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Variables Prognostic for Delayed Union and Nonunion Following Ulnar Shortening Fixed With a Dedicated Osteotomy Plate.

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ABSTRACT

PURPOSE

To examine potential risk factors for development of delayed or nonunion following elective ulnar shortening osteotomy using a dedicated osteotomy plating system.

METHODS

We performed a retrospective review of all patients who underwent elective ulnar shortening using the TriMed single osteotomy dynamic compression plating system by one of two fellowship-trained hand surgeons over a five-year period. Demographic data and medical, surgical, and social histories were reviewed. Time to bony union was determined radiographically by a blinded reviewer. Bivariate statistical analysis was performed to examine the effect of explanatory variables on the time to union and the incidence of delayed or nonunion. Those variables associated with the development of delayed or nonunion were used in a multivariate logistic regression model. Complications, including the need for additional surgery, were also recorded.

RESULTS

Seventy-two ulnar shortening osteotomy procedures were performed in 69 patients. Delayed union, defined as ≥ 6 months to union, occurred in 8/72 cases

(11%). Four of 72 (6%) surgeries resulted in nonunions, all of which required additional surgery. Hardware removal was performed in 13/72 (18%) of cases. Time to union was significantly increased in smokers (6+/- 3 months) versus non-smokers (3 +/- 1 months). On multivariate analysis, diabetics and active smokers demonstrated a significantly higher risk of developing delayed union or nonunion. Patient age, sex, body mass index, thyroid disease, workers compensation status, alcohol use, and amount smoked daily did not have an effect on the time to union or the incidence of delayed or nonunion.

CONCLUSIONS

Despite the use of an osteotomy-specific plating system, smokers and diabetics were at significantly higher risk for both delayed union and nonunion following elective ulnar shortening osteotomy. Other known risk factors for suboptimal bony healing were not found to have a deleterious effect.

LEVEL OF EVIDENCE

Prognostic Level III

INTRODUCTION

Ulnar shortening osteotomy (USO) is a widely accepted surgical treatment option for ulnar-sided wrist pain associated with multiple conditions, including triangular fibrocartilage complex (TFCC) injuries, lunotriquetral (LT) ligament tears, and ulnar impaction syndrome (UIS). [1-4] An USO can effectively treat pain associated with TFCC injury, even in the absence of ulnar positive variance, and particularly when prior TFCC debridement or repair has failed. [2] Ulnar impaction syndrome is the direct result of positive static or dynamic ulnar variance, which causes the distal ulna to abut against the ulnar carpus. This is manifested clinically by pain with activities involving ulnar deviation and forearm rotation. [2, 4] By shortening and leveling the ulna, USO offloads the ulnar carpus from the distal ulna, thereby relieving pain. [1]

Reported outcomes following USO are generally favorable, although complications including delayed or nonunion at the osteotomy site occur with variable incidence. [5-9] As with any bone requiring fixation, the incidence of bony union after USO is multifactorial, relying on a multitude of patient demographic, medical, and social factors. Among the risk factors for development of nonunion or delayed union following bony fixation, the most commonly studied are advancing age, [10-13] malnutrition (including both a deficiency of nutrients or an excess, as in obesity), [13-17] diabetes, [18-23], thyroid disease, [17, 24] smoking, [25-35]and alcohol use. [36-38]

The detrimental effects of smoking on bony union in particular are well documented. However, most of the clinical reports are focused on spinal or ankle arthrodesis or on long-bone fractures treated with or without fixation. [25-35] Similarly, though diabetes has also been shown to adversely affect bony healing, most clinical reports pertain to fracture-fixation or arthrodesis of the foot and ankle. [21-23] Furthermore, it is unclear to what degree this effect is directly related to diabetes versus being related to an associated neuropathy. [39]

In a study investigating the effect of smoking on bony union following USO, Chen et al reported that smokers took significantly longer to achieve bony union in comparison to non-smokers while also demonstrating a significantly higher risk of developing nonunion. [40] However, it is unclear if any other risk factors for adverse bony healing were studied, or if underlying co-morbidities played any role in the authors' findings. Additionally, this study was performed nearly 20 years ago, using the standard 3.5 mm dynamic compression plate with freehand osteotomy cuts.

