CLINICAL ARTICLE

Effect of the Blood HbA1c Level on Surgical Treatment Outcomes of Diabetics with Ankle Fractures

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Objective: To investigate whether blood haemoglobin A 1c (HbA1c) levels was predicative of diabetic patients' responsiveness to surgical treatment of ankle fractures.

Methods: The relationship between blood HbA1c levels and surgical treatment outcomes of 21 diabetic patients undergoing open reduction internal fixation (ORIF) for ankle fractures was analyzed with Pearson correlation testing and *t* testing. All patients were treated with ORIF using standard surgical techniques. Treatment outcomes were defined using radiological outcome, the American Orthopaedic Foot and Ankle Score (AOFAS) ankle-hindfoot scale score, surgical revision rate, and complication rate.

Results: HbA1c levels were found to have a statistically significant correlation with poor radiological outcomes ($r = 0.547$) and AOFAS ankle-hindfoot scores ($r = -0.592$). Additionally, though rates of poor radiological outcome, revision, and complication were high in the diabetic population as a whole, these rates were considerably higher among individuals with elevated HbA1c (≥6.5%) and considerably lower among individuals with lower HbA1c (<6.5%) levels.

Conclusion: Blood HbA1c levels appear to be predictive of risk and complication rates in the surgical treatment outcomes of diabetic patients with ankle fractures.

Key words: Ankle fracture; Diabetes mellitus; Hemoglobin A 1c

Introduction

Diabetes mellitus is a disease that affects multiple different organs and systems throughout the human body. As such, diabetes creates many concerns for healthcare professionals treating patients with the disease. Diabetic patients with ankle fractures are no exception and, due to the growing number of diabetic patients, represent a substantial portion of patients presenting with ankle fractures. As of 2010, diabetes affected 25.8 million people (8.3% of the population) in the United States, including 10.9 million individuals over the age of 65 (26.9% of the elderly population)[1]. Estimates predict that between the years 2000 and 2050, the prevalence of diabetes will increase by 165%[2]. In 2000, it was also estimated that the risk of developing diabetes at some point in one's lifetime was 32.5% for men and 38.5% for women[3].

Past studies have indicated that the incidence of ankle fractures is 187 per 100,000[4]. This high incidence rate, combined with the growing prevalence of diabetes in the US population, makes the treatment of and care for ankle fractures among diabetic individuals a significant concern for the medical community. In spite of this growing patient population, there is no standard protocol for the treatment of diabetic patients with ankle fractures and little research investigating treatment outcomes, even though complications and poor

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TABLE 1 Description of fracture type, HbA1c, and treatment outcomes for cases included in this study

Case No.	Age (years)	Sex	Weber fracture type	HbA1c (%)	Postsurgical complications	Radiological outcome
1	55	F	B	10.0	Persistent pain	Delayed union
2	48	M	C	9.9	Redisplacement, Persistent swelling, Infection	Delayed union
3	54	F	B	8.1	Osteoarthritis, Persistent swelling, Infection, Delayed surface healing	Delayed union, Malunion
4	65	M	B	7.7	Infection, Delayed surface healing, Numbness	Nonunion
5	78	M	C	7.7	Persistent swelling	Nonunion
6	58	F	B	7.5	—	Delayed union
7	64	F	A	7.1	Infection, numbness	Nonunion
8	52	F	A	7.0	Persistent swelling	Delayed union
9	70	F	C	6.5	Persistent swelling, Infection	Delayed union
10	60	M	A	6.2	Infection, Delayed surface healing, Numbness	Union
11	66	M	A	6.1	Infection	Union
12	69	F	B	5.9	—	Union
13	71	M	B	5.8	Redisplacement, Persistent swelling	Nonunion
14	53	F	B	5.5	Numbness	Nonunion
15	68	M	A	5.5	Persistent swelling, Infection, Delayed surface healing	Delayed union
16	49	F	C	5.5	—	Union
17	48	F	A	5.4	—	Union
18	75	F	B	5.4	Persistent pain	Union
19	42	M	C	5.3	Osteoarthritis, Persistent swelling	Malunion
20	63	F	B	5.3	—	Union
21	33	F	A	5.0	Persistent pain	Union

F, female; HbA1c, haemoglobin A 1c; M, male.

treatment outcomes are common. This study attempted to determine whether hemoglobin A 1c (HbA1c) levels, representing the long-term degree of diabetic control, are predictive of treatment outcomes in diabetic patients undergoing surgical reduction of ankle fractures.

