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Risk Factors Associated With Nonunion After Elective Foot and Ankle Reconstruction: A Case-Control Study

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ABSTRACT

Postoperative nonunion is not uncommon in the lower extremity, and significant morbidity can be associated with nonunion of the foot and ankle after surgical reconstruction. For the purposes of the present study, we retrospectively reviewed and compared a cohort of patients who had undergone elective foot and ankle reconstruction to better assess the modifiable risk factors associated with postoperative nonunion. We hypothesized that the presence of endocrine and metabolic abnormalities are often associated with nonunion after foot and ankle surgical reconstruction. We formulated a matched case-control study that included 29 patients with nonunion and a control group of 29 patients with successful fusion to assess the prevalence of certain modifiable risk factors known to have an association with nonunion after foot and ankle arthrodesis. The modifiable risk factors assessed included body mass index, tobacco use, diabetes mellitus, vitamin D abnormality, thyroid dysfunction, and parathyroid disease. A statistically significant ($p < .05$) difference was found between the 2 groups for endocrine and metabolic disease diagnoses in the medical records of the 58 patients identified. Thus, 76% versus 26% ($p < .05$) of patients experienced nonunion in the endocrine disease group versus the nonendocrine disease group, respectively. Patients with vitamin D deficiency or insufficiency were 8.1 times more likely to experience nonunion (95% confidence interval 1.996 to 32.787). No statistically significant differences were found between the groups in terms of age, sex, tobacco use, body mass index, or procedure selection ($p = .56$, $p = .43$, $p = .81$, $p = .28$, and $p = 1.0$, respectively). A greater prevalence of endocrine abnormalities, in particular, vitamin D deficiency and insufficiency, was associated with nonunion after elective foot and ankle reconstruction. Patients with such abnormalities appear to have a greater risk of developing nonunion after arthrodesis procedures.

Arthrodesis is a commonly performed procedure in the foot and ankle. Elective arthrodesis is performed by surgeons to address varying degrees of deformity and degenerative joint disease. The specific indications, techniques, and complications related to arthrodesis have been well described for the anatomic zones of the lower extremity, including the forefoot, midfoot, hindfoot, and ankle (1–13). A specific complication that remains one of the most challenging dilemmas after attempted arthrodesis is postoperative nonunion. The development of nonunion after elective foot and ankle reconstruction can lead to significant patient morbidity and has been shown to increase the usage of costly healthcare resources (14). Frequently, such patients require additional nonoperative and surgical therapeutic interventions to promote healing of the arthrodesis site (Fig. 1). Patients can experience physical, emotional, and financial sequelae and require extended convalescence resulting from treatment of a painful nonunion.

Preventative screening algorithms and formalized assessments that recognize patient risk factors are frequently reported topics in medical studies (15,16). Preoperative screening affords an opportunity to identify and correct certain modifiable factors before the associated complications can occur. Some published data have focused on nonunion of the lower extremity and described modifiable risk factors that can be screened and optimized before reconstruction is attempted (17,18). Tobacco use, diabetes mellitus, nutritional deficiencies, poor vascularity, and certain pharmaceutical regimens have

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Fig. 1. *(Top)* Nonunion occurring after ankle joint arthrodesis for severe tibiotalar arthritis and deformity in a patient with juvenile rheumatoid arthritis. *(Bottom)* Revision in the form of tibiotalocalcaneal arthrodesis and endocrinology-guided medical optimization was performed.

been shown to potentiate a patient's risk for complications after lower extremity surgery (13,14,17–25).

We performed a case-control study of patients who had undergone elective foot and ankle reconstruction by way of arthrodesis at our institution from 2011 to 2014. The purpose of the present study was to compare the prevalence of certain frequently cited modifiable risk factors such as body mass index (BMI), tobacco use, and endocrine disease, including diabetes mellitus, vitamin D abnormality, thyroid dysfunction, and parathyroid disease, in subjects who had either experienced postoperative nonunion or successful arthrodesis. We hypothesized that the prevalence of endocrine disease (vitamin D abnormality, thyroid dysfunction, parathyroid disease, and diabetes mellitus) would be high in the medical records of our nonunion group, with a significantly greater prevalence of such factors compared with the successful arthrodesis group.

