Predictors of Outcomes of Foot Ulcers among Individuals with Type 2 Diabetes Mellitus in an Outpatient Foot Clinic

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Abstract

Objectives. To determine the risk factors for recurrence and persistence of non-healing foot ulcers resulting in minor and major amputations.

Methodology. This was an ambispective cohort analysis of persons with diabetic foot ulcers consulting at the diabetic foot clinic of East Avenue Medical Center. Data were analyzed through multiple logistic regression.

Result. Two hundred sixteen patients with Type 2 Diabetes Mellitus and diabetic foot ulcers were included in the analysis; 50.9% were males and the mean age of the cohort was 55.8 ± 9.9 years. Outcomes of foot ulcers were: healed 44.5% (healed with no recurrence 30%, healed but with recurrence 14.5%) and not healed 55.5% (major amputation 11%, minor amputation 21.5%, and persistently non-healing ulcer 23%). Multivariate logistic regression showed the following were independent risk factors for persistent non-healing ulcer: osteomyelitis (OR 66.5; CI 19.7, 217.8), smoking (OR 28.9; CI 6.8, 129.3, and peripheral arterial disease (PAD) (OR 56.8; CI 2.5, 877.2). Independent risk factors for ulcer recurrence were: plantar location of ulcer (OR 16.8; CI 6.8, 89.4), presence of more than one ulcer (OR 7.8; CI 3.6, 31.6), and neuropathy (OR 11.2; CI 7.2, 19.9). For healed foot ulcers, mean healing time was 14 ± 3 weeks. Healing time was significantly reduced from 12 weeks to 4.5 weeks (p<0.001) if patients consulted earlier (within 4 weeks from sustaining an ulcer).

Conclusion. Only half (55%) of patients with diabetic foot ulcers consulting in a dedicated outpatient foot clinic had an adverse outcome of foot ulcers (major amputation 11%, minor amputation, 21.5%, and persistently non-healing ulcer 23%) while a small portion (14.5%) of patients had recurrent foot ulcers. Arterial obstruction, smoking, low hemoglobin, neuropathy, and osteomyelitis increase the likelihood of healing failure while the presence of multiple ulcers, plantar location of ulcers, and neuropathy increase the risk of ulcer recurrence.

Key words: foot ulcer, amputation, neuropathy, peripheral artery disease

INTRODUCTION

Foot ulcerations are still the leading cause of limb amputations in persons with diabetes. In South East Asia, major amputation rates vary from as low as 9% to as high as 56%; while minor amputation rates are estimated at 27% and mortality from diabetic foot ulcers can be as high as 11%. Internationally, major amputation rates vary - the major amputation rate in Pakistan was 14% while it was only 10.7% in the UK. These studies were both done in a dedicated outpatient foot clinic. Ulcer recurrence is also a serious outcome next to amputations, and two important risk factors for ulcer recurrence are peripheral vascular disease and ulcer location. Patients with an ulcer on the plantar surface of the big toe are more likely to have recurrent ulcers. The healing time of diabetic foot ulcers vary from as short as 52 days to as long 78 days. Factors that affect time of healing are Wagner staging, bacterial infection, osteomyelitis, and peripheral arterial disease (PAD). Finally, ulcers may also fail to heal – risk factors associated with persistent ulcers are longer wound duration, number of ulcers, presence of infection, Wagner stage, age of patient, dialysis therapy, and peripheral vascular disease.

In the Philippines there are no published foot ulcer related outcome studies done in dedicated outpatient foot clinics to date. However, numerous inpatient studies have shown major amputation rates as high as 56%. Predictors for major amputation include neuropathy, PAD, severity of ulcer staging, longer duration of diabetes, smoking, delayed consultation, delayed administration of antibiotics, and delayed surgical management.

Data collected from this study will be used to aid clinicians to properly identify patients at risk for amputations and adverse foot outcomes so early referral to a diabetic foot clinic may be immediately done. Likewise, patients at risk for recurrence will be monitored more intensively and home routine foot care is taught at first consult.
The East Avenue Medical Center is the only tertiary government hospital in the Philippines to have a dedicated out-patient foot clinic (established in 1996). The goal of the clinic is to lower extremity amputation prevention by doing high risk foot screening, regular annual foot exam and applying standards of care for diabetic foot ulcers like off-loading, antibiotic therapy, weekly debridement and wound dressings.

The objective of the study was to determine the risk factors for foot ulcer recurrence and complications such as major amputation, minor amputation, or persistent ulceration. As a secondary objective, this study aimed to identify factors associated with healing time (defined as the number of weeks until complete epithelialization).

