Acta Orthop. Belg., 2020, **86 e-supplement** 2, 31-36

ORIGINAL STUDY

Results following surgical intervention for fracture nonunions: Does diabetes predict poor outcomes?

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The purpose of this study was to compare the functional outcomes of diabetic patients who were treated for a fracture nonunion against matched controls.

Sixty-one diabetic patients (type 1 or type 2) were identified from a prospective database. This cohort was paired with matched controls and univariate analysis was performed to evaluate for differences in complication rates, time to bony union and functional outcomes at 3, 6, 12, and greater than 24 months post-operatively.

The diabetic group was composed of 29 females and 32 males, with an average age of 58 years, and 17 upper extremity nonunions and 43 lower extremity nonunions. Time to bony union, complication rate or functional outcomes at any follow-up time point did not significantly differ between groups.

The comorbidity of diabetes mellitus does not lead to worse functional outcomes or increased complications following surgical treatment for a fracture nonunion.

Keywords : diabetic ; complications ; fracture ; nonunion ; outcomes

INTRODUCTION

The global prevalence of diabetes mellitus is rapidly increasing, and estimated to affect approximately 439 million adults worldwide by 2030 *(21)*. It is well documented that diabetes can affect bone quality, thus increasing the risk of fracture *(1,2,4,8,11,12,13,20,27)*. One of the cited complications of type 1 diabetes includes inadequate bone formation, resulting in osteopenia and delayed fracture healing *(12,20)*. However, increased fracture risk, which has been traditionally associated with type 1 diabetics, is now of a greater concern in type 2 diabetic populations6. Patients with type 2 diabetes have been shown to have an increased risk of fragility fractures despite increased body weight and normal or higher bone mineral density *(8,20)*. Time to healing is prolonged in both insulin and oral hypoglycemic-controlled diabetics, and high glucose overall will lead to both poor bone formation and turnover *(2,11)*. Additionally, diabetes medications have also demonstrated anti-osteogenic effects compared to a control cohort *(6)*.

Diabetes mellitus has also been cited as a contributing factor for development of a nonunion within multiple fracture types *(3,9,14,17)*. The presence of diabetes can also lead to a higher complication rate following surgery, as well as

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Conflict of interest: All authors declare that they have not received any funding or other benefits in support of this study. No relevant financial relationships to disclose.

poorer clinical outcomes (19,22,25). Literature on functional outcomes following a fracture in diabetic patients is limited, although Norris et al. has demonstrated that diabetic hip fracture patients have a similar recovery of function at 1 year post-operatively (16). However, to our knowledge, there are no studies to date reporting on the functional outcomes of diabetic patients who undergo surgical repair for a nonunion. The purpose of this study was to examine the functional outcomes of diabetic patients who were surgically treated for a nonunion, and compare their functional outcomes against matched controls.

MATERIALS AND METHODS

Three hundred and thirty-three patients who were surgically treated for a fracture nonunion between September 2004 and May 2015 within one academic medical center were enrolled in an IRB-approved prospective research registry. All enrolled patients were evaluated pre-operatively, at which time demographics, past medical history and initial injury information were collected. VAS pain scores were also collected pre-operatively, and patients' pre-operative functional status was evaluated using the Short Musculoskeletal Functional Assessment (SMFA) (23). Patients were radiographically evaluated at baseline, to determine type of nonunion according to the system of Weber and Cech, and at 3 months, 6 months, 1 year, and at 2 years or more postoperatively to assess for fracture healing (28). At these time points, patients' functional status was also assessed using the SMFA, and VAS pain scores were recorded (24). Any complications and additional surgeries that occurred following the initial nonunion surgery were also recorded. All fracture nonunions were treated surgically in a similar manner. Surgical intervention consisted of revision or repair, depending on the patient's initial injury management, and utilization of one or more biological stimulation graft, including iliac crest aspirate, recombinant bone morphogenic protein [BMP] (Infuse Medtronic, Minneapolis Mn.), cancellous chips, and iliac crest bone graft. Sixty-one (18.3%) patients in our prospective research registry carried a diagnosis of diabetes mellitus. There were 7 (11.5%) patients with type 1 diabetes and 54 (88.5%) patients with type 2 diabetes. Medications (i.e. insulin) and routine lab values, including Hemoglobin A1c and Vitamin D levels, were not recorded as a part of our prospective database, so diabetic patients could only be classified based on type 1 or type 2 diabetes mellitus.