Materials and Methods

The treatment outcomes of 21 diabetic patients who sustained ankle fractures and had corrective surgery at a Level 1 Trauma Center between March 2008 and December 2011 were reviewed retrospectively. Participants were selected from the surgical records based upon their positive past medical history of diabetes mellitus. Data on age, sex, fracture type, relevant past medical history, status of comorbidities, medications, surgical treatment method, HbA1c level, American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale score, presence of postsurgical complications, and final radiological outcome were gathered via chart review for each patient. Patients were between the ages of 33 and 78 years, with a mean age of 59.1 years. Thirteen of the subjects were women; eight were men. Two of the patients sustained open fractures. Seven patients sustained Weber A fractures, nine sustained Weber B fractures, and five sustained Weber C fractures (Table 1).

All of the patients were treated by the same surgeon with open reduction internal fixation (ORIF), using the institution's standard surgical techniques. In general, this first included a lateral-approach reduction and fixation of fibular fractures, using plating held in place by partially threaded cancellous screws and cortical screws. When applicable, medial malleolar fractures were reduced and fixed next, usually using partially threaded cancellous screws. Posterior malleolus fractures were fixed if the fragment was large, using partially threaded cancellous screws. After reduction and fixation of fracture fragments, presence of syndesmotic injury was ascertained using intraoperative stress views by checking the medial clear space or tibiofibular clear space under fluoroscopy. This involved neutrally positioning the ankle and applying external rotational stress to get a mortise view radiograph. Direct inspection of the syndesmosis and bone hook techniques were also used to evaluate syndesmotic injury in cases of excessive movement. If necessary, the syndesmosis was then reduced and fixed using screws. Endocrinology consults attempted to control blood glucose perioperatively, according to the institution's standard operating procedures.

HbA1c levels during the three months after surgery were compared to treatment outcomes. For HbA1c level, numerical lab values were recorded. Four criteria were selected to evaluate treatment outcome: radiological outcome, AOFAS Ankle-hindfoot scale score, need for surgical revision, and presence of postsurgical complications.

Radiological outcome was classified and recorded as either union, delayed union, nonunion, or malunion. According to Srinivasan *et al.*, healing in most ankle fractures can be radiographically appreciated 4–6 weeks after surgery[5]. Because many severe fractures may require a longer period of time to heal, especially in diabetic patients, this study considered a normal time course for fracture healing to be double that suggested by Srinivasan *et al.*; thus, union was defined as normal, properly aligned bony union achieved < 3 months after surgical reduction. Smith *et al.* describe nonunion as the persistence of the fracture line without a bridging callus six months after the initial injury[6]. Therefore, this study defined nonunion as an absence of bony union six months after surgical reduction. Delayed union was defined as properly aligned bony union achieved outside the normal three-month time course but prior to six months post-surgery. Malunion was defined as improperly aligned bony union at any time. The presence of either delayed union, nonunion, or malunion in any given patient was considered a "poor radiological outcome."

AOFAS ankle-hindfoot scale scores were recorded as a numerical, three-part score based on pain, function, and alignment of the fractured ankle. The AOFAS scale allots a maximum of 40 points for pain, 50 points for function, and 15 points for alignment, with higher scores indicating a healthier ankle. AOFAS ankle-hindfoot scores were recorded at the time of diagnosis with ankle fracture and again at a six month post-operative visit. For patients who healed within that time, no additional follow-up was done. However, the five patients in the study who experienced nonunion were followed for one year. Two patients did not achieve union after one year, and the remaining three patients had additional procedures: two underwent ankle fusions, while one patient required a below-the-knee amputation.

Need for surgical revision was recorded based upon the presence or absence of any abnormal surgical intervention that was required by the patient after the initial reduction of the fracture. Possible reasons for revision included fracture redisplacement, delayed union, nonunion, unsatisfactory alignment, and infection. Additional surgery for the removal of hardware was considered normal and was not recorded in the data as revision.

Serious complications in postsurgical fracture healing included redisplacement, persistent swelling, infection, delayed surface healing, and numbness. These complications impart a high level of morbidity on the patient and are encountered frequently in the diabetic population[7]. Therefore, we considered the presence of any one of these complications to be indicative of poor outcomes.

Additionally, patients were divided into two groups: one group with HbA1c $\geq 6.5\%$ and one group with HbA1c $< 6.5\%$. An HbA1c level of 6.5 was used to define the two groups because the American Diabetes Association considers HbA1c $\geq 6.5\%$ to be diagnostic of diabetes mellitus. The HbA1c $\geq 6.5\%$ group consisted of 9 patients, while the HbA1c <6.5% group included 12 patients. The treatment outcomes and complication rates of these two groups were then compared to one another statistically.

