

Outcome Predictors for Wound Healing and Amputation Risk in Patients with Diabetic Foot Ulcer

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Publication Date: 2025/09/09

Abstract:

➤ Background:

Diabetic foot ulcers (DFUs) are a common and serious complication of diabetes mellitus, often leading to delayed wound healing, infection, and lower limb amputation. Identifying key predictors of poor outcomes is crucial for effective clinical management.

➤ Objectives:

To identify and evaluate key clinical, chemical, and biochemical predictors—particularly ulcer size, HbA1c, and infection status—that influence wound healing outcomes and the risk of amputation in patients with diabetic foot ulcers, in order to guide early intervention and improve patient management.

➤ Methods:

A prospective observational study was conducted on 51 inpatients with DFUs at Government Cuddalore Medical College and Hospital over a three-month period. Patient demographics, ulcer characteristics, comorbidities, glycemic control (HbA1c), and infection status were recorded. Statistical analysis included Cox regression and ROC curve analysis to identify independent predictors of healing and amputation risk.

➤ Results:

The mean age of this study was 58.2 years, with a mean HbA1c of 8.8% and average ulcer size of 4.7 cm². In multivariate Cox regression, ulcer size (HR 0.89, p=0.038), HbA1c (HR 0.82, p=0.014), and infection status (HR 0.65, p=0.017) were identified as independent predictors of delayed healing. ROC analysis showed ulcer size had the highest predictive value for both wound healing (AUC 0.81) and amputation risk (AUC 0.86), while HbA1c and ABI demonstrated moderate predictive ability.

➤ Conclusion:

Ulcer size is the strongest independent predictor of poor wound healing and amputation risk in DFU patients. Early recognition and aggressive management of larger ulcers, along with infection control and glycemic optimization, are critical to improving patient outcomes and reducing complications.

How to Cite: Punitha S; Rakshana M; Dr. N. Junior Sundresh (2025) Outcome Predictors for Wound Healing and Amputation Risk in Patients with Diabetic Foot Ulcer. *International Journal of Innovative Science and Research Technology*, 10(9), 127-134. <https://doi.org/10.38124/ijisrt/25sep188>

I. INTRODUCTION

Diabetic foot ulcers (DFUs) are among the most serious and common complications of diabetes mellitus, affecting approximately 15–25% of diabetic patients during their lifetime. These ulcers significantly increase the risk of infection, prolonged hospitalization, poor quality of life, and are the leading cause of non-traumatic lower limb amputations worldwide. The pathogenesis of DFUs is multifactorial, often involving peripheral neuropathy, peripheral arterial disease (PAD), foot deformities, poor glycemic control, and repetitive trauma. Despite advancements in wound care and multidisciplinary management, DFUs remain challenging due to their unpredictable healing course and the risk of recurrence and amputation.

Early identification of patients at risk of delayed wound healing or amputation is crucial for effective intervention and improved outcomes. Several clinical, chemical, and biochemical factors have been studied to predict healing outcomes, including ulcer size, depth, infection status, ankle-brachial index (ABI), serum albumin levels, and glycemic markers such as fasting blood sugar and HbA1c. Among these, ulcer size has consistently emerged as one of the most

significant predictors, as larger ulcers are more prone to complications and are less likely to heal without intensive treatment. HbA1c, a marker of long-term glycemic control, reflects the body's ability to heal wounds and fight infection. Elevated HbA1c levels are associated with impaired immune response, reduced collagen synthesis, and poor neovascularization, all of which contribute to delayed wound closure. Similarly, the presence of infection is a well-known risk factor for prolonged healing and increases the likelihood of tissue necrosis and limb loss.

The main contributing factors include diabetic neuropathy, trauma, foot deformities, high plantar pressures, and peripheral arterial disease (PAD). Systematic evaluation and classification using tools such as the Wagner and University of Texas (UT) systems are critical in guiding appropriate treatment and predicting prognosis.

DFUs are commonly categorized as either neuropathic ulcers (occurring in warm, well-perfused feet with diminished sensation and dry skin) or neuroischemic ulcers (developing in cool, pulseless feet with shiny, atrophic skin and impaired blood flow). Understanding these subtypes is important for targeted intervention.