The diabetic cohort was composed of 32 (52.5%) males and 29 (47.5%) females, with an average age at the time of nonunion surgery of 58.29±13.5 years. There were 45 (73.8%) lower extremity nonunions and 16 (26.2%) upper extremity nonunions. Within the diabetic cohort, specific location of the nonunion is as follows: 15 (24.6%) femurs, 2 (3.3%) fibulas, 1 (1.6%) 5th metatarsal, 1 (1.6%) forearm (both bones), 14 (23.0%) humeri, 2 (3.3%) medial malleoli, 1 (1.6%) patella, 25 (41.0%) tibias, and 1 (1.6%) ulna. All members of the diabetic cohort were paired with non-diabetic matched controls based on age at time of nonunion surgery, gender, and location of fracture nonunion (upper extremity versus lower extremity). The specific nonunion location of the age and gender matched controls is as follows: 2 (3.3%) clavicles, 20 (32.8%) femurs, 1 (1.6%) fibula, 13 (21.3%) humeri, 2 (3.3%) medial malleoli, 1 (1.6%) patella, and 21 (34.4%) tibias ($p = .697$).

The diabetic cohorts and matched controls were statistically compared in a univariate analysis in terms of SMFA scores and VAS pain scores at all study time points. Time to healing and complications were also analyzed. The Mann Whitney U test for continuous variables and Pearson's chi-squared analysis was used for non-continuous variables. Significance was set at $p < 0.05$.

RESULTS

Sixty-one diabetic nonunion patients were compared against age, gender, and fracture nonunion location matched controls. The results of this univariate analysis are demonstrated in Table I. There were 6 (9.8%) diabetic patients and 5 (8.2%) non-diabetic patients who were infected at initial nonunion presentation. All infected nonunions were treated with culture directed antibiotic following an infectious diseases consult. All 11 patients healed their nonunions and had no recrudescence of their infections to date.

There were no statistically significant differences between diabetics and non-diabetics with regard to: time from injury to nonunion surgery, time to healing, or VAS pain and SMFA scores at any study time point. The mean time to healing was 6.69±4.4 months for diabetics and 6.46±3.1 months for non-diabetics. Mean VAS pain scores never differed by more than 1 point between diabetic and non-diabetic cohorts. Mean SMFA scores differed by between 1 and 9 points between the cohorts depending on the study time point. However, although the diabetic cohort had consistently higher SMFA scores than the non-diabetic cohort, there was no statistically significant difference between functional scores at any study time point. Baseline SMFA scores are recorded prior to nonunion surgery, and thus represent the functional status of patients while they are living with a nonunion. In order to quantify improvement, we calculated the change in SMFA scores from baseline to the most recently available SMFA score. Diabetic nonunion patients saw a mean decrease in SMFA scores by 13.27±29.7 and non-diabetics had a mean decrease of 18.52±24.8 points in SMFA scores, yet this difference in mean SMFA reduction was not significantly different between the groups. The complication rate between the 2 cohorts was similar as well, with the most common complication in both groups being a second nonunion surgery (Table I).

Table I. — Univariate Analysis of Diabetics and Matched Controls

	Diabetics	Non-Diabetic Matched Controls	Sig.
Age at Nonunion Surgery	58.29±13.5	57.71±12.9	.808
Gender	Male: 32 Female: 29	Male: 32 Female: 29	.428
Age Adjusted CCI	2.87±1.6	1.61±1.3	<.0005
Nonunion Location	Upper: 16 Lower: 45	Upper: 16 Lower: 45	.500
Time from Injury to Nonunion Surgery (Months)	15.59±25.6	19.66±35.5	.481
Time to Healing (Months)	6.69±4.4	6.46±3.1	.764
Baseline SMFA	41.49±21.3	40.34±24.5	.788
Baseline Pain	5.27±2.8	4.91±2.4	.536
3 Month SMFA	34.14±19.4	30.73±19.0	.364
3 Month Pain	3.36±2.8	2.90±2.5	.387
6 Month SMFA	26.16±18.0	24.56±16.7	.642
6 Month Pain	3.56±2.8	2.57±2.9	.084
12 Month SMFA	27.09±21.6	22.83±18.8	.287
12 Month Pain	2.82±2.7	2.60±2.5	.684
Long Term Follow-Up Interval (Months)	37.68±12.8	41.70±23.7	.400
Long-Term SMFA	29.94±22.5	21.11±18.1	.078
Long-Term Pain	3.52±3.2	2.47±2.7	.153
Change in SMFA Score	13.27±29.7	18.52±24.8	.311
Complications	14.8% (9)	18.0% (11)	.625
Infected Nonunion at Presentation	9.8% (6)	8.2% (5)	.752