To determine whether HbA1c levels were correlated to specific treatment outcomes or complication rates, data were analyzed statistically using PASW (version 18.0; SPSS, Chicago, IL, USA). Pearson bivariate correlation analysis testing was used to determine whether there were statistically significant correlations between HbA1c level and radiological outcome, AOFAS ankle-hindfoot scale score, need for surgical revision, or presence of postsurgical complication. Outcome rates of patients with an HbA1c level $\geq 6.5\%$ and patients with an HbA1c level $< 6.5\%$ were compared using independent two-tailed t tests. Data with $r > 0.5$, $r < -0.5$, and $P < 0.05$ were considered statistically significant for this analysis.

Results

HbA1c Levels

HbA1c levels for the 21 patients analyzed in this study showed statistically significant correlations to several of the treatment outcome criteria. HbA1c levels were inversely correlated to radiological union ($r = -0.547$, $P = 0.010$); thus, high HbA1c levels were associated with lower rates of union, while low HbA1c levels were associated with higher rates of union. HbA1c levels were also inversely correlated to improvement in AOFAS ankle-hindfoot scale scores at six month follow-up appointments ($r = -0.592$, $P = 0.005$); thus, high HbA1c levels were associated with lower average function scores, while low HbA1c levels were associated with higher average function scores.

HbA1c levels were positively correlated to delayed union ($r = 0.595$, $P = 0.004$), but were not correlated to either nonunion or malunion. However, HbA1c levels were positively correlated to poor radiological outcome as a whole (delayed union, nonunion, or malunion) ($r = 0.547$, $P = 0.010$). Thus, high HbA1c levels were associated with high rates of delayed union and poor radiological outcome, while low HbA1c levels were associated with low rates of delayed union and poor radiological outcome.

There were no correlations between HbA1c levels and revision rates or complication rates. Therefore, HbA1c levels were not associated with the likelihood of revision or postsurgical complications.

Treatment Outcomes and Complication Rates

Overall, treatment outcomes were extremely poor in patients with diabetes mellitus. Radiologically, only 38.1% of patients achieved successful union, while 61.9% of patients had poor bone healing (delayed union, nonunion, or malunion). 100% of patients with an HbA1c $\geq 6.5\%$ had poor radiological outcomes, while only 33.3% of patients with an HbA1c $< 6.5\%$ had poor radiological outcomes. Additionally, there were statistically significant differences in the prevalence of both union and delayed union between the two groups (Table 2).

TABLE 2 Prevalence of radiological outcomes in the diabetic patients studied (21 cases)

Radiological outcome	Total occurrence (%)	Occurrence(%) in patients with HbA1c ≥ 6.5% (9 cases)	Occurrence(%) in patients with HbA1c < 6.5% (12 cases)
Union (8 cases)	38.1	0	66.7
Delayed union (7 cases)	33.3	66.7	8.3
Nonunion (5 cases)	23.8	33.3	16.7
Malunion (2 cases)	9.5	11.1	8.3
Poor radiological outcomes (13 cases)	61.9	100	33.3

HbA1c, haemoglobin A 1c.

For all patients with diabetes mellitus in this study, the average improvement in AOFAS Ankle-Hindfoot Scale score between the initial patient encounter and the six month follow-up was 39.8 points. The average improvement for patients with an HbA1c ≥ 6.5% was 26.7 points. The average improvement for patients with an HbA1c < 6.5% was 49.6 points. However, *t* test analysis comparing the average score improvement of the high and low HbA1c groups did not show a statistically significant difference between them ($P < 0.05$).

The rate of surgical revision for all diabetic patients was 42.9%. For patients with an HbA1c level ≥ 6.5%, the revision rate was 55.6%, while only 25.0% of patients with an HbA1c < 6.5% required revision. Again, despite the large disparity in the numbers between the high and low HbA1c groups, the differences were not statistically significant upon *t* test analysis ($P < 0.05$).

Complication rates were very high; 76.2% of all diabetic patients had some sort of serious postsurgical complication. 88.9% of patients with an HbA1c ≥ 6.5% had complications, and 66.7% of patients with an HbA1c < 6.5% had complications. Infection and persistent swelling were the most common complications, both of which occurred in 38.1% of patients. For patients with an HbA1c ≥ 6.5%, however, the infection rate was 55.6%, compared to 25% in patients with an HbA1c < 6.5% (Table 3).