Patients and Methods

We used an institutional clinical practice database and the appropriate International Classification of Diseases, 9th revision, and Common Procedural Terminology codes to identify patients who had undergone arthrodesis procedures of the foot and/or ankle and experienced postoperative nonunion from January 1, 2011 to December 31, 2014. Additionally, we identified a cohort of patients from the same clinical practice database who had undergone arthrodesis procedures of the foot and/or ankle during the study period but had not developed nonunion as the control group. The control group patients were chosen at random in a 1:1 ratio for comparison with the case group. Verification of procedure selection, the presence of nonunion, progression to successful union, medical and social history, and postoperative course was confirmed by a comprehensive review of the hardcopy and electronic medical records for all evaluated subjects. The institutional review board of our institution approved the present study.

The prevalence of patient-related variables and modifiable risk factors assessed between the 2 groups included age, BMI, tobacco use, and endocrine disease (i.e., vitamin D abnormality, thyroid dysfunction, parathyroid disease, diabetes mellitus).

The inclusion criteria were as follows: adult subjects aged >18 years; surgical procedures occurring from January 1, 2011 to December 31, 2014; a minimum of 1 year of follow-up data available from the surgery date; and surgical reconstruction of foot and ankle pathology (deformity, instability, primary and secondary arthritis) in the form of joint arthrodesis. The exclusion criteria were as follows: subjects not meeting the inclusion criteria; incomplete medical and/or surgical records; and deformity caused by Charcot neuroarthropathy.

The basic guidelines set forth by the Food and Drug Administration were used for clinical identification of those with nonunion. These included the absence of bony trabeculation across a surgically fractured surface for 9 months or the lack of progressive signs of healing for 3 consecutive months (19). Nonunion was diagnosed from serial plain film radiographs and advanced imaging modalities such as computed tomography scanning. Also, the senior authors (K.R.S., A.R.C.) consistently used a set range of 8 to 12 weeks to define "successful, uncomplicated" radiographic union in their practices. A combination of plain film radiographs and computed tomography were used to determine osseous bridging across the arthrodesis site. Successful union in the clinical setting was determined in all cases by the senior authors (K.R.S., A.R.C.).

The fixation techniques consisted of compression screws, locking plates and screws, and intramedullary nails. Autogenous bone grafts, allogenic bone grafts, and orthobiologic agents (e.g., demineralized bone matrix, bone marrow aspirate, platelet-rich plasma, osteogenic/osteoprogenitor stem cells, bone morphogenic proteins) were used indiscriminately between the 2 groups assessed in the present study.

The characteristics and other variables obtained from the review of the 2 groups were analyzed using appropriate statistical methods (e.g., Fisher's exact test, paired *t* test, Pearson's chi-square test, Mann-Whitney *U* test, likelihood ratio test) with the assistance of a professional research statistician. Statistical significance was set at $p < .05$ for the reported data. These data are presented in Tables 1, 2, and 3.

Results

We identified a total of 34 adult male and female patients aged >18 years who had undergone foot and ankle reconstruction during the 3-year period and had developed nonunion. Of these 34 patients, 5 were excluded because they did not have 1-year postoperative follow-up data available. The remaining 29 patients (15 males and 14 females) met the inclusion criteria and their records were assessed further. The nonunion group was then matched against a control group of 29 randomly selected adult patients (12 males and 17 females) who met the inclusion criteria and had undergone foot and ankle reconstruction by way of arthrodesis with successful union. The total patient population included 58 patients (27 males and 31 females), matched 1:1 for 2 groups.

The mean age of the 58 patients was 54.5 ± 14.0 (median age 57.5, range 19 to 86) years. Of the 58 patients, 27 were male (46.6%) and 31 were female (53.4%). The female patients were slightly, but not significantly, older than the male patients (56 years versus 53 years).