DISCUSSION

Sixty-one diabetic nonunion patients were compared against age, gender, and nonunion location matched controls. Although diabetics did have on average a higher VAS pain scores and SMFA scores than non-diabetics at each time point, these differences were not significantly different. Non-diabetics on average had a greater reduction in SMFA scores from baseline to last available follow-up time point, consistent with diabetics having higher SMFA scores at each time points. However, since none of the differences in VAS pain scores and SMFA scores were statistically significantly different, we interpreted that a difference of several points does not represent a significant difference in functional abilities and thus diabetics and non-diabetics are comparable in terms of pain levels and functional outcomes following nonunion surgery. The mean time to healing was nearly identical for both diabetic and non-diabetic nonunions, suggesting that proper improvement of local biology through surgical treatment of nonunions can lead to successful healing regardless of underlying diabetic mechanisms interfering with bone healing. Diabetic patients with a fracture nonunion pursued surgery on average 4 months sooner than their non-diabetic counterparts, yet this difference was not significant. The majority of patients included in this study did not undergo their initial surgery at our institution, so it remains unclear what delayed the non-diabetic cohort with respect to presentation for non-union surgery. It is possible that the original treating physician was more tolerant in expectation for normal fracture healing in non-diabetic patients and more apt to refer for treatment in diabetics sooner, due to belief that healing success was not achievable. Furthermore, since both groups had comparable functional outcomes, suggesting that time to nonunion surgery does not seriously impact long-term outcomes. The complication rate was also comparable between diabetics and non-diabetics, although 1 of the diabetic patients who had wound healing problems died from unrelated medical complications 6 months after surgery and another developed Charcot collapse of the ankle joint. With the exception of these 2 diabetic nonunion patients, the type of complications experienced by both groups (infection, hardware failure, and need for second surgery) were seen equally in the 2 groups.

The diagnosis of diabetes mellitus can be considered a risk factor for nonunion as it negatively impacts bone healing *(1,3,9,27,29)*. While there have been no previous studies evaluating the outcomes of diabetics undergoing surgical repair for a nonunion, the effects of diabetes has been discussed in regards to acute fracture patterns. It has been previously suggested that patients with well-controlled diabetes without other co-morbidities will have similar outcomes to non-diabetic patients following orthopaedic surgery *(29,30)*. However, diabetic patients are at a higher risk for post-operative complications and longer hospital stays following orthopaedic trauma, incurring greater associated costs *(7,16,19,22,26)*. Furthermore, there are conflicting reports as to whether diabetics can expect similar functional outcomes to their non-diabetic counterparts *(10,16,29)*. Our analysis contributes to the current body of literature regarding functional outcomes for diabetic orthopaedic trauma patients, and demonstrates that, despite being at an increased risk for nonunion, this sub-group of patients can expect similar functional results following surgical intervention for a fracture nonunion.

While this analysis was conducted using only prospectively-collected functional data, it is limited by the use of matched controls. Matching has been shown to limit the statistical power of analysis *(5)*. Although matching on factors such as age and sex is commonly used in case-control studies, matching does not control for confounding by the matching factors *(18)*. However, we felt that age and gender matched-controls was the most appropriate method for examining the functional outcomes of diabetics treated for a fracture nonunion. Other possible confounding variables could not be taken into consideration during the matching process, such as duration of nonunion, comorbidities, smoking status, and diabetic control (i.e. hemoglobin A1c levels), yet the matched controls were selected based on location of the nonunion, so as to reduce confounding results based on the discrepancies in functional outcomes between upper and lower extremity nonunions *(15)*.

CONCLUSIONS

Our results demonstrate that the comorbidity of diabetes mellitus does not lead to significantly worse clinical or functional outcomes following surgical treatment for a fracture nonunion. While patients with diabetes mellitus may be more likely to go on to nonunion following an acute fracture, comparison with matched controls demonstrates that diabetes mellitus has little impact on the healing, outcomes and complications that occurs following surgical revision for fracture nonunion. Orthopaedic surgeons can effectively counsel diabetic patients undergoing surgical intervention for a fracture nonunion to expect a similar return to function and time to healing as non-diabetic patients

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