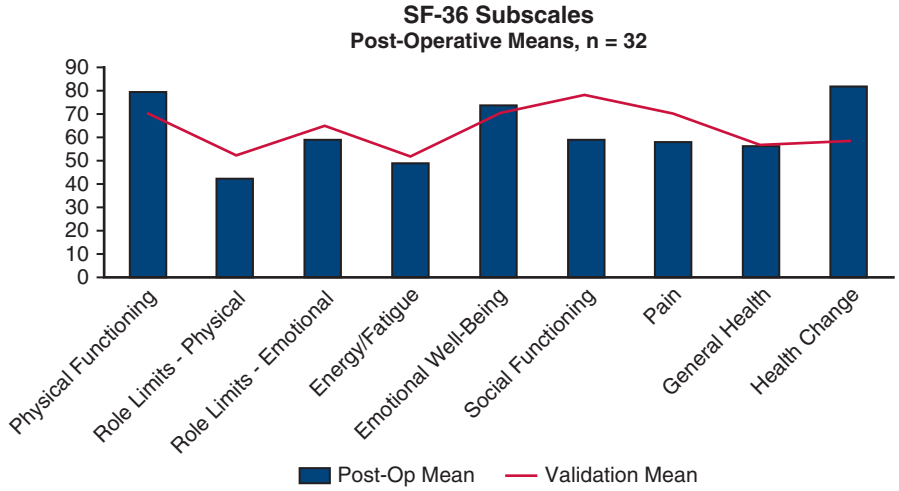

FIGURE 2. The 36-Item Short Form Health Survey[18,19] (*SF-36*) quality of life results in the study population retrospectively available for survey (n = 32) compared with population-based validation means. *Post-op*, Postoperative.

standard for evaluating patients with suspected metal allergy because it is simple to perform, widely available, and offers a variety of possible testing.[12] Scratch or prick testing should be performed as well to identify unrecognized immunoglobulin E-mediated metal contact urticaria. Indeed, in our patient cohort, there was a sizeable group (17%) of patients who were patch-negative, but scratch/prick-positive and benefited from device removal.

Unfortunately, preimplant testing is neither recommended nor reliable in this patient population. The vast majority of patients with metal implants (even with documented sensitivities) have no implant-related adverse events.[23] Negative preimplant testing only reflects the current state of allergy, and does not predict future hypersensitivity resulting from implantation of a device.[12] Patient reports of metal allergy before implantation are associated with decreased functional and mental health outcomes and postoperative morbidity.[24,25] Combined with our current report, select patients (eg, those with a history of cutaneous reactions to inexpensive jewelry) should be considered for preimplant metal testing in coordination with a contact dermatitis specialist.

An issue that is difficult to definitively reconcile relates to the large number of other intracardiac devices that contain nickel yet apparently do not initiate this problem. Compared with patients who receive stented biologic valves (either surgical or transcatheter) or coronary stents, our cohort represents a unique patient population of predominantly young, white women with PFO defects and a history of potential nickel sensitization. An additional, perhaps

TABLE 4. The 36-Item Short Form Health Survey[18,19] (SF-36) scores in prospectively enrolled patients (n = 12 preoperative (pre-op), n = 11 1-month postoperative (post-op), and n = 8 6-months post-op)

SF-36 subscale	Validation	Pre-op (n = 12)	1-mo post-op (n = 11)	6-mo post-op (n = 8)
Physical functioning	71	44 ± 5.7	65 ± 3.6*	80 ± 9.0†
Role limits, physical	53	11 ± 8.4	16 ± 8.9	59 ± 16.3†
Role limits, emotional	66	33 ± 10.1	79 ± 8.5*	88 ± 12.5†
Energy/fatigue	52	15 ± 4.2	30 ± 4.2*	62 ± 6.9†
Emotional well-being	70	58 ± 4.5	76 ± 3.4*	81 ± 6.0†
Social functioning	79	41 ± 7.1	47 ± 5.8	78 ± 7.4†
Pain	71	36 ± 4.6	39 ± 3.6	74 ± 9.8†
General health	57	26 ± 5.1	50 ± 4.2*	59 ± 7.6†
Health change	59	27 ± 5.7	70 ± 4.2*	91 ± 4.6†

Values are presented as mean ± standard error (validation group is mean only). *$P < .05$, pre-op versus 1-mo post-op. †$P < .001$, pre-op versus 6 mo using the 8 participants with full longitudinal data.