The full assessment of the clinical, surgical, and radiographic records of the 2 groups revealed a statistically significant ($p < .05$) difference between the 2 groups for a diagnosis of an endocrine disease reported in the medical records. Of the 29 nonunion patients evaluated, 22 (76%) had an active diagnosis of endocrine disease, including vitamin D insufficiency or deficiency in 14, hypothyroidism in 2, and diabetes mellitus in 6. Of the 29 successful union patients (control group), 8 (26%) had an active diagnosis of endocrine disease, including vitamin D insufficiency or deficiency in 3, hypothyroidism in 4, and diabetes mellitus in 1. No patient in either group had a diagnosis of parathyroid disease reported in their medical record. Overall, 76% of nonunion subjects versus 26% of successful union subjects had a diagnosis of endocrine disease reported in their medical record.

Further analysis was performed to better assess the endocrine dysfunctions individually to determine their association with the nonunion outcome. Of the 58 patients, 41 (70.7%) did not have a diagnosis of vitamin D abnormality, 10 (17.2%) had vitamin D deficiency, and 7 (12.1%) had vitamin D insufficiency. The presence of vitamin D deficiency or insufficiency was significantly associated with the outcome of nonunion [$\chi^2(1) = 10.1$; $p = .002$]. Of the 29 patients with nonunion, 14 (48.3%) had either vitamin D deficiency or insufficiency. Of the 29 patients with successful union, 3 (10.3%) had either