Discussion

Past studies have shown that control of blood glucose is essential for proper wound healing in diabetic patients[8], and animal studies observed that uncontrolled diabetes leads to longer fracture healing times than in animals where blood sugar is well controlled[9]. Lengthy fracture healing times have also been described in diabetic patients with ankle fractures[10]. The literature has focused on the pathophysiological basis of these effects.

Hyperglycemia due to insulin dysregulation—the hallmark of diabetes—causes nonenzymatic glycosylation of proteins, along with increased intracellular formation of polyols, such as sorbitol, and these changes damage tissue in a wide range of organ systems throughout the body[11]. Many manifestations of this pathology interfere with the treatment of ankle fractures, including diabetic neuropathy. Patients suffering from diabetic neuropathy sustain oxidative damage to nerve cells due to the accumulation of polyols in the neurons[12]. This results in abnormal nerve function—including dysfunction of sensory, motor, or autonomic nerves—and may cause reduced proprioception, pain, thermal, and light touch sensations[11,13]. In its more advanced stages, peripheral neuropathy can cause the loss of protective sensation in the distal limb. It may also increase blood flow and osteoclast activity secondary to the aforementioned autonomic dysfunction, resulting in osteope-

TABLE 3 Prevalence of different complications in the diabetic patients studied (21 cases)

Complications	Total occurrence (%)	Occurrence(%) in patients with HbA1c ≥ 6.5% (9 cases)	Occurrence(%) in patients with HbA1c < 6.5% (12 cases)
Infection	38.1	55.6	25.0
Delayed surface healing	19.0	22.2	16.7
Persistent swelling	38.1	55.6	25.0
Osteoarthritis (ankle)	9.5	11.1	8.3
Numbness	19.0	22.2	16.7
Persistent pain	14.3	11.1	16.7
Redisplacement	9.5	11.1	8.3
Overall*	76.2	88.9	66.7

*Some patients had more than one serious complication. HbA1c, haemoglobin A 1c.

nia. Along with microtrauma resulting from the loss of protective sensation, this weakened bone structure contributes to the development of arthropathy[14–18]. Osteopenic pathology may initially put neuropathic individuals at increased risk of fracture, but it may also delay bone healing after fracture has occurred, even with proper surgical treatment and postoperative management of the injury[11,15].

Angiopathies are well documented in diabetics and develop progressively as a result of atherosclerotic damage secondary to hyperglycemia. Glycosylated molecules in the blood have been shown to contribute to the formation of atherosclerotic plaques and decreased arterial compliance in the peripheral vessels, and the concentration of these molecules is increased with continued hyperglycemia[19,20]. Occlusion of peripheral vessels that are crucial to proper perfusion of the ankle tissues results in poor nutrient supply, which in turn contributes to increased risk of infection, delayed fracture healing, and impaired wound healing[11].

The hyperglycemic, hypoxic environment produced by diabetic pathology in the distal limbs also decreases immune function. Immune cells in this environment display impaired attachment and migration into tissue that sustains traumatic damage[21,22]. The body's ability to clear necrotic debris from the area of injury is compromised, increasing the probability of infection. Subsequently, bacteria surviving in damaged or healing tissues release metalloproteinases and other enzymes that degrade fibrin and growth factors integral to the healing process[21]. Local wound healing is further affected by the diabetic environment's effect on fibroblasts. Fibroblasts necessary for the production of collagen show decreased migration and proliferation in hypoxic conditions[23]. Consequently, collagen synthesis is dramatically diminished in the wounds of diabetics, and its production is directly proportional to the amount of oxygen that is present in the damaged tissue[23,24].

The decreased collagen synthesis that impairs wound healing may also impair fracture healing and weaken the stability of new, healed bone[25,26]. Studies conducted in both animal models and humans have illustrated the consequences of this pathophysiology by demonstrating delayed fracture healing among diabetic individuals versus their non-diabetic counterparts[11,27].

The literature describes the manifold effects of elevated blood glucose on the surgical site, bone metabolism, and fracture healing, and it suggests that control of blood glucose plays an important role in successfully treating diabetic ankle fractures. However, the extent to which average long-term blood glucose levels (HbA1c) affect surgical treatment outcomes remains largely undescribed. Our study attempted to illustrate whether an observable relationship between HbA1c level and treatment outcome exists.