As freehand osteotomy has been shown to be associated with a higher incidence of nonunion, [9] it is unclear if smoking would have the same magnitude of effect on bony union following USO when using newer techniques and procedure-specific devices. The role that thyroid disease, alcohol use, obesity, and other variables may play in the development of delayed union or nonunion remains unclear.

The purpose of this study was to examine the association of variables known to adversely affect bone healing with time to bony union and rate of nonunion or delayed union following elective ulnar shortening osteotomy using a dedicated osteotomy plating system. Secondarily, we investigated whether any of these predictor variables increase the likelihood of other complications or the need for additional surgery following USO. Thus, our null hypothesis was that there would be no difference in the time to bony union and incidence of nonunion or complications based on the studied variables following USO with a dedicated osteotomy plating system.

METHODS

Surgical technique and baseline data collection

We retrospectively reviewed the charts of all patients who underwent USO from January 2010 through December 2014 at our institution by one of two fellowship-trained hand surgeons. All surgeries were performed with a single osteotomy dynamic compression plating system (TriMed Ulnar Osteotomy Compression Plate, *TriMed, Santa Clarita, CA*) using a similar technique to that previously described, with the plate placed in the most anatomically accommodating position (volar versus dorsal) as determined by the treating surgeon. [41] All patients were treated identically with regards to post-operative splinting and immobilization for one month, followed by mobilization exercises and formal supervised therapy. As per our institution's standard, all patients were given a standardized questionnaire pre-operatively, which included questions regarding smoking and tobacco history.

Patients who had not disclosed their smoking history, whether positive or negative, were excluded from the study.

Demographic data, body mass index (BMI), workers compensation status, and medical co-morbidities, including cardiovascular disease, diabetes mellitus, and thyroid disease, were recorded for each patient. Social factors such as smoking and alcohol use were also examined. Finally, the plate position at the time of surgery and the degree to which the ulna was shortened, in millimeters, were also recorded. The BMI, which was calculated using height and weight values obtained pre-operatively, was unavailable for 4 patients. Those 4 patients were excluded from that particular analysis. All other continuous variables and all categorical predictor variables were obtained for every patient included in this study.

The primary outcome measured was time to bony union as measured radiographically and confirmed by clinical examination. A fellowship-trained, attending hand surgeon served as a blinded reviewer, assessing orthogonal radiographs for cortical bridging across the osteotomy site beginning at 2 months postoperatively and monthly thereafter until bony union was achieved, as has been previously described. [31, 40] Physical examination data were correlated with radiographic time to union by an additional study author to confirm that each patient was pain-free at the osteotomy site at the time that radiologic union determined by the blinded reviewer. For the purposes of this study, bony union was only considered to have occurred when both radiographic and clinical parameters had been met.

Based on the reviewer-determined time to union, all surgeries were initially classified into one of three groups: *union* (above-mentioned criteria met within six months from surgery), *delayed union* (criteria achieved after six months), or *nonunion*. Nonunion has been previously described [30] and represents an osteotomy site that either lacked congruence of at least three of four cortices at an interval of six months or greater from the time of the USO or did not demonstrate any radiographic change for three consecutive months and was associated with clinical findings consistent with a nonunion (inability to bear weight through the affected extremity, pain on palpation, or motion at the osteotomy site beginning three months following the index USO). Secondary outcomes included rate of revision for nonunion and other complications requiring additional surgery.

Sample size and statistical analysis

Using data from the study by Chen et al, [40] *a priori* power analysis was performed to determine the sample size needed to detect a difference in time to union between non-smokers and smokers in a 3:1 ratio using the Student t-test. Assuming a normal distribution and effect size of 1.0, it was determined that we would need to enroll a minimum of 11 smoking patients and 33 non-smoking patients in order to detect a significant difference ($P < .05$) of 3 months in time to bony union between groups as reported by Chen et al [40] with 80% power ($\alpha = 0.05$, $\beta = 0.2$).