**METHODOLOGY**

The outpatient treatment of foot ulcers is done at the diabetic foot clinic of East Avenue Medical Center in Quezon City, Philippines - which is managed by an endocrine consultant and four endocrine fellows working in collaboration with orthopedic and vascular surgeons. The clinic sessions are held once a week. Patient management follows standards of care as defined by international recommendations. Upon consult patients are evaluated according to standards of care as given by international endocrine consultant and four endocrine fellows working in collaboration with orthopedic and vascular surgeons. The clinic sessions are held once a week. Patient management follows standards of care as given by international recommendations. Upon consult patients are evaluated according to standards of care as given by international recommendations.13 Upon consult patients are evaluated by etiology, presence of infection, and limb threatening/life threatening state. Those with limb threatening infection, extensive osteomyelitis, or needing major amputation or revascularization are subsequently admitted. Appropriate antibiotics are prescribed according to severity of infection; sharp debridement is done to remove gangrene and slough tissue; ulcer dressings and autolytic ointments are given by taking into consideration the wound bed, presence of granulation tissue, and degree of exudation. Patients are educated on off-loading, and follow-up is scheduled weekly at the minimum.

This was an ambispective study and ulcer outcomes were defined 1 year after initial consult. The retrospective cohort arm reviewed all charts from 2014-2017. For the prospective arm, patients consulting at the Out-Patient Foot Clinic recruited consecutively from January 2018 to May 2018 and were followed up for 1 year. Informed consent was obtained and privacy and confidentiality were emphasized. Individual case record forms contained only the initials of patient plus the code numbers assigned. Approval was obtained from the Institutional Ethics Review Board.

Inclusion criteria include: All adult patients, 18 years old and above, able to give written informed consent, consulting in the Diabetic foot clinic, diagnosed with Type 2 Diabetes Mellitus, presenting with ischemic/neuropathic/ neuroischemic foot ulcers, of any duration, and all charts of patients in the Diabetic foot clinic from 2014-2017.

Exclusion criteria include: patients unable to give written informed consent, patients with mental illness, patients with disease that may impair judgment and consent, non-diabetic foot ulcers, venous ulcers, cellulitis without ulcer, Charcot arthropathy without diabetic foot ulcer, and other unrelated skin diseases. Patients with missing data from the retrospective chart review were likewise excluded from the study. All charts from the retrospective arm with missing data and all patients from the prospective arm who were lost to follow up were excluded from the study.

Data collection included demographic data, duration of diabetes, presence of hypertension, atherosclerotic cardiovascular disease (ASCVD), or chronic kidney disease; laboratories collected were fasting blood sugar, HbA1c, lipid profile, creatinine, and hemoglobin at the time of initial consult (i.e., lipid profile were categorized as either “high” or “low” following clinical practice guideline targets of total cholesterol 200 mg/dL, Triglycerides 150 mg/dL, and HDL 40 mg/dL for male and 50 mg/dL for female14 and hemoglobin, defined as “low” if lower than normal range); also noted were history of past foot ulcers and previous amputations, onset and duration of foot ulcer, presence of infection, PAD, neuropathy, osteomyelitis and Wagner staging.

The presence of peripheral neuropathy was assessed using the Michigan Neuropathy Screening Instrument.15,16 PAD was assessed by palpation of the posterior tibial and dorsalis pedis pulses and by measuring the Ankle Brachial Index using a hand held Doppler. PAD is defined as at least one of the following: ABI <0.9, a history of a peripheral artery revascularization procedure or angiography confirming PAD, non-compressible arteries (defined as ABI >1.4), abnormal waveforms (monophasic or biphasic) with ABIs of 0.9 –1.4, or absence of two or more pedal pulses on palpation.17

Osteomyelitis was diagnosed through probe to bone or X-ray findings.

Outcomes of this study were defined as:

1. **Healed:** (complete epithelialization of a foot ulcer)
   a. Healed (complete epithelialization) with no recurrence within the observation period of 1 year.
   b. Recurrent foot ulcers (those who presented with foot ulcers that eventually healed within the observation period of 1 year but had another foot ulcer on the same site as the healed ulcer). If the recurrent ulcer eventually healed within the observation period, this was still included in the population of “recurrence.”

2. **Not healed:**
   a. Resolved foot ulcer through Minor amputation (amputation below the malleolus)
   b. Resolved foot ulcer through Major amputation (amputation above the malleolus)
   c. Persistence of ulcer (non-healing of ulcer beyond the study period)

These outcomes were assessed by the primary investigator. Healed foot ulcers are defined as complete epithelialization of a foot ulcer with no signs of infection such as erythema, swelling, or exudative discharge. Recurrence is defined as a new foot ulcer occurring at the same site of a previous foot ulcer at any time during the study period. For persistent ulcers, these were diabetic foot ulcers that required major or minor amputation, or ulcers that failed to epithelialize beyond the study period.13 Healing time was defined as the number of weeks it took for a foot ulcer to have complete re-epithelialization with resolution of any sign of infection.
Statistical analysis
Summary statistics were reported as mean ± standard deviation for continuous data with normal distribution or as median (interquartile range) for quantitative data with skewed distribution or as count (percent) for qualitative measures. Minimum and maximum values were also reported. Shapiro-Wilk’s test was used to check for normality of quantitative data. Checks for homogeneity of patient characteristics were also performed. Multivariate regression analyses were performed to identify demographic and clinical characteristics independently associated with healed and unhealed ulcers, and healing time.