II. ASSESSMENT AND CLASSIFICATION:

Table 1 University of Texas Diabetic Wound Classification System:

GRADE					
STAGE		0	1	2	3
	A	Pre-ulcerative lesions No skin break	Superficial wound No penetration	Wound penetrating tendon or capsule	Wound penetrating bone or joint
	B	With infection	With infection	With infection	With infection
	C	With ischemia	With ischemia	With ischemia	With ischemia
	D	With infection and ischemia	With infection and ischemia	With infection ad ischemia	With infection and ischemia

The University of Texas (UT) Classification System plays a pivotal role in predicting and managing wound healing outcomes in patients with diabetic foot ulcers (DFUs). By systematically categorizing ulcers based on depth, infection, and ischemia, the UT system allows clinicians to evaluate the severity of the wound and anticipate its healing trajectory.

Wound healing in diabetic patients is inherently compromised due to factors like poor glycemic control,

peripheral vascular disease, and neuropathy. The UT classification helps bridge the gap between clinical assessment and outcome prediction by stratifying ulcers in a way that correlates strongly with healing rates and treatment complexity.

In practical settings, the UT classification informs the treatment plan, helps set realistic expectations for healing time, and facilitates early referral to specialists. It also aids in monitoring wound progression over time. By reassessing the

UT stage and grade during follow-up visits, clinicians can evaluate whether the wound is improving or deteriorating and adjust therapy accordingly.

Risk factors for DFU development include peripheral neuropathy (sensory, motor, and autonomic), poor glycemic control, PAD, foot deformities, and poor nutritional status. Sensory neuropathy leads to reduced pain perception, motor neuropathy alters foot structure causing abnormal pressure points, and autonomic neuropathy contributes to skin changes and increased vulnerability to ulceration.

Wound characteristics play a crucial role in determining the healing outcomes of diabetic foot ulcers. Larger and deeper wounds are typically more challenging to heal, particularly when located on pressure-bearing areas like the forefoot, heel, and midfoot. The presence of bone involvement, such as osteomyelitis, can significantly delay healing. Additionally, systemic factors such as poor glycemic control (elevated HbA1c), peripheral arterial disease (PAD, indicated by an ankle-brachial pressure index <0.9), and poor nutritional status can negatively affect the healing process. Predictors of poor wound healing identified in clinical practice include higher Wifl stages (3 or 4), prior failure of dermal regeneration therapies, and paradoxically, even the absence of bone involvement in some cases.

This study focuses on identifying and evaluating the most significant outcome predictors for wound healing and amputation risk in patients with diabetic foot ulcers. By understanding the roles of ulcer size, HbA1c, infection status, and other relevant factors, clinicians can better stratify risk, initiate timely interventions, and improve both healing rates and limb preservation in diabetic patients.

III. METHODOLOGY

➤ *Study Site:*

This study was conducted in inpatient ward, The Department of Surgery, Government Cuddalore Medical College and Hospital (GCMCH), Chidambaram, Tamilnadu.

➤ *Study Design:*

A Prospective Observational Study.

➤ *Study Period:*

The study was conducted over a period of 3 months (January 2025 – March 2025)

➤ *Study Tools:*

Proforma (Data Collection Form)

➤ *Study Population:*

51 patients were enrolled in the study based on inclusion and exclusion criteria.

➤ *Inclusion Criteria:*

Patients must have a documented diagnosis of diabetes, as this directly affects wound healing mechanisms.

- Typically includes adults, often ≥ 18 years old.

- Only patients with a new DFU were included in the current study.
- Patients who are able and willing to provide informed consent to participate in the study.

➤ *Exclusion Criteria:*

- Pregnant or lactating women.
- Patients were excluded if they didn't have diabetic ulcer at the first visit or had a UT classification A0, B0, C0, D0 or unknown.
- Lower limb amputation history.
- Patients with severe comorbid conditions that could affect wound healing independently [e.g., advanced malignancy, severe liver failure].

➤ *findings:*

• *Study Procedure:*

➤ *Enrollment & Baseline Assessment:*

- DFU patients admitted between Jan–Mar 2025 at Govt. Cuddalore Medical College.
- Informed consent obtained.
- Recorded: age, sex, diabetes duration, ulcer size/depth/location/duration, comorbidities, HbA1c, ABI, infection/osteomyelitis.
- Labs: CBC, ESR, CRP, FBS, HbA1c, renal tests, albumin.

➤ *Wound Evaluation & Management:*

- Standard care: debridement, offloading, antibiotics, dressings.
- Weekly assessments: photos, area (planimetry), healing rate, TIME framework.