The percentage of poor treatment outcomes for patients in the high HbA1c group ($\geq 6.5\%$) was consistently higher than the percentage of poor treatment outcomes in the total diabetic population studied, while the percentage of poor treatment outcomes for patients in the low HbA1c group ($<6.5\%$) was consistently lower than that in the total diabetic population (Tables 2 and 3). These data, coupled with the statistically significant differences between the prevalence of union and delayed union in the high HbA1c and low HbA1c groups (Table 2), suggest that there is a relationship between HbA1c and treatment outcome. Specifically, it appears that the risk of poor treatment outcomes is increased considerably in patients with elevated HbA1c. We postulated that patients with elevated HbA1c are more likely to have suffered pathological changes in the extremities due to long-term lack of glycemic control, accounting for these results. This inference is further supported by the presence of statistically significant correlations between elevated HbA1c levels and poor treatment outcomes.

Diabetic patients who are at greater risk of treatment complications may be better identified by using blood HbA1c levels as a predictive marker. Prisk and Wukich[11], report that surgical fixation is the preferred treatment for diabetic ankle fractures in the majority of cases. They assert that more rigid fixation, lengthy nonweight bearing, and extra follow-up are critical for successful treatment outcomes in diabetic patients. The treatment methods set forth by Prisk and Wukich have proven to be effective in healing diabetic ankle fractures. Despite the use of these surgical and postsurgical methods, the data reported in our study suggest that the level of glycemic control achieved in a given patient could make a significant difference in outcome. Physicians should be aware of this when treating diabetic patients. Even with effective control of blood glucose, diabetic ankle fractures will continue to challenge physicians attempting to treat them—as evidenced in this study by the abundance of poor treatment outcomes and high complication rates in patients with HbA1c $< 6.5\%$ (Tables 2 and 3). However, the difference in treatment outcomes between high HbA1c and low HbA1c groups is distinct enough to warrant further consideration by the medical and scientific communities.

Because this study is retrospective in nature and could not completely control for all other variables (outside of HbA1c) that might influence fracture healing, it is difficult to make definitive statements about the degree of impact that HbA1c level has on ankle fracture healing in diabetics. However, major variables were similar enough among the groups of diabetic patients studied, that the findings described in this study may have significant value to the medical and scientific communities (Table 4). This study presents these findings as a preliminary examination of this subject.

While these data provide some evidence that HbA1c is indicative of underlying diabetic pathology and increased risk of poor treatment outcome, further research is needed on this subject. Both the retrospective nature and relatively small sample size of this study limit its ability to show a cause–effect relationship between HbA1c levels and treatment outcomes. Specifically, *t* test results comparing the prevalence of outcomes between the high HbA1c and low HbA1c groups were affected by the low number of patients in each group. Increasing the sample size could allow us to draw more definitive conclusions about the relationship between HbA1c and

TABLE 4 Characteristics of the high HbA1c (≥6.5%) and low HbA1c (<6.5%) groups

Group	Mean age (years)	Time to do ORIF (days)	Male : female	Initial AOFAS score*
HbA1c ≥6.5% (9 case)	60.4	3.8	3:6	27.4
HbA1c <6.5% (12 cases)	58.1	3.9	5:7	21.2

*Initial AOFAS Ankle-Hindfoot Scale Score used here as a representation of initial fracture severity.
HbA1c, haemoglobin A 1c.

treatment outcomes. Furthermore, this study was limited to using correlation analysis due to its retrospective design. This approach was necessary because patient groups in this study differed by more than one variable. In order to completely describe the extent of the relationship between HbA1c and treatment outcome in the different patient groups, a prospective study would be needed that controlled for factors such as age, severity of the fracture, quality of the bone, soft tissue conditions, and other potential confounding variables. Thus, larger prospective studies comparing patients with elevated HbA1c to control patients are necessary to confirm and further elucidate the findings described here.

HbA1c levels appear to be predictive of treatment outcomes and complication rates in the surgical reduction of fractures in patients with diabetes mellitus. Our findings imply that, despite appropriate perioperative control of blood sugar, patients with high HbA1c levels may have preexisting pathology that contributes to poor treatment outcomes. Further prospective analyses of larger populations of diabetic patients are needed to confirm these findings.

Author Contributions

N. Ebraheim designed the study, provided the data for the study and critically reviewed the analysis. T. Ludwig contributed to the review of current literature, data analysis, and writing of the manuscript. J. Liu designed the study, oversaw the interpretation of data and assisted in writing the manuscript.

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