Subgroup analysis was done for 2 data sets: the first was for patients with “healed” ulcers – factors for recurrence vs. no recurrence were compared using all data collected. The second subgroup analysis using the Mann Whitney U test was done for patients with “healed” ulcers with no recurrence – specifically, the factors for number of weeks it took for complete epithelialization (healing time) were identified. Odds-ratios and 95% confidence intervals were estimated. Statistical significance was based on \( p \)-value \( \leq 0.05 \).

RESULTS

Cohort description
There were a total of 216 adults with Type 2 diabetes mellitus and diabetic foot ulcers seen in this study. There were 130 charts for the retrospective arm and 86 patients for the prospective arm. The demographic and clinical characteristics of the study are summarized in Table 1. The average age was 55.8 years and there was an equal distribution of male and female (male 50.9%). Average duration of diabetes was 5 years. Only 22% of the cohort were smokers (n=48) and the most common comorbidity was hypertension seen in 38.9% of the cohort (n=84). Only 4.6% of the entire cohort had regular or routine foot care at home. The mean fasting blood sugar (FBS) was 145 mg/dL, mean HbA1c was 7.9%, mean creatinine was 0.9 mg/dL, and the mean lipid profile of the cohort has total cholesterol less than 200 mg/dL but LDL greater than 100 mg/dL.

A plantar foot ulcer was seen in 25.5% of patients (n=54) and only 14.8% (n=17) had more than 1 foot ulcer upon consult. The average duration of diabetic foot ulcers prior to initial consult was 9 weeks.

Upon presentation, 38.4% (n=83) had PAD, while a similar percentage had osteomyelitis 34.7% (n=75). Majority of all patients (58.3%, n=126) had neuropathy.

Table 1. Characteristics of patients with diabetic foot ulcer according to healing outcome

|                      | All (n = 216) | Not Healed Ulcers (n = 120) | Healed Ulcers (n = 96) |
|----------------------|--------------|-----------------------------|------------------------|
|                      | [Major amputation 24; Minor amputation 46; Persistently unhealed 50] | [Recurrence 31; No recurrence 65] |                      |
| Age in years         | 55.8 ± 9.9   | 55.1 ± 10.7                 | 56.2 ± 9.2             |
| Male gender          | 110 (50.9%)  | 60 (50.0%)                  | 50 (52.1%)             |
| Duration of diabetes in years | 5.0 (9.6)       | 8.0 (9.5)                   | 3.0 (9.7)              |
| Smoker               | 48 (22.2%)   | 40 (33.3%)                  | 8 (8.4%)               |
| Comorbidities        |              |                             |                        |
| Hypertension         | 84 (38.9%)   | 46 (38.3%)                  | 38 (39.5%)             |
| Chronic kidney disease | 22 (10.2%)  | 9 (15.0%)                   | 14 (14.6%)             |
| Retinopathy          | 52 (24.1%)   | 30 (25.0%)                  | 22 (22.9%)             |
| With routine foot care | 10 (4.6%)    | 4 (3.33%)                   | 6 (6.25%)              |
| Serum biochemistry   |              |                             |                        |
| FBS in mg/dL         | 145.0 (86.0) | 173.5 (96.5)                | 121.0 (83.0)           |
| HbA1c in %           | 7.9 (3.2)    | 8.9 (4.0)                   | 7.7 (2.0)              |
| Creatinine in mg/dL  | 0.9 (0.3)    | 0.9 (0.2)                   | 0.8 (0.3)              |
| Hemoglobin in g/dL   | 14.0 (2.4)   | 11.1 (3.4)                  | 14.1 (1.6)             |
| Cholesterol in mg/dL | 189.0 (47.0)| 196.0 (50.0)                | 151.0 (43.0)           |
| Triglyceride in mg/dL| 146.0 (87.0)| 189.5 (91.0)                | 110.0 (54.5)           |
| HDL in mg/dL         | 37.2 (11.0)  | 35.0 (11.3)                 | 41.0 (11.0)            |
| LDL in mg/dL         | 122.7 (46.0) | 146.5 (39.5)                | 99.5 (32.5)            |
| Plantar location of ulcer | 54 (25.5%) | 36 (30.0%)                  | 18 (18.8%)             |
| More than 1 ulcer on foot | 17 (14.8%)  | 37 (30.8%)                  | 7 (7.3%)               |
| Duration of ulcer in weeks | 9.0 (3.4)   | 12.0 (4.8)                  | 3.0 (1.0)              |
| Peripheral Arterial Disease | 83 (38.4%) | 68 (56.7%)                  | 15 (15.6%)             |
| Osteomyelitis         | 75 (34.7%)   | 60 (50.0%)                  | 15 (15.6%)             |
| Neuropathy            | 126 (58.3%)  | 86 (71.7%)                  | 30 (31.3%)             |
| Wagner staging system |              |                             |                        |
| I                    | 11 (5.1%)    | 1 (0.8%)                    | 10 (10.4%)             |
| II                   | 120 (55.6%)  | 44 (36.7%)                  | 76 (79.2%)             |
| III                  | 12 (5.6%)    | 9 (7.5%)                    | 3 (3.1%)               |
| IV                   | 76 (35.2%)   | 70 (58.3%)                  | 6 (6.25%)              |
| V                    | 6 (2.8%)     | 6 (5.0%)                    | -                      |