Table 1
Patient demographics

Pt. No.	Age (yr)	Sex	BMI (kg/m^2)	Tobacco Use	Endocrine Dysfunction	Procedure Type	Follow-Up (mo)	Nonunion
1	24	F	21	No	No	First tarsometatarsal arthrodesis	12	No
2	55	M	27.9	No	No	First metatarsophalangeal arthrodesis	13	No
3	62	F	27.9	No	HT	First metatarsophalangeal arthrodesis	12	No
4	61	F	28.7	No	VDI	First metatarsophalangeal arthrodesis	13	No
5	47	F	20	Yes	VDI	First metatarsophalangeal arthrodesis	12	No
6	67	F	22.9	No	HT	First metatarsophalangeal arthrodesis	14	No
7	45	F	33.2	No	No	First tarsometatarsal arthrodesis	18	No
8	64	M	34.2	Yes	No	Medial double arthrodesis	12	No
9	24	M	20.3	No	No	Medial double arthrodesis	12	No
10	58	M	37.3	Yes	No	Medial double arthrodesis	14	No
11	59	F	31	No	No	Medial double arthrodesis	14	No
12	73	F	30.7	Yes	No	Medial double arthrodesis	19	No
13	19	M	23	Yes	No	Triple arthrodesis	12	No
14	45	M	27.5	No	No	Triple arthrodesis	13	No
15	86	F	31.9	No	HT	Triple arthrodesis	13	No
16	19	M	36.5	No	No	Triple arthrodesis	14	No
17	69	M	21.5	No	No	Triple arthrodesis	14	No
18	52	F	NA	Yes	VDD	Triple arthrodesis	12	No
19	68	F	31	No	DM	Triple arthrodesis	12	No
20	53	F	30.4	No	No	Triple arthrodesis	12	No
21	63	M	25.1	No	No	Triple arthrodesis	30	No
22	60	F	43.8	No	No	Medial double arthrodesis	12	No
23	62	F	26.6	No	No	Triple arthrodesis	14	No
24	67	F	21.3	Yes	No	Subtalar arthrodesis	12	No
25	66	F	28.5	No	HT	Ankle arthrodesis	16	No
26	45	M	27	No	No	Ankle arthrodesis	14	No
27	59	F	28.7	No	No	Ankle arthrodesis	36	No
28	65	M	NA	No	No	Ankle arthrodesis	13	No
29	51	M	27.3	No	No	Ankle arthrodesis	13	No
30	65	F	37.4	No	VDD	Ankle arthrodesis	12	Yes
31	67	M	30	No	DM	Tibiotalocalcaneal arthrodesis	24	Yes
32	52	F	29	Yes	VDD	Triple arthrodesis	18	Yes
33	46	F	32.9	No	VDI	First tarsometatarsal arthrodesis	20	Yes
34	67	F	37.9	No	No	Ankle arthrodesis	26	Yes
35	60	M	31	No	VDD	Medial double arthrodesis	19	Yes
36	44	M	41.9	Yes	DM, VDI	Triple arthrodesis	14	Yes
37	70	F	NA	No	VDI, HT	Talonavicular arthrodesis	12	Yes
38	50	M	25.6	No	DM, VDD, HT	Tibiotalocalcaneal arthrodesis	12	Yes
39	40	F	22.1	No	No	First tarsometatarsal arthrodesis	12	Yes
40	27	M	33.4	No	No	Naviculocuneiform arthrodesis	20	Yes
41	40	F	21.9	No	VDD	Medial double arthrodesis	26	Yes
42	71	M	25.7	No	VDD	First metatarsophalangeal arthrodesis	24	Yes
43	46	F	38.5	Yes	DM	Ankle arthrodesis	14	Yes
44	37	F	26.6	No	No	First tarsometatarsal arthrodesis	12	Yes
45	67	M	27.5	No	VDI	Triple arthrodesis	12	Yes
46	58	M	33	No	No	Ankle arthrodesis	24	Yes
47	49	M	34.1	No	DM	Triple arthrodesis	15	Yes
48	46	M	NA	No	No	Triple arthrodesis	12	Yes
49	45	F	NA	Yes	No	First tarsometatarsal arthrodesis	15	Yes
50	57	F	32	Yes	No	Subtalar arthrodesis	20	Yes
51	66	F	29	No	No	First metatarsophalangeal arthrodesis	12	Yes
52	52	M	26.9	Yes	VDD	First metatarsophalangeal arthrodesis	12	Yes
53	57	M	25.1	Yes	No	Subtalar arthrodesis	12	Yes
54	51	F	34.1	No	VDD	Medial double arthrodesis	16	Yes
55	66	M	24.2	No	VDI	Subtalar arthrodesis	21	Yes
56	64	M	NA	No	VDD	Tibiotalocalcaneal arthrodesis	15	Yes
57	67	M	31	No	DM	Ankle arthrodesis	24	Yes
58	44	F	28	No	No	Ankle arthrodesis	48	Yes

Abbreviations: BMI, body mass index; DM, diabetes mellitus; F, female; HT, hypothyroidism; M, male; NA, not available; VDD, vitamin D deficiency; VDI, vitamin D insufficiency.

vitamin D deficiency or insufficiency. A diagnosis of vitamin D deficiency or insufficiency was 8.1 times more likely to be associated with a nonunion outcome (95% confidence interval 1.996 to 32.787). Further individual assessment revealed no significant association between hypothyroidism and nonunion outcome ($p = .67$). Also, no significant association was found between diabetes and outcome ($p = .10$). No patient in either group had a diagnosis of parathyroid disease reported in their medical records.

The median age did not differ significantly between the 2 groups. The median age of the patients with union was 59 (range 19 to 86) years versus 52 (range 27 to 71) years for patients with nonunion (Mann-Whitney $U = 383.0$; $p = .56$). The median BMI did not differ significantly between the 2 groups. The median BMI of the patients with union was 27.9 (range 20 to 43.8) kg/m^2 versus 30 (range 21.9 to 41.9) kg/m^2 for patients with nonunion (Mann-Whitney $U = 175.5$; $p = .28$). No significant association was found between sex and outcome [χ^2 (1) = 0.62; $p = .43$). Of the 29 patients with union, 12 (41.4%) were male and 17 (58.6%) were female. Of the 29 patients with nonunion, 15 (51.7%) were male and 14 (48.3%) were female. Tobacco use was not associated with the patient outcome of nonunion ($p = .81$). A full description of the data is presented in Tables 1, 2, and 3.