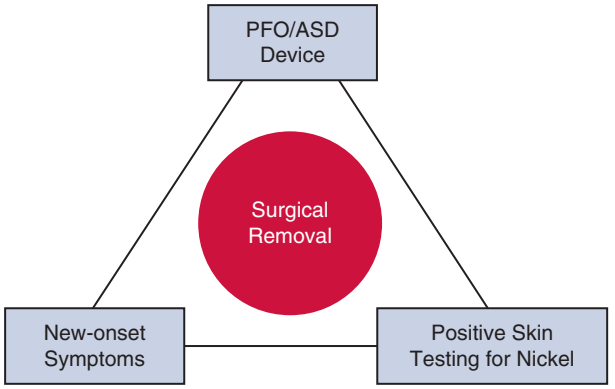

FIGURE 3. Current approach to management of patients with symptomatic patent foramen ovale or atrial septal defect (*PFO/ASD*) device rejection. Enhanced quality of life after surgical explant necessitates linking 3 defined points: the presence of the PFO/ASD device, symptoms (preferentially new-onset symptoms that occur relatively soon after device placement), and positive dermatologic evidence of nickel hypersensitivity either by patch and/or scratch testing.

more hypothesis-driven explanation relates to the physical concentration of nitinol in the respective devices and their ability to leach nickel. For example, a typical bioprosthetic aortic valve (including transcatheter valves) have, amongst other alloys, roughly 15% nickel. In comparison, the pure nitinol frames of the ASO and HSO devices have a nickel concentration closer to 55%. In vitro elution of nickel from 3 different closure devices (ASO, HSO, and Septal [W. L. Gore & Associates, Flagstaff, Ariz]) appeared to be proportionally related to the amount of exposed nickel, with the ASO having the highest nickel levels.[22] Our patient experience suggests that both ASO and HSO devices are susceptible to this complication. Extending this logic to other intracardiac devices, one could surmise that the cumulative volume of exposed nickel is much lower than that which is present in the occluding devices. Quite possibly, the less nickel released with nonoccluder devices would provide less substrate for sensitization (either de novo or recurrent).

This study has several additional limitations and represents an evolution of our experience. Most patients are retrospectively reviewed with only 11 patients being prospectively followed for patient-reported outcomes. Hence, preoperative objective assessment of their quality of life scores was not available and subjective scores based on questionnaires can be biased. That said, the general experience in the postoperative clinic, ultimately leading to this study, as well as the result of our provider-generated qualitative surveys, was of marked, favorable change in quality of life postexplant. Although we cannot completely rule out the possibility of a placebo effect, this anecdotal experience was robustly supported by the prospectively collected data. When compared with the SF-36 validation cohort, preoperative quality of life reflected the debilitated state of these patients. Despite undergoing surgery, the scores were profoundly improved compared with their preoperative state, even 1 month postoperatively.

An additional, important caveat that influences the decision process preoperatively is related to the denominator. We fully acknowledge that the number of patients with nickel allergies and ASD/PFO devices who experience no symptoms is unknown. As such, and based on our experience, our current approach requires intersection of 3 elements: presence of the device, positive dermatologic testing, and symptoms (Figure 3). It can often be challenging to link all 3 of these points, and we will not offer surgery if we are unable to do so. If possible, we try to distinguish symptoms postimplant from those that existed preimplant. For example, headache is a common symptom, but is the quality/type of headache different? The ideal story is the development of new-onset symptoms within a short time period after device implantation. Indeed, this was the case in 67% of patients. More recently, we have extended the temporal relationship to include patients that have developed symptoms that are months, if not years, following device placement. There are a number of patients who presented with typical symptoms, yet their dermatologic testing was either negative or very weakly positive. Although it is unclear whether these patients would benefit from device removal (perhaps nonimmune mediated), we remain reluctant to extend our explant criteria to that patient population.

