

Correlation between metal allergy and treatment outcomes after ankle fracture fixation

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ABSTRACT

Purpose. To determine correlation between metal hypersensitivity and long-term foot and ankle function and pain after internal fixation using stainless steel implants.

Methods. 60 men and 46 women (mean age, 47 years) who underwent internal fixation for ankle fractures completed a questionnaire 13 to 38 (mean, 26) months after surgery to assess their existing medical condition, history of metal hypersensitivity, problems and outcome of the implant (revision or removal), and the American Academy of Orthopaedic Surgeons (AAOS) foot and ankle score. A subset of 12 men and 15 women then underwent patch testing for metal hypersensitivity to molybdenum, chromium, iron, manganese, and nickel. Patients with positive and negative reactions were compared.

Results. 21 of the 106 patients underwent removal of the metal implants. The AAOS score was not associated with any of the variables, except for a history of metal hypersensitivity from dental implants and irritation around the surgical scar. Multiple linear regression analysis showed that

only irritation around the surgical scar remained associated with poorer AAOS scores. Five of the 27 tested patients had a positive reaction. The mean AAOS scores did not differ significantly between patients with positive and negative reactions (34 vs. 31, $p=0.73$). Gender was not associated with the test results ($p=0.63$). None of the 5 patients with a positive reaction underwent revision surgery or reported any history of asthma or metal hypersensitivity. Of the 27 patients, one of the 8 who reported itching, irritation, redness or rash around the surgical scar had a positive reaction, compared to 4 of 19 patients who reported no such symptoms ($p=1$). Two of the 27 patients reported development of eczema after fixation, one of whom had a positive reaction. Only one of the 27 patients reported a history of metal hypersensitivity to jewellery, but had a negative reaction..

Conclusion. Neither a history of metal hypersensitivity nor positive patch testing correlated with poor outcomes after internal fixation for ankle fractures using stainless steel implants.

Key words: dermatitis, allergic contact; fracture fixation, internal; outcome assessment (health care); patch tests; stainless steel

INTRODUCTION

Ankle fractures are commonly treated with open reduction and internal fixation using metal implants.¹ Long-term outcomes in 52% to 83% of patients are good to excellent,²⁻⁴ yet 24 to 63% of patients had poor outcomes with persistent pain, swelling or stiffness.^{2,5,6}

Stainless steel is commonly used for internal fixation.⁷ However, products of its degradation may affect outcomes mediated by metal hypersensitivity.⁸ Metal corrosion occurs in contact with biological fluids through mechanical wear, physiochemical corrosion, or both.⁸ Although ions released by metal corrosion are not antigenic, they may form complexes with proteins in the blood and stimulate hypersensitivity reactions.⁹ The presence of metal implants can convert patients from non-sensitive to sensitive to metals.^{9,10}

Persistent pain after internal fixation with metal implants may relate to metal hypersensitivity.¹¹ 31% of patients reported pain overlying tibial and fibular hardware at postoperative month 6; 50% of them reported a significant decrease in their pain scores from 6 ± 3 to 3 ± 3 after implant removal.¹¹

Metal hypersensitivity is not uncommon. About 10 to 15% of the population are sensitive to metals, mostly to nickel, cobalt, and chromium.⁸ Modern stainless steel implants have a very low zinc content and contain 13 to 16% nickel, 17 to 19% chromium, and 2 to 4% molybdenum.⁸ We evaluated outcomes of 106 patients who underwent ankle fixation using a stainless steel implant. 27 of them were patch-tested for metal hypersensitivity to determine any correlation between metal hypersensitivity and long-term foot and ankle function and pain after internal fixation.

MATERIALS AND METHODS

This study was approved by the Sydney South West Area Health Service Human Research Ethics Committee. 205 patients aged 18 to 80 years who underwent ankle or tarsal fixation with a stainless steel implant at Liverpool Hospital between May 2007 and August 2009 were sent a questionnaire. The questionnaire contained 10 questions enquiring patient's existing medical conditions, history of metal hypersensitivity (from jewellery, watches or dental fillings), and problems and outcome with the implant (revision or removal). The American Academy of Orthopaedic Surgeons (AAOS) foot and ankle score was also assessed using only 25 questions. It

measures functional outcome and pain around the ankle and has a high validation score¹²; lower scores indicate worse outcome, and the maximum possible score is 56.