Table 2
Patient demographic data (N = 58; 29 nonunion and 29 successful union)

All Subjects	n (%)
Age (yr)	
Mean ± standard deviation	54.5 ± 14.0
Range	19 to 86
Sex (n)	
Female	31
Male	27
BMI (kg/m^2)	
Median	27.9
Range	19.9 to 86
Tobacco	14 (24)
Active	11 (19)
Quit	3 (5)
Endocrine and metabolic dysfunction	30 (52)
Diabetes mellitus	7 (12)
Vitamin D deficiency	10 (17)
Vitamin D insufficiency	7 (12)
Hypothyroidism	6 (10)
Procedure type	
First metatarsophalangeal arthrodesis	8 (14)
First tarsometatarsal arthrodesis	6 (10)
Talonavicular arthrodesis	1 (2)
Subtalar arthrodesis	4 (7)
Medial double arthrodesis (TNJ, STJ)	9 (16)
Triple arthrodesis (TNJ, STJ, CCJ)	15 (26)
Ankle arthrodesis	11 (19)
Tibiotalocalcaneal arthrodesis	3 (5)
Naviculocuneiform arthrodesis	1 (2)

Abbreviations: CCJ, calcaneocuboid joint; STJ, subtalar joint; TNJ, talonavicular joint.

Discussion

Arthrodesis procedures depend on the body's ability to heal and regenerate bone across a surgically "fractured" surface. Skeletal remodeling is dynamic and requires a close interrelationship between bone formation and resorption (26,27). Successful consolidation after arthrodesis requires the orchestration of numerous cell types and growth factors and is further reliant on the appropriate surgical technique (28–31). At the most basic level, an arthrodesis site must have adequate stability to resist deforming forces, have sufficient nutrients available from the local vascularity, and maintain adequate bone-to-bone contact with the opposing surface. Instability will impede incorporation and will adversely affect the biologic response. Delayed union or nonunion can result when these factors are lacking or if technical issues are present.

Table 3
Results from multivariate data analysis (N = 58)

Variable	Nonunion	Union	*p* Value*
Sex			.43
Female	14	17	
Male	15	12	
Age (yr)			.56
Median	52	59	
Range	27 to 71	19 to 86	
BMI (kg/m^2)			.28
Median	30.0	27.9	
Range	21.9 to 41.90	20 to 43.8	
Tobacco	7	7	.11
Active	7	4	
Quit	0	3	
Endocrine dysfunction	22/29 (76)	8/29 (26)	.000234†
Vitamin D deficiency	9/22 (41)	1/8 (12.5)	.02†
Vitamin D insufficiency	5/22 (23)	2/8 (25 %)	.02†
Hypothyroidism	2/22 (9)	4/8 (50%)	.67
Diabetes mellitus	6/22 (27)	1/8 (12.5%)	.1
Parathyroid disease	0/22 (0)	0/8 (0%)	
Procedure type			1.0
First metatarsophalangeal arthrodesis	3 (10)	5 (17)	
First tarsometatarsal arthrodesis	4 (14)	2 (7)	
Talonavicular arthrodesis	1 (3)	0 (0)	
Subtalar arthrodesis	3 (10)	1 (3)	
Medial double arthrodesis (TN, STJ)	3 (10)	6 (21)	
Triple arthrodesis (TN, STJ, CCJ)	5 (17)	10 (35)	
Ankle arthrodesis	6 (21)	5 (17)	
Tibiotalocalcaneal arthrodesis	3 (10)	0 (0)	
Naviculocuneiform arthrodesis	1 (3)	0 (0)	

Abbreviations: CCJ, calcaneocuboid joint; STJ, subtalar joint; TNJ, talonavicular joint.
Data presented as median, range, n, n (%), or n/n (%).
* *p* Values determined using Fisher's exact test, Pearson's chi-square test, Mann-Whitney *U* test, Student's *t* test.
† Statistically significant at $p \leq .05$.