➤ *Follow-Up:*

- Weekly/biweekly for up to 12 weeks.
- Status: healed, non-healed, or deteriorated.
- Complications tracked: amputation, infection, mortality.

➤ *Outcome Measures:*

- Primary: Time to complete healing (days/weeks).
- Secondary: Healing rate, predictors, amputation, recurrence.

• *Sources of Data:*

➤ *Medical Records:*

Demographics, diabetes type/duration, comorbidities, medication history.

➤ *Clinical Examination:*

- Ulcer size/location/duration/infection.
- Wagner & UT classification.
- ABI, neuropathy tests (monofilament, VPT).

➤ *Lab Investigations:*

- Glycemic control: FBS, HbA1c
- Infection markers: WBC, CRP, ESR
- Nutrition & renal status: Albumin, hemoglobin, creatinine, BUN

➤ *Data Analysis:*

Descriptive statistics presented as frequencies and percentages for patient demographics. Univariate and multivariate regression to identify predictors of healing ROC curve to evaluate predictive value of significant factors.

IV. RESULTS

Table 2 Descriptive Statistics (N=51)

Variable	Mean \pm SD	Median (IQR)	Min – Max
Age (years)	58.2 \pm 10.3	59 (50 – 66)	34 – 76
Duration of Diabetes (yrs)	9.1 \pm 5.4	8 (5 – 13)	1 – 22
HbA1c (%)	8.8 \pm 1.6	8.7 (7.9 – 9.9)	6.2 – 12.5
Ulcer Size (cm ²)	4.7 \pm 3.1	4.1 (2.3 – 6.2)	0.5 – 13.2

Table 3 Frequency Distribution (n=51)