FBS: fasting blood glucose, HbA1c: glycated hemoglobin, HDL: High density lipoproteins, LDL: low-density lipoproteins
Data presented as mean ± standard deviation, median (interquartile range) or count (percent).

*Single case
Non-healing foot ulcers

For non-healing foot ulcers vs. healed foot ulcers a significant proportion were smokers (33.3% vs 8.4%); had evidence of PAD (56.7% vs 15.6%); neuropathy (71.7% vs 31.3%); osteomyelitis (50.0% vs 15.6%); had multiple ulcers (30.8% vs 7.3%); had higher levels of fasting blood glucose (173.5 vs. 121 mg/dL); cholesterol (196 vs. 151 mg/dL); triglyceride (189.5 vs. 110 mg/dL); LDL (146.5 vs. 99.5 mg/dL); plus lower levels of hemoglobin (11.1 vs. 14.1 mg/dL); lower HDL (35 vs. 41 mg/dL) and a longer ulcer duration prior to consult (12 vs 3 weeks). A higher proportion of the non-healing group had worse ulcer severity - majority presenting with Wagner IV (58.3% vs. 6.25%) or Wagner V (5% vs. 0%).

The prevalence of non-healing ulcer was 55.5% (n=120). The major amputation rate was 11% (n=24), minor amputation rate 21.5% (n=46), and persistently unhealed 23% (n=50). The major amputation rates in an outpatient setting are expectedly lower compared to inpatient rates of 50%.11,12 In the outpatient setting, patients present with less severe ulcer staging and milder infections – these, along with prompt antibiotic treatment, weekly sharp debridement, offloading education, all contribute in lowering major amputation rates.11

Risk factors independently associated with major amputation, minor amputation, or persistent non-healing are shown in Table 2. Independent factors with the highest odds for non-healing are osteomyelitis (OR 66.5; CI 19.7, 217.8), PAD (OR 56.8; CI 2.5, 877.2), and smoking (OR 28.9; CI 6.8, 121.9). The data concurs with current literature that osteomyelitis and infection are the leading causes of major amputation in diabetic foot ulcers.18-21 Our study did not analyze the location of osteomyelitis as a predictor of amputation – but other studies have found that osteomyelitis is more frequently found in the forefoot (90% of the time) - which has a better prognosis than if the osteomyelitis was in the hindfoot, because a hindfoot osteomyelitis significantly increases the chance of major amputation.22

Dyslipidemia (high TG and LDL, low HDL) is significant but only barely increased the odds for non-healing: high TG (OR 1.09; CI 1.0, 2.4), high LDL (OR 1.1; CI 1.0, 1.1), low HDL (OR 0.9; CI 0.8, 0.9).

We also found that every 1 g/dL decrease in hemoglobin from normal increased the chance of non-healing of a diabetic foot ulcer by 29% (p<0.0001).

| Factor | Adjusted OR | 95% CI | p-value |
|--------|-------------|--------|---------|
| Smoking | 28.9 | (6.8, 129.3) | <0.0001* |
| Hemoglobin in g/dL | 0.7 | (0.4, 0.9) | <0.0001* |
| Triglyceride in mg/dL | 1.1 | (1.0, 2.4) | 0.010* |
| HDL in mg/dL | 0.9 | (0.8, 0.9) | 0.010* |
| LDL in mg/dL | 1.1 | (1.0, 1.1) | 0.009* |
| Peripheral Arterial Disease | 56.8 | (2.5, 877.2) | <0.0001* |
| Osteomyelitis | 66.5 | (19.7, 217.8) | <0.0001* |
| Neuropathy | 9.9 | (7.4, 19.0) | 0.010* |

| Factor | Adjusted OR | 95% CI | p-value |
|--------|-------------|--------|---------|
| Plantar location of ulcer | 16.8 | (6.8, 89.4) | 0.031* |
| More than 1 ulcer on foot | 7.8 | (3.6, 31.6) | 0.006* |
| Neuropathy | 11.3 | (7.2, 19.9) | 0.010* |

Osteomyelitis: yes vs. no 12 (8) 15 (9) <0.0001*.