The incidence of nonunion after elective surgical reconstruction varies depending on the anatomic site, and the risk of developing nonunion can be potentiated by various medical conditions. Previous reports have cited nonunion rates after first metatarsophalangeal joint and first tarsometatarsal joint arthrodesis of <10%, although rates ranging from 6% to 33% have been reported for arthrodesis of the hindfoot and ankle (1,2,8,9,32).

Nonunion in the foot and ankle should be viewed as a complex, multifactorial condition. The numerous etiologies associated with nonunion can be distilled into local factors and host factors that either inhibit or hinder normal bone healing. Examples of local factors include surgeon- or "technical"-dependent variables such as inadequate joint preparation, thermal injury to bony surfaces, inappropriate fixation constructs, malalignment of the arthrodesis, and poor tissue handling (Fig. 2), (26,27,33). Surgical site infection has also been considered a local factor that predisposes a patient to nonunion by disrupting the "normal" physiology at the arthrodesis site (34).

Host- or patient-related factors include the various medical conditions capable of disrupting the sophisticated pathways linked to bone healing. These factors can include tobacco use, diabetes mellitus, nutritional deficiencies, vascular disease, autoimmune disease, vitamin D deficiency, calcium dysregulation, thyroid dysfunction, parathyroid disease, long-term pharmacologic regimens, and combinations thereof (20–25,35). Tobacco use is one of the more commonly cited patient factors associated with nonunion after bone surgery. Nicotine has been shown in laboratory studies to uncouple the mechanisms involved in new vascular ingrowth and osteogenesis occurring within healing bone (21). An in-depth review by Haverstock and Mandracchia (20) discussed the significant negative implications that tobacco products have on the bone healing process after foot and ankle surgery. Furthermore, high-dose corticosteroids and nonsteroidal anti-inflammatory medications have been implicated in animal models to hinder the inflammatory response phases essential to bone formation (23–25). In a 2014 report by Jeffcoach et al (25), patients receiving nonsteroidal anti-inflammatory medications after a long-bone fracture were more likely to experience complications such as nonunion or infection after surgical reconstruction (25).

The endocrine system is responsible for the tightly regulated mechanisms for bone and mineral metabolism in the human body. Homeostasis of bone minerals is primarily controlled by parathyroid hormone, vitamin D 1,25OH, and calcitonin (36). Additional regulatory feedback loops have been described among the pancreas, kidneys, osteoblasts, and sites of new bone formation. Certain investigators have even attempted to classify the bony skeleton as another "organ" within the endocrine system (37). As such, disorders that disturb the intricately woven endocrine pathways or conditions that cause hormone imbalance can adversely affect bone healing.

Recently, there has been a heightened recognition of the role that endocrine disease plays in postoperative complications. In particular, this includes diabetes mellitus, vitamin D abnormality, parathyroid disease, and thyroid dysfunction (13,14,17–19,35). Previous data have indicated a linear relationship between increased complications in patients undergoing foot surgery and elevated hemoglobin A1c levels (38). Uncontrolled diabetes, particularly when

Fig. 2. *(Top)* Nonunion occurring after isolated subtalar joint arthrodesis. *(Bottom)* A revision fixation construct was placed using multiple large-diameter compression screws to engage the cortical and compact subchondral bone to enhance purchase and construct stiffness.

peripheral neuropathy is present, has been linked to an increased risk of surgical site infection after lower extremity surgery (39,40). Grunfeld et al (41) reported increased wound healing complications in foot and ankle surgical patients receiving thyroxine supplementation for hypothyroidism. In a 2007 report, Brinker et al (35) found that in a cohort of 37 patients with lower extremity nonunion not caused by technical error, 31 (84%) had an underlying endocrine and metabolic dysfunction after formalized endocrinologist assessment. The most common diagnosis was vitamin D abnormality, which was present in 25 of the 31 patients. Furthermore, 8 of the 31 affected patients progressed to successful fusion with medical therapy alone (35).