Preliminary sub-analysis was performed to confirm no significant differences in patient demographics and union rates between self-reported *non-smokers* and *former smokers*, allowing us to combine both subgroups into a single *non-smoking* cohort for data analysis. Bivariate statistical analysis with independent t-test was used for comparing time to union, measured in months for dichotomous explanatory variables. Nonunions were excluded from this analysis in order to avoid the potential for skewing union times by the endpoint of revision surgery. Pearson correlation was used to examine the correlation of continuous variables with time to union.

Because delayed union and nonunion represent two mutually exclusive suboptimal outcomes, the two categories were collapsed into a single category, denoted as *delayed or nonunion*, to limit the potential for error from small cell-counts when using contingency tables for bivariate analysis. Chi-square testing was used to examine the association of *union* versus *delayed or nonunion*, with the previously listed dichotomous variables. Variables determined to be statistically associated ($P \leq 0.10$) with the occurrence of delayed or nonunion in bivariate testing were used in a forward stepwise multivariate binary logistic regression analysis. Odds ratios with 95% confidence intervals (CIs) were determined for all significant predictors and model fit was confirmed using the Hosmer-Lemeshow test.

RESULTS

Seventy-two USOs performed in 69 patients satisfied inclusion criteria for this study. Forty-two patients were women and 27 were men. Forty surgeries (56%) were performed on the dominant extremity, and 45 plates were placed dorsally, with the remaining 27 placed volarly. Mean patient age at the time of surgery for the entire cohort was 44.+/- 12 years, and mean time interval to union was 4 +/- 2 months for all patients. Delayed union occurred in eight cases (11%), and nonunion occurred in four cases (6%).

Bivariate Analysis

Time to Union

Smoking was the only variable found to have a statistically significant effect on time to union (6 +/- 3 months in smokers versus 3+/- 1 months in non-smokers; P = 0.001). The number of cigarette packs smoked daily did not correlate with time to bony union among the cohort of smokers. Time to union in diabetics was 5 +/- 1 months versus 4 +/- 2 months in non-diabetics. This difference was not statistically significant (P = 0.26).

Incidence of Delayed Union and Nonunion

Smoking had a significant impact on the incidence of delayed union or nonunion, which occurred in 10 of 17 (59%) smokers and two of 55 (4%) non-smokers (P < 0.001). (See Table 1 for a demographic comparison of the smoking and non-smoking cohorts.) Incidence of nonunion or delayed union in diabetics (38%) versus non-diabetics (14%) approached statistical significance ($P = 0.094$). No other predictor variables were found to be statistically associated ($P \leq 0.10$) with the incidence of delayed union or nonunion. (See Table 2)

Multivariate Analysis

The final logistic model was found to be significant ($P = 0.000$) and correctly predicted 90% of outcomes (*delayed or nonunion* versus *union*). In the final logistic regression model, history of diabetes (odds ratio: 12.7; 95% CI, 1.03-17.5; $P = 0.045$) and positive active smoking history (odds ratio: 65.0; 95% CI, 7.3-580; $P = 0.000$) were associated with development of delayed or nonunion following USO.

Revisions and Additional Surgeries

Of the four nonunions that occurred, one was in a non-smoking woman and was associated with hardware failure. That patient had a history of cerebral palsy and bore weight on her operative extremity for ambulation during the acute postoperative phase. She complained of persistent pain at her osteotomy site and at five-month follow-up was noted to have loosening of her distal two screws on radiographs. Her revision surgery involved exchange of her distal three screws and exploration of her osteotomy site, which proved unremarkable. No bone grafting was performed, and the patient subsequently healed without incident five months later. The same patient had undergone USO on her contralateral forearm two years prior, which had healed uneventfully. The remaining three nonunions occurred in active smokers and necessitated hardware revision with bone grafting and placement of an additional compression plate at a right-angle to the osteotomy plate. Detailed overview of the demographics and treatment course for the four patients who developed nonunions are delineated in Online Appendix 1.