Recurrent

The prevalence for healed foot ulcers was 44.5% (n=96). Out of the 96 patients who had healed foot ulcers, only 14% of them had ulcer recurrence (n=31). Three important factors (Table 3) were found that predicted recurrence in healed foot ulcers: plantar location of ulcer (OR 16.8; CI 6.8, 89.4), presence of more than one ulcer (OR 7.8; CI 3.6,31.6), and neuropathy (OR 11.2; CI 7.2, 19.9).

Healing time

Table 4 shows the factors that affect healing time. Of the 65 adults with completely healed ulcer (no recurrence), the mean healing time was 14 weeks (98 days) ±3 weeks. Many studies have established various factors that affect healing time of ulcers which include: duration of ulcer, size and depth of ulcer, smoking, increased HbA1c, male gender, and presence of infection.23-25 In our study, the only significant factor associated with time of healing was ulcer duration – those who consulted within 4 weeks of sustaining the ulcer healed faster (healing time 4.5 weeks) than those who delayed more than 4 weeks (healing time 12 weeks).

DISCUSSION

Out of 216 patients with diabetic foot ulcers the prevalence of healed foot ulcers was 44% (n=96) and the prevalence of non-healing was 55% (n=120). For the non-healing foot ulcers, major amputation rate outcome 20% (n=24), minor amputation outcome 38% (n=46), and non-healing outcome was 42% (n=50). For the healed foot ulcers, 32% (n=31) had recurrence within 1 year.

The major and minor amputation rates in an out-patient setting are expectedly lower than those of in-patient studies such as those located at the Philippine General Hospital (PGH) where the major amputation rate is 50%.11,12 This can be attributed to factors such as ulcer severity presenting in the out-patient setting is less severe compared to the in-patient setting; or that an out-patient...
setting provides patients early consult, prompt antibiotic treatment, and weekly sharp debridement that are not done in most cases that are eventually admitted.11

Risk factors independently associated with non-healing of ulcers were smoking, low hemoglobin, dyslipidemia, and the presence of PAD, osteomyelitis, and neuropathy. Although dyslipidemia increased non-healing by only a small percentage, smoking was found to increase the risk of non-healing nearly 29 times compared to non-smokers. The significance of smoking in these patients reflect an acceleration of macrovascular disease and atherosclerosis prevalent in many persons with diabetes and is in itself, together with dyslipidemia, already an independent risk factor for developing peripheral arterial disease.19

Our study also found that for every 1 g/dL decrease in hemoglobin, the chance of non-healing of diabetic foot ulcer is increased by 52%.

The data also concurs with the study of Jeffcoate et al.,5 where PAD was an independent risk factor for major amputation. As mentioned previously, the co-existence of CAD and PAD in patients with diabetes is well established. In a study by Poredos and Jug,20 50% of patients with macrovascular disease have co-existing PAD – reflecting the underlying atherosclerosis that plagues these patients predisposing to foot ulcer formation resulting in major amputation.

Neuropathy is an established risk factor for recurrence because this predisposes the feet to “unrecognized repetitive trauma.”27 Neuropathy also delays and impairs detection of new foot ulcers which tend to recur on the same site as old ulcers when healed patients begin to walk again.28 Multiple ulcers are twice as likely to recur than single ulcers, have poor 12-month outcomes, and are almost invariably associated with ischemic ulcers and PAD.

Peters et al., found that patients had a 61% chance of increase in recurrence if the ulcer was located in the plantar area.6 An ulcer on the plantar surface, when not offloaded properly, is subjected to repeated pressures which delay its healing.

This concurs with our finding that a plantar ulcer increased risk of recurrence; and if the ulcer was on the dorsal side of the foot, the non-healing outcome was reduced by 83%.

For ulcer recurrence, other risk factors were neuropathy and presence of more than 1 ulcer at the time of consult. These risk factors differ from two studies of Cardino and Panuda et al.,11,12 where smoking and PAD were both significant risk factors for non-healing.

Possible sources of difference in these risk factors are that our patients are treated and seen in an outpatient foot clinic where their presentation is less severe than the population seen by in the PGH studies where the patients were admitted and had severe infection or ischemia.