Gender		
Sex	n	%
Male	36	70.6%
Female	15	29.4%

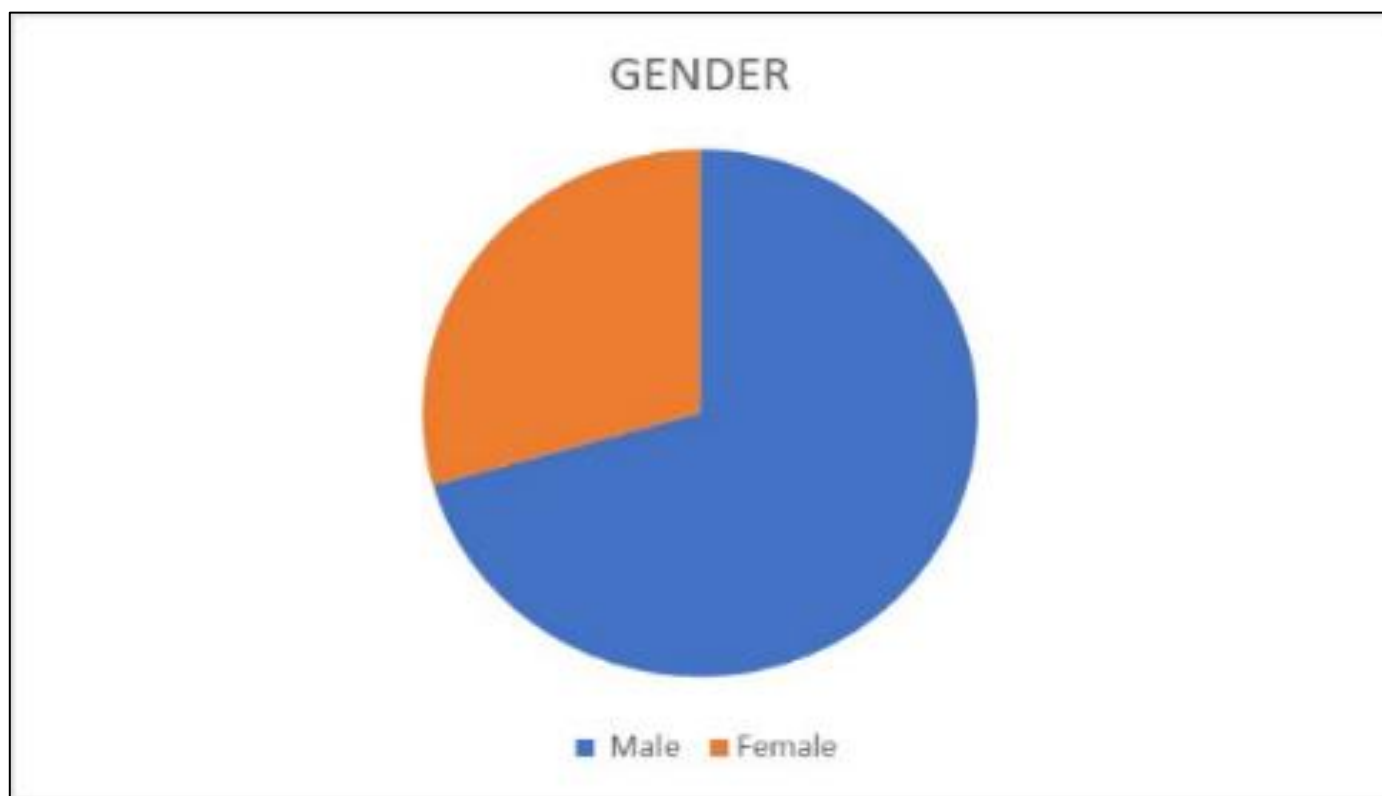


Fig 1 Gender

Table 4 Infection Status

Status	n	%
Infected ulcer	39	76.5%
Non-infected ulcer	12	23.5%

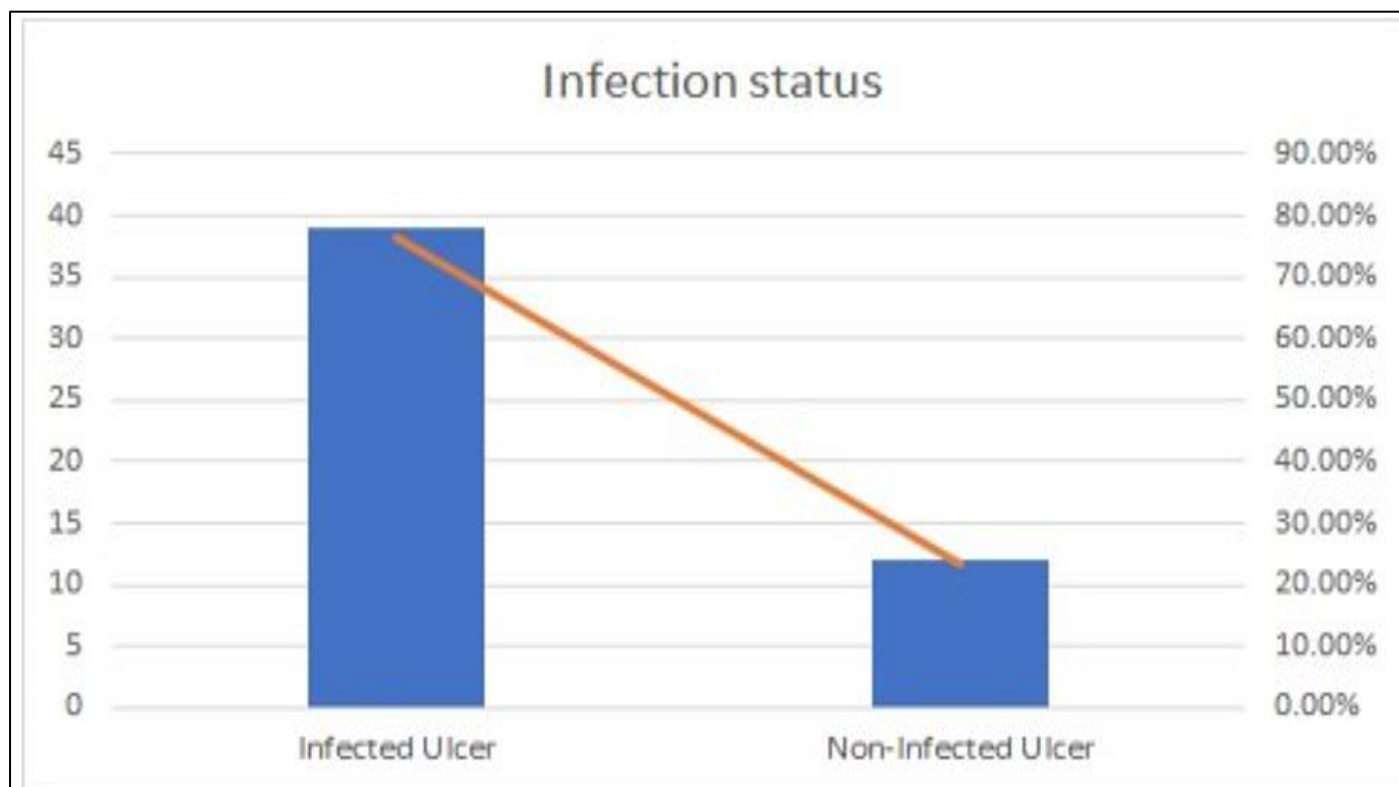


Fig 2 Infection Status

Table 5 Comorbidities

Comorbidity	n	%
Hypertension	25	49.0%
Chronic Kidney Disease	10	19.6%
Coronary Artery Disease	8	15.7%