60 men and 46 women (mean age, 47 years) completed the questionnaire via telephone or mail 13 to 38 (mean, 26) months after surgery. The remaining 54 men and 45 women aged 18 to 78 (mean, 40) years were excluded, as they were not contacted (n=63), refused to participate (n=16), unable to speak English (n=19), or mentally disabled (n=1).

A subset of 12 men and 15 women then underwent patch testing for metal hypersensitivity to molybdenum, chromium, iron, manganese, and nickel. Each patient's skin was photographed before and after the patch test, which lasted 48 to 72 hours. According to the International Contact Dermatitis Research Group guidelines,¹³ skin reactions were classified as (1) weak positive reaction: homogeneous redness throughout the entire test area, non vesicular reaction (+), (2) moderate positive reaction: homogeneous redness throughout the entire test area, oedematous or vesicular reaction (++), (3) severe positive reaction: intense homogeneous redness throughout the entire test area, bullous or ulcerative reaction (+++), and (4) negative reaction: an irritant reaction, doubtful or negative reading.

Patients with positive and negative reactions were compared in terms of patient characteristics and AAOS scores using the Student's *t*-test (for continuous variables) and the Chi-squared test or Fisher's exact test (for categorical variables). Multiple backward stepwise linear regression was used to assess the correlation between patient characteristics and AAOS scores. A *p* value of <0.05 was considered statistically significant.

RESULTS

The mean AAOS score of the 106 patients was 39 (median, 47; standard deviation, 19; range, -16 to 56, Table 1). 21 of the patients underwent removal of the metal implants, owing to discomfort and/or limitation of movement (n=10), breakage of the implant (n=2), chronic infection and/or failure of the surgical site to heal (n=2), pain and swelling (n=1), and uncertain reasons (n=6). Two additional patients were awaiting removal of the implants owing to pain and swelling. The AAOS score was not associated with any of the variables, except for a history of metal hypersensitivity from dental implants and irritation around the surgical scar (Table 2). Multiple linear regression analysis showed that only irritation

Table 1
Patient characteristics

Characteristic	No. (%) of patients who responded (n=106)	No. (%) of patients who were patch- tested (n=27)
Gender		
Male	60 (57)	12 (44)
Female	46 (43)	15 (56)
Age groups (years)		
19–29	21 (20)	-
30–39	21 (20)	1 (4)
40–49	17 (16)	5 (19)
50–59	14 (13)	6 (22)
60–69	26 (25)	12 (44)
70–79	7 (7)	3 (11)
Existing medical conditions		
Allergies	20 (19)	7 (26)
Asthma	11 (10)	1 (4)
Eczema	8 (8)	3 (11)
History of metal hypersensitivity to		
Jewellery	17 (16)	1 (4)
Dental implants	3 (3)	-
Revision surgery	22 (21)	-
Removal of metal implants	21 (20)	4 (15)
Revision of improperly inserted pin	1 (1)	-
American Academy of Orthopaedic Surgeons foot and ankle score		
-20 to -11	1 (1)	1 (4)
-10 to -1	4 (4)	0 (0)
0 to 9	9 (9)	4 (15)
10 to 19	5 (5)	2 (7)
20 to 29	7 (7)	1 (4)
30 to 39	14 (13)	8 (30)
40 to 49	22 (21)	8 (30)
50 to 59	44 (42)	3 (11)

Table 2
Association between variables and foot and ankle scores

Variable	No. (%) of patients who responded (n=106)	p Value
Age		0.08
Sex		0.48
Existing medical conditions		
Allergies	20 (19)	0.82
Asthma	11 (10)	0.52
Eczema	8 (8)	0.28
History of metal hypersensitivity to		
Jewellery	17 (16)	0.13
Dental implants	3 (3)	0.02
Irritation around the surgical scars	28 (26)	0.0002
Revision surgery	22 (21)	0.32
Presence of additional metal implants	15 (14)	0.11
Irritation around the additional implant sites	1 (1)	0.23

around the surgical scar remained associated with poorer AAOS scores ($p=0.0002$).