The mean healing time was 14 weeks (98 days) ±3 weeks and only one factor was significant in affecting healing time, namely, the duration of foot ulcer prior to consult. Patients who consulted within 1 month of sustaining a foot ulcer tended to heal within 4.5 weeks while patients who waited after 1 month healed within 12 weeks (p<0.001). This again reinforces the findings of Cardino et al., that delayed treatment of foot ulcers lead to untoward foot complications.2,11

Compare this to the study of Messenger et al., where 335 patients consulting in an out-patient podiatry clinic were analyzed and foot ulcers had a median healing time of 52 days (7.5 weeks) and the factors that affected healing time were more severe wound staging, bacterial infection, osteomyelitis, and PAD.7 In the study by Jeffcoate et al.,5 of 449 patients with diabetic foot ulcers, the median healing time was 78 days (11 weeks) and again factors that affected healing time were severity of infection and presence of PAD. Once persons with diabetes sustain a foot ulcer it is imperative they consult immediately for prompt assessment and treatment of PAD, neuropathy, and infection to prevent non-healing.

Glycemic control (as tracked by fasting blood sugar and HbA1c) plays a major role in wound healing and diabetic foot ulceration. In two reasonably large prospective studies by Xiang et al., and Christman et al., their data found that an HbA1c of 7-8% increased the healed outcome of diabetic foot ulcers by 3 (OR 3.01, CI 1.32, 6.86) and “for each 1.0% point increase in HbA1c, the daily wound area healing rate decreased by 0.028 cm²/day.”29,30

Other studies done on diabetic foot ulcers in the inpatient and outpatient settings found no correlation between blood sugar control and healing of diabetic foot ulcers. In a prospective study by Fesseha et al., they found that “baseline A1c was not associated with wound healing in univariate or fully adjusted models.” Furthermore, as they monitored the HbA1c changes in their 4-year study, they found that mean HbA1c changes were not associated with wound healing.31 This finding was also seen by Ozenc et al., in 137 patients with diabetic foot ulcers that HbA1c was not a factor in developing diabetic foot ulcers or healing.32 Sarinnapakorn et al., in a prospective study of 593 patients in Thailand found that blood glucose control is not markedly related to foot ulcer onset and healing. Their study identified that the significant factors for foot ulcer healing are age, duration of diabetes, dyslipidemia, neuropathy, cardiovascular disease, foot deformities, decreased pulses, prior amputation, and abnormal ankle-brachial index.33

Taking into account all these studies, the information at hand indicates foot ulcer healing is affected not just by glycemic control but also by the additional interplay of other factors like smoking, osteomyelitis, peripheral arterial disease, number of ulcers on consult, severity of infection, and delay of consult and treatment – important factors also found in our study.

The data obtained from this study are from patients presenting at a dedicated outpatient clinic. The profile of patients who are admitted for diabetic foot ulcers are much different because by definition, their admission may already be an indicator of a more severe infection necessitating intravenous antibiotics, limb threatening ischemia, or life-threatening sepsis. Thus, the data and independent risk factors presented in this study should be able to guide
clinicians seeing patients with foot ulcers in the outpatient setting – facilitating early referral to a diabetic foot clinic or specialist for those patients who have risk factors for non-healing, or intensive monitoring and education for patients who are at risk for foot ulcer recurrence.

**CONCLUSION**

Outcomes of foot ulcers can be classified into two groups: Healed and Not Healed. For unhealed foot ulcers whose specific outcomes can lead to major amputation, minor amputation, and persistent ulceration - the presence of PAD, smoking, dyslipidemia, low hemoglobin, neuropathy, and osteomyelitis all increase the likelihood of amputation or persistent non-healing.

For patients who have healed foot ulcers the presence of multiple ulcers, plantar location, and neuropathy all increase the risk for ulcer recurrence. When patients present to a foot clinic early (less than 4 weeks) the healing time is significantly shortened from 12 weeks to 4.5 weeks.

We recommend early identification of risk factors in patients with type 2 Diabetes Mellitus presenting with foot ulcers so that timely and early referral to an outpatient foot clinic or diabetic foot specialist may be immediately initiated.

Likewise, for patients with a past history of foot ulcers that have healed, identification of risk factors should lead to closer monitoring and education for routine home foot care. Ultimately, primary prevention is still the key to avoiding adverse foot outcomes. We encourage all persons with diabetes to have regular foot screening and foot care education.

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**Statement of Authorship**

Both authors certified fulfillment of ICMJE authorship criteria.