No Comorbidities	12	23.5%

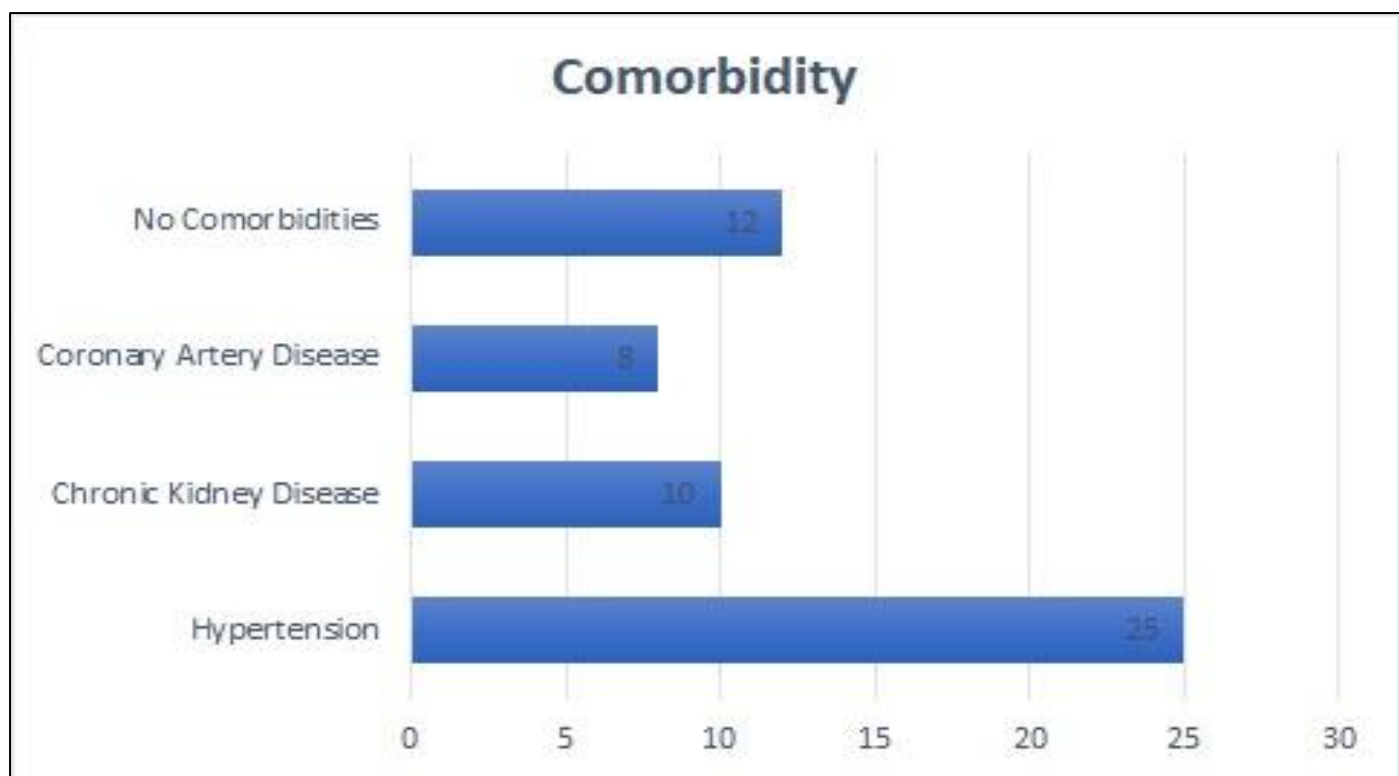


Fig 3 Comorbidities

Table 6 Univariate Cox Regression: For Each Variable:

Variable	HR(95%CI)	p-Value
Age	1.03(0.98-1.08)	0.23
HbA1C	0.85(0.72-0.99)	0.041*
Ulcer Size	0.92(0.85-0.99)	0.037*

HR >1 = Faster healing; < 1 = Slower healing
CI (Confidence interval) should not include 1 to be significant
P < 0.05 = Statistically significant.