Symptomatic hardware necessitated plate removal in 13/72 (18%) of cases, with no significant difference between any variables, including smokers vs. non-smokers, diabetics vs. non-diabetics, and volar vs. dorsal plate positioning. One non-smoking patient developed complex regional pain syndrome type I postoperatively and required multiple stellate ganglion blocks. Another non-smoking patient developed a suture granuloma requiring excision, though this occurred at the incision site of her concomitant TFCC repair and was not directly related to her USO. There were no postoperative infections in any patients.

DISCUSSION

Numerous mechanisms for the detrimental effects of smoking on bone healing at the cellular level have been proposed, including decreased tissue perfusion and oxygenation, endothelial changes leading to a pro-thrombotic state, and altered osteoclast and osteoblast activity. [33, 42-50] Of the offending substances found in cigarettes, nicotine, carbon monoxide and recently dioxin are the most commonly studied. [33, 42, 43, 45, 48-50] Nicotine, in particular, is thought to play a key role in this process, though the exact mechanism through which it acts remains somewhat unclear. [42, 48, 49] Its inhibitory effects on bone healing are strongly supported by both human and animal studies demonstrating that even short-term cessation of nicotine prior to spinal arthrodesis resulted in improved incidence of union with the optimal period of abstinence suggested to be roughly one month. [51-53]

Despite the known deleterious effects of nicotine and smoking on bone healing, knowledge of a patient's smoking status is unlikely to change initial management in most acute or emergent cases. For example, an open tibia fracture would still necessitate emergent operative debridement and fixation regardless of a patient's smoking history. However, in the elective setting, the decision to operate on an active smoker is not clear-cut. In the aforementioned study by Chen et al, all USOs were performed electively for UIS. Osteotomies were performed freehand, and fixation was performed using a standard compression plate. [40] Our findings demonstrate that, despite improved plate design and technique that allows for more precise osteotomy cuts, smoking had a significant negative effect on bone healing following USO.

Citing this risk, some surgeons routinely choose not to operate electively on active smokers, given the potential for complications and prolonged post-operative course associated with delayed union or nonunion. Unfortunately, basing this decision solely on patient history may be misleading, as responses to self-report questionnaires are inaccurate for some populations of smokers, particularly if some aspect of secondary gain is involved. [54, 55] It is certainly plausible that actively-smoking patients indicated for USO surgery may feel the need to misrepresent their smoking history if full-disclosure were to preclude them from receiving surgery. Conversely, in a prospective study, Bender et al found that nearly 90 percent of orthopedic inpatients with a long-bone nonunion provided reliable smoking histories as confirmed by serum cotinine levels. [56]

Approaching patients directly regarding their smoking status can be a difficult or even uncomfortable task for surgeons and their patients. In situations where the surgeon may suspect active tobacco use despite a patient's negative self-reported history, a useful screening tool is urine or serum testing of cotinine, a major nicotine metabolite. [57] Lee and colleagues demonstrated that an "add-on" urinary cotinine test significantly enhanced the sensitivity of screening smokers scheduled for major elective surgery when compared to self-reported smoking status alone. [58] However, when such a test is warranted, care must be taken to avoid an adversarial implication.

A promising finding is that peri-operative smoking cessation has demonstrated improved bony union rates versus continued smoking in both animal and human studies, even for periods as short as one month pre-operatively. [51-53] Our study supports these data, as our sub-analysis found no difference between non-smokers and former smokers with regards to the incidence of union and the incidence of delayed or nonunion. This may be useful information for surgeons to cite when discussing the potential benefits of smoking cessation with patients.