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**References**

1. Boulton AJ. The diabetic foot: Grand overview, epidemiology and pathogenesis. Diabetes Metab Res Rev. 2008;24(Suppl 1):S3–6. PMID: 18442166. https://doi.org/10.1002/dmr.533.
2. Cardino M, Josol C, Isip-Tan I. Quality of care and outcomes of diabetic extremity patients after the implementation of the revised Diabetes Extremity Care Team Protocol of the Philippine General Hospital. Philipp J Intern Med. 2009;47(2):57-63. https://drive.google.com/file/d/1D7qrRr6hdtaI3POF3nBxDczoy6HqIMIg/view.
3. Penayun TGD, Naibaho RM. Clinical profile and outcome of diabetic foot ulcer, a view from tertiary care hospital in Semarang, Indonesia. Diabet Foot Ankle. 2017;16(1):1312974. PMID: 28649286. PMID: PMC547294. https://doi.org/10.1016/j.dfa.2016.12.001.
4. Riaz M. Miyan Z, Zaidi SI, et al. Characteristics and outcomes of subjects with diabetic foot ulceration. Diabetes Care. 2012;35(9):e63. PMID: 22928685. PMID: PMC3425011. https://doi.org/10.2337/dc11-1906.
5. Jeffcoate WJ, Chipchase SY, Ince P, Game FL. Assessing the outcome of the management of diabetic foot ulcers using ulcer-related and person-related measures. Diabetes Care. 2006;29(9):1784-7. PMID: 16875786. https://doi.org/10.2337/dci06-0306.
6. Peters EJ, Armstrong DG, Laverey LA. Risk factors for recurrent diabetic foot ulcer: Site matters. Diabetes Care. 2007;30(8):2077-9. PMID: 17506793. https://doi.org/10.2337/dci07-0445.
7. Messinger G, Masaebia R, Husen I, Dvaragan S, Lahromi M. Diabetic foot ulcer outcomes from a podiatry led tertiary service in Kuwait. Diabet Foot Ankle. 2018;11(1):471-92. PMID: 28968165. PMCID: PMC5974709. https://doi.org/10.1016/j.diabfo.2018.03.047.
8. Fike CE, Horn SD, Smout RJ, Barrett RS, Thomson B. A predictive model for diabetic foot ulcer outcome: The wound healing index. Adv Wound Care (New Rochelle). 2016(5(7)):279–87. PMID: 27366589. PMCID: PMC4980227. https://doi.org/10.1089/wound.2015.05686.
9. Chang AO, Elao EA, Quimpo JA. Diabetic foot ulcer - experience at the Philippine General Hospital. Philipp J Intern Med. 2016;34(6):205-9. https://drive.google.com/file/d/1LGgk871_TokTeXn3TayP5yfE8wH-U/view.
10. Balderas JA, Orbiso R, Racho V, Lim-Abraham MA. Diabetic foot extremity management by a multidisciplinary care team: The PFGH Experience. Philipp J Intern Med. 1999;37 (5):246-52. https://drive.google.com/file/d/1G92oS9S9EciCQgBuSyVCyVAcbVnQ6MDMA1/view.
11. Cardino MIT, Josol CV, Isip-Tan I, Jimeno CA. Risk factors for major amputation of diabetic foot ulcers. Philipp J Intern Med. 2011;49(2):74-8.
12. Panuda JP, Macalad-Josue AA, Buenaust-Sedurante M. Factors associated with in-hospital mortality among patients with diabetes admitted for lower extremity infections. J ASEAN Fed Endocr Soc. 2019;34(1):336-43. PMID: 33442135. PMCID: PMC7784136. https://doi.org/10.15605/jafes.034.01.07.
13. Schaper NC, van Netten JJ, Apelqvist J, et al. IWGDF practical guidelines on the prevention and management of diabetic foot disease. https://iwgdfguidelines.org/wp-content/uploads/2021/03/IWGDF-2019-final.pdf. Accessed June 1, 2020.
14. Gonzalez-Santos LE, Oliva R, Jimeno CA, et al. Executive summary of the 2020 Clinical Practice Guidelines for the management of dyslipidemia in the Philippines: 2020 Dyslipidemia CPG. J ASEAN Fed Endocr Soc. 2021;36(1):5-11. PMID: 34177882. PMCID: PMC8214350. https://doi.org/10.15605/jafes.036.01.01.
15. Moghtaderi A, Bahkshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument. Clin Neurol Neurosurg. 2006;108(5):477-81. PMID: 16150538. https://doi.org/10.1016/j.clineuro.2005.08.003.
16. Herman WH, Pop-Busari R, Braffett BH, et al. Use of Michigan Neuropathy Screening Instrument as a measure of distal symmetrical peripheral neuropathy in type 1 diabetes: results from the diabetes control and complications trial/epidemiology of diabetes interventions and complications. Diabet Med. 2012;29(7):933-44. PMID: 22417277. PMCID: PMC3641573. https://doi.org/10.1111/j.1464-5491.2012.03644.x.
17. Aboyans V, Ho E, Denenberg JO, Ho LA, Natarajan L, Criqui MH. The association between elevated ankle systolic pressures and peripheral occlusive arterial disease in diabetic and nondiabetic subjects. J Vasc Surg. 2008;48(5):1197–203. PMID: 18692981. https://doi.org/10.1016/j.jvs.2008.06.005.
18. Reiber GE, Pecoraro RE, Koepsell TD. Risk factors for amputation in patients with diabetes mellitus. A case-control study. Ann Intern Med. 1992;117(2):97–105. PMID: 1605439. https://doi.org/10.7547/1000052.
19. Boulton AJ, Vileikyte L, Ragnarsson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. Lancet. 2005;366(9498):1719–24. PMID: 16299106. https://doi.org/10.1016/S0140-6736(05)67698-2.
20. Lavery LA, Ashry HR, van Houtum W, Pugh JA, Hankless LB, Basu S. Variation in the incidence and proportion of diabetes-related amputations in minorities. Diabetes Care. 1996;19(1):48-52. PMID: 8720533. https://doi.org/10.2337/diacare.19.1.48.
21. Nicolau DP, Stein GE. Therapeutic options for diabetic foot infections: a review with an emphasis on tissue penetration characteristics. J Am Podiatr Med Assoc. 2010;100(12):52–63. PMID: 20093545. https://doi.org/10.7547/1000052.
22. Faglia E, Clerici G, Caminiti M, Curci V, Somalvico F. Influence of osteomyelitis location in the foot of diabetic patients with transstibial amputation. Foot Ankle Int. 2015;34(2):222–7. PMID: 25413061. https://doi.org/10.1177/1071100714537436.
23. Musa HG, Ahmed ME. Associated risk factors and management of chronic diabetic foot ulcers exceeding 6 months’ duration. Diabet Foot Ankle. 2012;3. PMID: 2311925. PMCID: PMC3465402. https://doi.org/10.1016/j.dfa.2011.09.003.
24. Marston WA, Dermagraft Diabetic Foot Ulcer Study Group. Risk factors associated with healing chronic diabetic foot ulcers: The importance of hyperglycemia. Ostomy Wound Manage. 2006;52(3):96–9. PMID: 16569785.
25. Margolis DJ, Kantor J, Santanna J, Strom BL, Berlin JA. Risk factors for delayed healing of neuropathic diabetic foot ulcers: A pooled analysis. Arch Dermatol. 2000;136(12):1531-5. PMID: 11151660. https://doi.org/10.1001/archderm.136.12.1531.
26. Poredos P, Jug B. The prevalence of peripheral arterial disease in high risk subjects and coronary or cerebrovascular patients. Angiology. 2007;58(3):309-15. PMID: 17626985. https://doi.org/10.1177/0003319707302494.