CONCLUSIONS

Patients with nickel allergy and severe refractory symptoms after implantation with an ASD/PFO device experience resolution of symptoms after device explantation with improved quality of life. Device-related symptoms are debilitating. Not only should nickel allergy be discussed before device insertion, but providers should also have a low threshold for considering explant as definitive treatment.

Webcast

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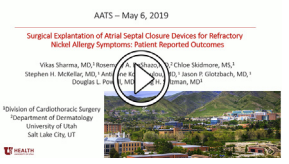

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

The authors thank the dedicated staff and members of the Division of Cardiothoracic Surgery at the University of Utah. The authors also thank Jamie Heaton, Catherine Mihlfeith, Michele Tyson, Tonna Russell, Cole Johnson, Thomas Lewis, Ike Collard, and Erik Sivertsen for their engagement and provision of compassionate care.

References

1. Karamlou T, Diggs BS, Ungerleider RM, McCrindle BW, Welke KF. The rush to atrial septal defect closure: is the introduction of percutaneous closure driving utilization? *Ann Thorac Surg*. 2008;86:1584-9.
2. Handke M, Harloff A, Bode C, Geibel A. Patent foramen ovale and cryptogenic stroke: a matter of age? *Semin Thromb Hemost*. 2009;35:505-14.
3. Saver JL, Carroll JD, Thaler DE, Smalling RW, MacDonald LA, Marks DS, et al. Long-term outcomes of patent foramen ovale closure or medical therapy after stroke. *N Engl J Med*. 2017;377:1022-32.
4. Sondergaard L, Kasner SE, Rhodes JF, Andersen G, Iversen HK, Nielsen-Kudsk JE, et al. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. *N Engl J Med*. 2017;377:1033-42.
5. Du ZD, Hijazi ZM, Kleinman CS, Silverman NH, Larntz K, Amplatzer I. Comparison between transcatheter and surgical closure of secundum atrial septal defect in children and adults: results of a multicenter nonrandomized trial. *J Am Coll Cardiol*. 2002;39:1836-44.
6. Verma SK, Tobis JM. Explantation of patent foramen ovale closure devices: a multicenter survey. *JACC Cardiovasc Interv*. 2011;4:579-85.
7. Jones TK, Latson LA, Zahn E, Fleishman CE, Jacobson J, Vincent R, et al. Results of the U.S. multicenter pivotal study of the HELEX septal occluder for percutaneous closure of secundum atrial septal defects. *J Am Coll Cardiol*. 2007;49:2215-21.
8. Schram SE, Warshaw EM, Laumann A. Nickel hypersensitivity: a clinical review and call to action. *Int J Dermatol*. 2010;49:115-25.
9. Warshaw EM, Maibach HI, Taylor JS, Sasseville D, DeKoven JG, Zirwas MJ, et al. North American contact dermatitis group patch test results: 2011-2012. *Dermatitis*. 2015;26:49-59.
10. Goldenberg A, Vassantachart J, Lin EJ, Lampel HP, Jacob SE. Nickel allergy in adults in the U.S.: 1962 to 2015. *Dermatitis*. 2015;26:216-23.
11. Rietschel RL, Fowler JF, Warshaw EM, Belsito D, DeLeo VA, Maibach HI, et al. Detection of nickel sensitivity has increased in North American patch-test patients. *Dermatitis*. 2008;19:16-9.
12. Schalock PC, Crawford G, Nedorost S, Scheinman PL, Atwater AR, Mowad C, et al. Patch testing for evaluation of hypersensitivity to implanted metal devices: a perspective from the American Contact Dermatitis Society. *Dermatitis*. 2016;27:241-7.
13. Dasika UK, Kanter KR, Vincent R. Nickel allergy to the percutaneous patent foramen ovale occluder and subsequent systemic nickel allergy. *J Thorac Cardiovasc Surg*. 2003;126:2112.
14. Fukahara K, Minami K, Reiss N, Fassbender D, Koerfer R. Systemic allergic reaction to the percutaneous patent foramen ovale occluder. *J Thorac Cardiovasc Surg*. 2003;125:213-4.
15. Vincent RN, Raviele AA, Diehl HJ. Single-center experience with the HELEX septal occluder for closure of atrial septal defects in children. *J Interv Cardiol*. 2003;16:79-82.
16. Wertman B, Azarbal B, Riedl M, Tobis J. Adverse events associated with nickel allergy in patients undergoing percutaneous atrial septal defect or patent foramen ovale closure. *J Am Coll Cardiol*. 2006;47:1226-7.
17. Saluja SS, Davis CL, Chong TA, Powell DL. Contact urticaria to nickel: a series of 11 patients who were prick test positive and patch test negative to nickel sulfate 2.5% and 5.0. *Dermatitis*. 2016;27:282-7.
18. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item health survey 1.0. *Health Econ*. 1993;2:217-27.
19. 36-Item short form survey from the RAND Medical outcomes study. Available at: http://www.rand.org/health/surveys_tools/mos/mos_core_36item.html. Accessed November 27, 2019.
20. Mas JL, Derumeaux G, Guillon B, Massardier E, Hosseini H, Mechtouff L, et al. Patent foramen ovale closure or anticoagulation vs. antiplatelets after stroke. *N Engl J Med*. 2017;377:1011-21.
21. Ries MW, Kampmann C, Rupprecht HJ, Hintereder G, Hafner G, Meyer J. Nickel release after implantation of the Amplatzer occluder. *Am Heart J*. 2003;145:737-41.
22. Verma DR, Khan MF, Tandar A, Rajasekaran NS, Neuharth R, Patel AN, et al. Nickel elution properties of contemporary interatrial shunt closure devices. *J Invasive Cardiol*. 2015;27:99-104.
23. Kim HJ, Shin JU, Lee J, Lee H, Jin S, Kim SH, et al. Positive reactions to nickel on a patch test do not predict clinical outcome of nickel alloy-based atrial septal defect occluder implantation. *Dermatology*. 2015;230:184-8.
24. 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.
25. Perruccio AV, Davis AM, Hogg-Johnson S, Badley EM. Importance of self-rated health and mental well-being in predicting health outcomes following total joint replacement surgery for osteoarthritis. *Arthritis Care Res (Hoboken)*. 2011;63:973-81.