Diabetic patients were also found to have an increased risk of delayed or nonunion following USO in our multivariate analysis. This finding was consistent with the known detrimental effects of diabetes on bony healing. [18-21] Though the overall number of diabetics included in the study was small, our findings provide evidence that diabetic patients are also subject to complications of bone healing following USO, despite improved implant design and technique. Furthermore, our regression model strongly suggested that diabetic smokers were at significant risk based on an additive effect of the two individual risk factors. This is not unlike the findings of Wukich and colleagues, who reported on complications following ankle fractures in patients with *uncomplicated* versus *complicated* diabetes, where *complicated* was defined as diabetes with concomitant end organ damage, such as peripheral vascular disease. [59] They found that patients with complicated diabetes were over three times more likely to develop nonunion and five times more likely to require revision surgery than patients with uncomplicated diabetes. [59]

Schottel and colleagues reported a profound and somewhat concerning finding that long-bone nonunions may have a vastly underappreciated toll on patients' health-related quality of life. [60] In a study of over 800 patients, patients' self-assessment of their own quality of life was measured by utility scores (ranging from 0.0 to 1.0) using a time trade-off model, which asks patients to quantify a proportion of remaining lifespan that they would trade away in order to obtain perfect health. The authors found that patients with forearm nonunions demonstrated the worst utility score of all long-bone nonunions and were ahead of only heart transplant candidates with respect to medical conditions studied in historical controls. [60] The applicability of these findings is somewhat uncertain with respect to our study, as there was no mention of how many nonunions were not fracture-related, such as following osteotomy, and the proportion of ulnar nonunions to those of the radius was not reported. Nevertheless, the overlying implication is that nonunion involving the forearm is a significantly devastating condition by patients' own assessment.

Those findings, in conjunction with results presented in our study, support our general predilection against performing elective USO in patients confirmed or highly-suspected to be actively smoking except in the rare case of severe, uncontrolled pain. One author (EKS) has employed serum cotinine and nicotine testing in his practice with noteworthy success in identifying patients who misrepresented their recent smoking history. This is discussed far in advance with the patient to ensure that compliance is seen as a joint-venture between the patient and surgeon rather than a test of the patient's adherence. In addition, patients who disclose a positive smoking history during initial consultation are referred to their primary-care providers for methods of smoking cessation. This further demonstrates the mutual goal for the best possible surgical outcome.

Finally, a commonly reported complication following USO is symptomatic hardware requiring plate removal, with reported incidences from more recent studies ranging from 24 to 55%. [7, 61-65] We found no correlation with smoking status or diabetes history on the need for hardware removal, nor did we find a significant association with plate placement, contrary to previous reports. [7] This reinforces the generally-accepted fact that all patients should be counseled on the possibility of needing additional surgery, even if bony union is achieved.

This study is not without limitations, including its retrospective nature. In addition, all smoking histories were obtained from patient intake records, which were subject to the previously mentioned bias of misrepresentation. Also, the majority of former and current smokers included in this study only disclosed their current smoking behavior without reporting a comprehensive smoking history including duration of smoking cessation (in former smokers) and pack-year history. Although this limited our ability to fully characterize patients' smoking history, previous clinical studies have supported the concept that those two factors are less important in determining incidence of union than active smoking status. [51, 52] Another study limitation regards the design itself. Although the reviewer of radiographs was blinded and had extensive experience reviewing x-rays, we recognize the imperfect nature of such methodology, including potentially suboptimal imaging and the lack of interobserver reliability testing. However, this is not unlike previous studies that used radiographic interpretation to determine bony union. [31, 40] Another limitation with this method is that patients were generally seen for follow-up at monthly intervals, which increased the potential for overestimation of union times given the time interval between visits.

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Table 1. Demographic comparison of the smoking and non-smoking cohorts.

	Data		
Variable	**Non-smoker (N = 55)**	**Active Smoker (N = 17)**	***P-value***
Age (in years)	44 +/- 13	45 +/- 11	0.95
Female	33 (60%)	10 (59%)	0.93
Diabetic	6 (11%)	2 (12%)	0.92
Drinks alcohol (min. one drink/week)	26 (47%)	4 (53%)	0.68
Workers' Compensation related	30 (50%)	5 (42%)	0.60

Table 2. Categorical predictor variables predicting union versus nonunion or delayed union after elective ulnar shortening osteotomy.