27. Waaijman R, de Haart M, Arts ML, et al. Risk factors for plantar foot ulcer recurrence in neuropathic diabetic patients. Diabetes Care. 2014;37(6):1697–705. PMID: 24705610. https://doi.org/10.2337/dc13-2470.

28. Khalifa WA. Risk factors for diabetic foot ulcer recurrence: A prospective 2-year follow-up study in Egypt. Foot (Edinb). 2018;35:11–5. PMID: 29753996. https://doi.org/10.1016/j.foot.2017.12.004.

29. Xiang J, Wang S, He Y, Xu L, Zhang S, Tang Z. Reasonable glycemic control would help wound healing during the treatment of diabetic foot ulcers. Diabetes Ther. 2019;10(1):95-105. PMID: 30465160. PMCID: PMC649267. https://doi.org/10.1007/s13300-018-0536-8.

30. Christman AL, Selvin E, Margolis DJ, Lazarus GS, Garza LA. Hemoglobin A1c predicts healing rate in diabetic wounds. J Invest Dermatol. 2011;131(10):2121-7. PMID: 21697890. PMCID: PMC3174328. https://doi.org/10.1038/jid.2011.176.

31. Fesseha BK, Abularrage CJ, Hines KF, et al. Association of hemoglobin A1C and wound healing in diabetic foot ulcers. Diabetes Care. 2018;41(7):1478-85. PMID: 29661917. PMCID: PMC614359. https://doi.org/10.2337/dc17-1683.

32. Ozenc S, Simsek K, Yildirim AO, et al. Association between the development of diabetic foot and serum fetuin-A levels. Pol Arch Med Wewn. 2013;12(10):513-8. PMID: 23974250. https://doi.org/10.20452/pamw.1921.

33. Sarinnapakorn, V, Sunthorntepwarakul T, Deerochanawong C, Niramitmahapanay S, Napartvaunmuay N. Prevalence of diabetic foot ulcers and risk classifications in type 2 diabetes mellitus patients at Rajavithi hospital. J Med Assoc Thai. 2016;99(Suppl 2):S99-105. PMID: 27266223.