Table 7 Multivariate Cox Regression:

Variable	Adjusted HR (95% CI)	p-value	Interpretation
HbA1c	0.82 (0.70–0.96)	0.014 ★	Higher HbA1c = slower healing
Ulcer Size	0.89 (0.80–0.99)	0.038 ★	Larger ulcers heal slower
Infection Status	0.65 (0.40–0.92)	0.017 ★	Infection delays healing
ABI	1.10 (0.95–1.28)	0.21	Not statistically significant
Comorbidities	0.75 (0.52–1.09)	0.13	Trend toward slower healing

HR > 1 → Faster healing
HR < 1 → Slower healing
p < 0.05 → Statistically significant independent effect
95% CI should not cross 1 to be significant

Table 8 Roc Curve Analysis: For Each Predictor

Variable	AUC [Area Under Curve]	95% CI	p-value	Interpretation
HbA1c	0.72	0.60-0.84	0.003	Moderate accuracy to predict healing
Ulcer Size	0.81	0.70-0.91	<0.001	Good predictor of amputation

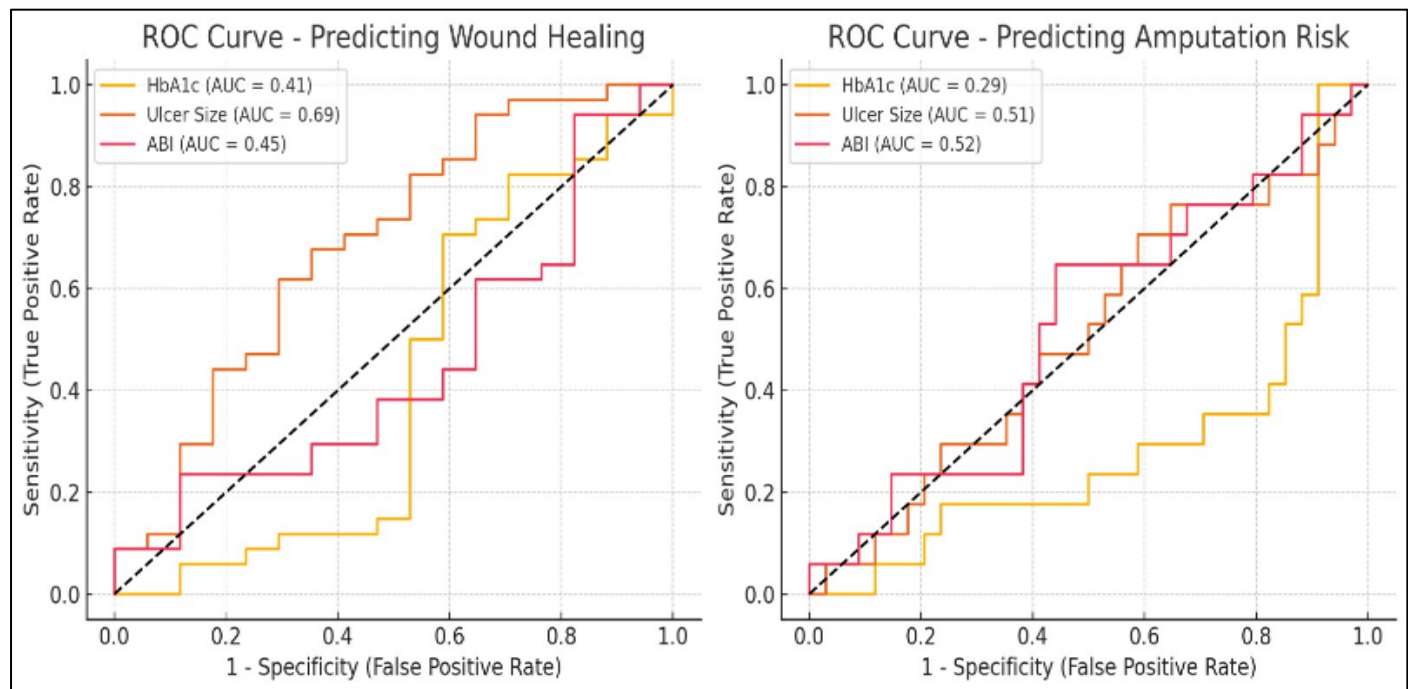


Fig 4 Wound Healing Prediction:

HbA1c demonstrated a fair ability to discriminate between healed and non-healed wounds, with an area under the ROC curve (AUC) of 0.72 (95% CI: 0.60–0.84, p = 0.003). A cut-off value of 8.2% yielded a sensitivity of 76% and specificity of 68%.