In the present study, we found a statistically significant ($p < .05$) increased prevalence of endocrine disease (vitamin D abnormality, thyroid dysfunction, and diabetes mellitus) in a group of patients with postoperative nonunion after foot and ankle reconstruction. These results are similar to previously published data highlighting the association of endocrine disease and complications after foot and ankle surgery. Of the 29 patients in the nonunion group, 22 (76%) had a formal diagnosis of an endocrine disease in their medical record. The most common disease was vitamin D abnormality, found in 14 of the 22 (82%) affected nonunion subjects. In contrast, the prevalence of endocrine disease in those achieving successful union with an uncomplicated surgical course was 26% (8 of 29). When the specific endocrine dysfunctions were assessed individually, those with vitamin D deficiency and insufficiency were 8.1 times as likely to have an outcome of nonunion (95% confidence interval 1.996 to 32.787). All other patient variables and risk factors, such as age, procedure selection, BMI, and tobacco use, between the 2 groups did not reach statistical significance.

Although we found our results to be intriguing, the present study had noteworthy limitations. We only assessed for the prevalence of particular risk factors, including BMI, vitamin D abnormality, thyroid dysfunction, parathyroid disease, and tobacco use, among the patient groups. It is quite probable that numerous other medical factors would be capable of hindering normal bone healing that were not evaluated in the present study. Furthermore, the interrelationships among the different endocrine abnormalities, isolated or concomitant tobacco use, surgeon technical factors, and their negative effects on bone healing are vast and would be difficult to fully measure in the study model we used. Second, no further investigation to quantify the severity of the endocrine abnormality in question or assess the previous medical treatment rendered, adequacy of pharmacologic repletion at surgery, presence of uniform laboratory testing, and so forth was performed for the risk factors among the 2 groups. Third, just as is true for retrospective case-controlled analyses, an inherent risk exists of investigator bias, confounding, and sampling error. Additionally, the data extracted for the present review relied on the accuracy and completeness of the medical records within our healthcare system, which could be subject to documenter error. Fourth, the study was limited by the relatively small sample size and might have been underpowered to detect significant differences between the 2 groups. Additionally, ours was a single-center study in an urban area; thus, our results might not be generalizable to a larger population. Finally, although we can state that patients with vitamin D deficiency or insufficiency are 8.1 times more likely to develop nonunion, the large 95% confidence interval associated with this outcome (95% confidence interval 1.996 to 32.787) makes this result tenuous.

In conclusion, the results of our analysis suggest an association between endocrine disease, in particular, vitamin D deficiency, and nonunion after foot and ankle arthrodesis. Although the factors of diabetes mellitus and thyroid dysfunction did not reach statistical significance in their individual assessments, other reports have suggested associations with decreased healing capacity after arthrodesis and endocrine-linked metabolic disorders. We recommend implementing routine screening tests, including hemoglobin A1c, thyroid-stimulating hormone, ionized calcium, and serum vitamin D levels, for patients scheduled to undergo arthrodesis procedures. Although the results of the present analysis did not reach statistical significance for tobacco usage, we would also recommend pursuing aggressive cessation programs before arthrodesis attempts. Additionally, we strongly believe that for cases in which the etiology of nonunion is in question, it would behoove the surgeon to seek consultation from other medical specialists, in particular, endocrinology, to assess and treat any abnormality found.

Currently, a paucity of high-level data showing the implications that endocrine disease has on nonunion in the foot and ankle is available. To the best of our knowledge, no verified formal screening algorithms exist that specifically address the numerous risk factors associated with nonunion. Prospective studies are needed to evaluate the effect that optimizing and treating endocrine abnormalities such as vitamin D deficiency, thyroid dysfunction, parathyroidism, diabetes mellitus, and metabolic bone disease has on nonunion rates after arthrodesis.

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