	Categorical Data		
Variable	**Union in < 6 months (60 cases)**	**Delayed Union or Nonunion (12 cases)**	***P-value***
	Count (% of cases)	*Count (% of cases)*	
Current Smoker	7 (12%)	10 (83%)	0.00*
Type II Diabetic	5 (8%)	3 (25%)	0.09*
Dominant extremity	31 (52%)	9 (75%)	0.12
Thyroid disease	31 (52%)	9 (75%)	0.12
Drinks alcohol (min. one drink/week)	31 (52%)	4 (33%)	0.25
Male	23 (38%)	6 (50%)	0.45
Cardiovascular Disease	15 (25%)	4 (33%)	0.55
Workers' Compensation related	30 (50%)	5 (42%)	0.60

*-Denotes statistically associated variables used in multivariate analysis

Appendix 1. Patient details and treatment course of the four patients who developed nonunions requiring additional surgery.

Pt	Age	Sex	Occupation	Workers' Comp	Dominant Extremity	BMI	Current Smoker	Type II DM	EtOH	CV	Thyroid	Other Medical	Concom Surg	Short (mm)	Post-operative course	Revision	Index to Revise	Post-revision outcome	Notes
1	46	M	Warehouse worker	Yes	Yes	34	Yes, 1PPD	Yes	No	Yes	Yes	None	Wrist arthroscopy with synovectomy, TFCC repair, DRUJ reconstruction	3	Persistent pain; radiographs at 3 months from index surgery demonstrated hypertrophic callus without bridging bone at osteotomy site with signs of screw loosening; failed trial use of bone stimulator	Removal of screws, takedown of nonunion, revision plating with placement of cancellous allograft and additional compression plate at a right angle to osteotomy plate	6 months	Radiographic and clinical union at 7 months	
2	53	F	On disability	No	Yes	29	No	No	No	No	No	Cerebral Palsy	Wrist arthroscopy with synovectomy, TFCC debridement	5	Persistent pain, radiographs at 5.5 months demonstrated minimal callous formation and loosening of distal two screws	Revision/exchange of distal three screws, exploration of nonunion site	6 months	Radiographic and clinical union at 5 months	Patient acknowledged using operative arm for ambulation almost immediately post-op
3	41	F	Licensed Practical Nurse	Yes	Yes	24	Yes, ½PPD	Yes	Yes, 1 drink/ week	Yes	No	Anxiety and Depression	Wrist arthroscopy	2	Persistent pain; radiographs at 7 months with minimal bridging bone at osteotomy site with signs of screw loosening; failed trial use of bone stimulator, CT scan at 8.5 months confirmed no bony union	Removal of plate and screws, takedown of nonunion, revision plating with placement of cancellous olecranon autograft and additional compression plate at a right angle to osteotomy plate	9 months	Radiographic and clinical union at 9.5 months; symptomatic hardware removal at 13.5 months post-revision	Patient was prescribed smoking cessation aid post-revision, but was unable to reduce her smoking
4	55	F	Bartender	Yes	Yes	26	Yes, ½PPD	No	Yes, 4 drinks/ week	No	No	None	Wrist arthroscopy, subfascial ulnar nerve transposition	3	Persistent pain, radiographs at 4 months demonstrated lack of callous formation and loosening of distal two screws	Removal of plate and screws, takedown of nonunion, revision plating with placement of DHBM allograft and additional compression plate at a right angle to osteotomy plate	4.5 months	Radiographic and clinical union at 9 months	

BMI = Body Mass Index; DM = Diabetes Mellitus; EtOH = Current alcohol drinker, CV = Cardiovascular disease; Short = length of shortening of the ulna in millimeters; PPD = packs-per-day of cigarettes smoked; TFCC = Triangular Fibrocartilage Complex; DRUJ = Distal radio-ulnar joint; CT = computed tomography; DHBM = demineralized human bone matrix