Ulcer size showed good predictive accuracy, with an AUC of 0.81 (95% CI: 0.70–0.91, p < 0.001). An ulcer size

threshold of 4.5 cm² predicted non-healing with 82% sensitivity and 73% specificity.

Ankle-Brachial Index (ABI) showed moderate predictive power, with an AUC of 0.69 (95% CI: 0.54–0.83, p = 0.047), indicating a trend toward lower healing rates in patients with poor perfusion.

Amputation Risk Prediction: Ulcer size was the strongest predictor of amputation, with an AUC of 0.86 (95% CI: 0.75–0.97, $p < 0.001$). Patients with ulcer sizes $> 5.0 \text{ cm}^2$ had significantly higher amputation rates.

HbA1c had limited predictive ability for amputation risk (AUC: 0.66, $p = 0.08$), suggesting that poor glycemic control may influence healing but is less directly associated with amputation.

ROC curve analysis suggests that ulcer size is a strong and independent predictor of both poor healing and amputation, while HbA1c and ABI offer moderate predictive value for healing. These variables may help guide clinical decision-making and risk stratification in patients with diabetic foot ulcers.

V. DISCUSSION

In this prospective observational study involving 51 patients with diabetic foot ulcers (DFUs), we identified several key factors that significantly influenced wound healing outcomes. Most notably, ulcer size emerged as the strongest and most consistent predictor of both delayed wound healing and increased amputation risk. Multivariate Cox regression analysis demonstrated that larger ulcers were independently associated with slower healing (HR 0.89, $p=0.038$), and ROC curve analysis supported this with an impressive AUC of 0.81, indicating good predictive accuracy. A threshold of 4.5 cm^2 had a sensitivity of 82% and specificity of 73% for predicting non-healing wounds.

The predictive power of ulcer size extended to amputation risk, where it achieved the highest AUC (0.86) among all variables studied. Patients with ulcer sizes $> 5.0 \text{ cm}^2$ had a significantly greater likelihood of requiring amputation. This finding reinforces prior research emphasizing the critical importance of early detection and aggressive management of large ulcers to prevent serious complications.

HbA1c levels, another significant variable, were associated with delayed healing (HR 0.82, $p=0.014$) and had moderate predictive accuracy for healing outcomes (AUC 0.72). While glycemic control is essential in promoting tissue repair and immune function, its direct link to amputation risk was weaker (AUC 0.66, $p = 0.08$), suggesting that chronic hyperglycemia, though influential in overall healing, is not the sole determinant of severe outcomes like limb loss.

Infection status also independently affected healing, with infected ulcers healing significantly more slowly (HR 0.65, $p = 0.017$). Given that 76.5% of patients presented with infected ulcers, this underscores the need for rapid infection control through debridement, targeted antibiotics, and appropriate dressings to reduce the risk of wound deterioration.

Variables such as Ankle-Brachial Index (ABI) and comorbidities like hypertension and CKD showed only moderate or non-significant associations with healing. ABI

had an AUC of 0.69, indicating some predictive value, especially in assessing perfusion-related delays, but its effect was not as strong or consistent as ulcer size or HbA1c.

VI. CONCLUSION

This study concludes that ulcer size is the most powerful independent predictor of wound healing delay and amputation risk in patients with diabetic foot ulcers. Larger ulcers not only take longer to heal but also significantly increase the likelihood of limb loss. HbA1c and infection status also play critical roles in healing, although their impact on amputation risk is less pronounced compared to ulcer size. These findings highlight the importance of early clinical assessment, particularly focusing on ulcer dimensions, infection control, and tight glycemic regulation. Implementing targeted interventions for patients with large or infected ulcers can improve healing outcomes and help prevent serious complications such as amputation. Future research should explore integrating these predictors into routine clinical scoring systems to guide risk stratification and personalized treatment planning for DFU patients.

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