Key Words: atrial septal defect, occluding devices, patent foramen ovale, nickel hypersensitivity

APPENDIX E1. ATRIAL SEPTAL DEFECT (ASD)/ PATENT FORAMEN OVALE (PFO) QUESTIONNAIRE

1. Do you have a primary care physician? If so, what is their name and place of practice.
2. Do you have a cardiologist? If so, please indicate their name and place of practice.
3. Were you diagnosed with ASD or PFO?
4. What was the indication for having the device placed/ what were your symptoms?

   Headaches/migraines

   History of stroke

   Asymptomatic

   Other
5. What device did you have placed?

   Amplatzer

   Helex
6. Did you have any complications during the placement of the device?

   Bleeding

   Migration of device

   Other
7. What were your symptoms after the device was placed, if any?

   Chest pain

   Headaches

   Breathlessness on exertion

   Palpations

   Skin rash

   Fever

   Fatigue

   Asymptomatic

   Other
8. How long after the placement of the device did your symptoms begin, if any?
9. How would you rate your quality of life after the device was placed?

   Poor

   Fair

   Good

   Very good

   Excellent
10. How satisfied were you with your level of well-being after the placement of the device?

    Not at all satisfied

    Somewhat satisfied

    Very satisfied
11. Do you have allergies to jewelry?
12. Do you have a documented nickel allergy?
13. Approximately when did you have your allergy testing, or your patch/scratch testing done?
14. Did you have an ASD/PFO repair device removal surgery?
15. How have your symptoms improved after surgery?

    Completely improved

    Are somewhat better

    About the same

    Somewhat worse

    Much worse
16. How satisfied were you with your level of well-being after the removal of device?

    Not at all satisfied

    Somewhat satisfied

    Very satisfied