Patients who were patch-tested ($n=27$) were older (58 ± 11 vs. 43 ± 16 years, $p<0.0001$) and had lower mean AAOS score (31 ± 18 vs. 42 ± 19 , $p=0.01$) than those who were not patch-tested ($n=79$). Five of the 27 tested patients had a positive reaction (Table 3). The mean AAOS scores did not differ significantly between patients with positive and negative reactions (34 ± 17 vs. 31 ± 18 , $p=0.73$). Gender was not associated with the test results ($p=0.63$). None of the 5 patients with positive reactions underwent revision surgery or reported any history of asthma or metal hypersensitivity to jewellery, watches, chains or dental implants. Of the 27 patients, one of the 8 who reported itching, irritation, redness or rash around the surgical scar had a positive reaction, compared to 4 of 19 patients who reported no such symptoms ($p=1$). Two of the 27 patients reported development of eczema after fixation, one of whom had a positive reaction. Only one of the 27 patients reported a history of metal hypersensitivity to jewellery, but had a negative reaction.

DISCUSSION

The association between irritation around the surgical scar and poorer AAOS scores could be accounted for by allergic contact dermatitis in skin overlying metal implants,^{14,15} which may indicate metal hypersensitivity, but there was no such association on patch testing in our study. In 3 nickel-allergic patients who underwent fixation using stainless steel implants, there was no complication after one year and no significant difference in the prevalence of implant revision between those allergic and not allergic to metals.^{16,17} Metal hypersensitivity also does not influence the development of pain.⁹

In our study, a discrepancy between the proportion of women and men reporting irritation, rash, redness or itching in reaction to jewellery was significant (26% [12/46] vs. 8% [5/60], $p=0.017$). This may have been attributed to the fact that women are more commonly exposed to jewellery.¹⁸ Of 3 men and 2 women of the 27 patients tested positive for metal hypersensitivity, the number of women tested positive would have been higher if jewellery was a cause. Thus, increased exposure to jewellery merely increases women's awareness of their allergy status and does not induce hypersensitivity, as the nickel content in jewellery is small. The amount of nickel exposure directly correlates with its ability to sensitise humans.¹⁹ Nickel is the most common

Table 3
Patients with a positive metal patch testing reaction

Sex/age (years)	Time since surgery (months)	Severity of reaction	Sensitivity to	Allergies	Eczema	Irritation around scars
M/44	23	Moderate (++)	Nickel	No	Yes	Yes
F/47	38	Weak (+)	Manganese, nickel	Yes, grasses	No	No
M/35	20	Moderate (++)	Nickel	No	No	No
M/63	16	Weak (+)	Nickel, chromium	No	No	No
F/65	17	Moderate (++)	Chromium	No	No	No

metal sensitizer in humans; about 14% of the population display dermal reactivity to this metal,⁸ Cobalt and chromium are the next most common metal sensitizers; the prevalence of chromium hypersensitivity is 2.4 to 5.9%,²⁰ which is lower than the 7.4% in our study.

In our study, 2 men reported development of eczema after fixation; one of whom was sensitive to nickel. Another study reported 3 previously non-sensitive subjects that became sensitized to metal implants and developed eczema.²¹

There has been association between metal hypersensitivity and functional outcomes of metal implants.^{8,22–27} In our study, neither a history of metal hypersensitivity nor positive patch testing correlated with poor AAOS scores, but the number of patients was small. Patients who were patch-tested were not representative of the entire cohort; they were older and had significantly lower AAOS scores than those not patch-tested. The use of patch testing to determine metal hypersensitivity has limitations. Although the test is the cheapest and least invasive, its diagnostic

utility is questionable. Cutaneous sensitivity may not necessarily reflect deep-tissue sensitivity. Patients who lack cutaneous metal sensitivity in patch tests may nevertheless display moderate-to-strong inflammatory reactions in peri-implant tissue.²⁸ Nonetheless, it is unclear whether this is due to diagnostic inaccuracy of patch tests or physiological differences in the immunological responses to cutaneous and deep-tissue sensitivity. Ideally, patients should be tested before and after surgery to gauge the pre-surgical allergic state, as implantation of a metal prosthesis may induce both tolerance and hypersensitivity to metals.^{29–31} The patches themselves may also induce cutaneous sensitivity in previously insensitive patients,³² although this risk is extremely low and has only been reported with strong sensitizers.¹⁹ Larger trials exploring associations between metal hypersensitivity, poor outcomes, and risk factors should be undertaken. The influence of preoperative allergy status, the duration of the implant *in situ*, and the type of prosthesis should all be assessed.¹⁰

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