

Statement of Purpose

The purpose of this study is to evaluate the factors influencing healing times in diabetic foot ulcers (DFUs) to improve patient outcomes and inform targeted treatment strategies. By analyzing key variables such as ESR, CRP, A1c, ABI, and wound area, and integrating retrospective data from 22 studies, this research quantifies their impact on healing. The findings aim to guide evidence-based interventions and provide clinicians with predictive tools to optimize care for individuals with DFUs.

Literature Review

A retrospective review of the literature was conducted to identify factors influencing healing times in diabetic foot ulcers (DFUs). The search included peer-reviewed articles published in English. Search terms used were: 'diabetic foot ulcers,' 'healing times,' and 'factors that affect healing.' Relevant studies were identified through databases such as PubMed, Scopus, and Google Scholar. A total of 22 articles met the inclusion criteria and were used for data extraction. Articles were selected based on their focus on healing outcomes and quantitative analysis of factors such as inflammation, vascular status, metabolic control, and wound size. A custom app was developed using Swift in Xcode on MacOS to integrate the equations and compute healing times based on input parameters. The app utilizes user-provided data for ESR, CRP, A1c, ABI, wound size, and smoking status to predict total healing time. To enhance predictive accuracy, a supervised machine learning model was trained using the aggregated data. Seventy percent (70%) of the dataset was used for training, and the remaining 30% was reserved for validation. The model analyzed the influence of systemic inflammation, glycemic control, vascular status, and wound characteristics on healing outcomes. This approach allowed for the refinement of equations and the identification of key predictors of healing time.

Case Study

Diabetic foot wounds (DFWs) present a significant clinical challenge due to delayed healing and the risk of complications such as infection and amputation. Multiple physiological factors influence wound healing time, including inflammatory markers, metabolic control, vascular status, and wound characteristics. This study examines the impact of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hemoglobin A1c (A1c), ankle-brachial index (ABI), and wound area on total healing time in DFWs. Elevated ESR and CRP, markers of systemic inflammation, are strongly associated with delayed wound healing. ESR levels above 30 mm/h contribute to additional healing delays, with every unit increase in ESR extending healing time by 0.5 days. Similarly, CRP levels above 5.1 mg/L add 0.1 days per unit, reflecting prolonged inflammatory responses that impede tissue repair. Poor metabolic control, represented by elevated A1c, significantly reduces healing rates. Wounds in patients with A1c levels above 7% experience a linear decrease in healing rate, from 0.3 cm²/day at baseline to 0.005 cm²/day at A1c levels exceeding 11.1%. Vascular insufficiency, assessed using ABI, further exacerbates healing delays. ABI values outside the optimal range (0.9 to 1.1) contribute additional time to healing, with a cubic relationship quantifying the extent of the delay. Larger wound areas directly correlate with prolonged healing times, as they require greater cellular and vascular resources for tissue repair. This study highlights the importance of addressing systemic inflammation, glycemic control, vascular status, and wound size to optimize healing outcomes in diabetic foot wounds. Clinical management strategies must integrate these parameters to reduce healing times, improve patient outcomes, and minimize complications.

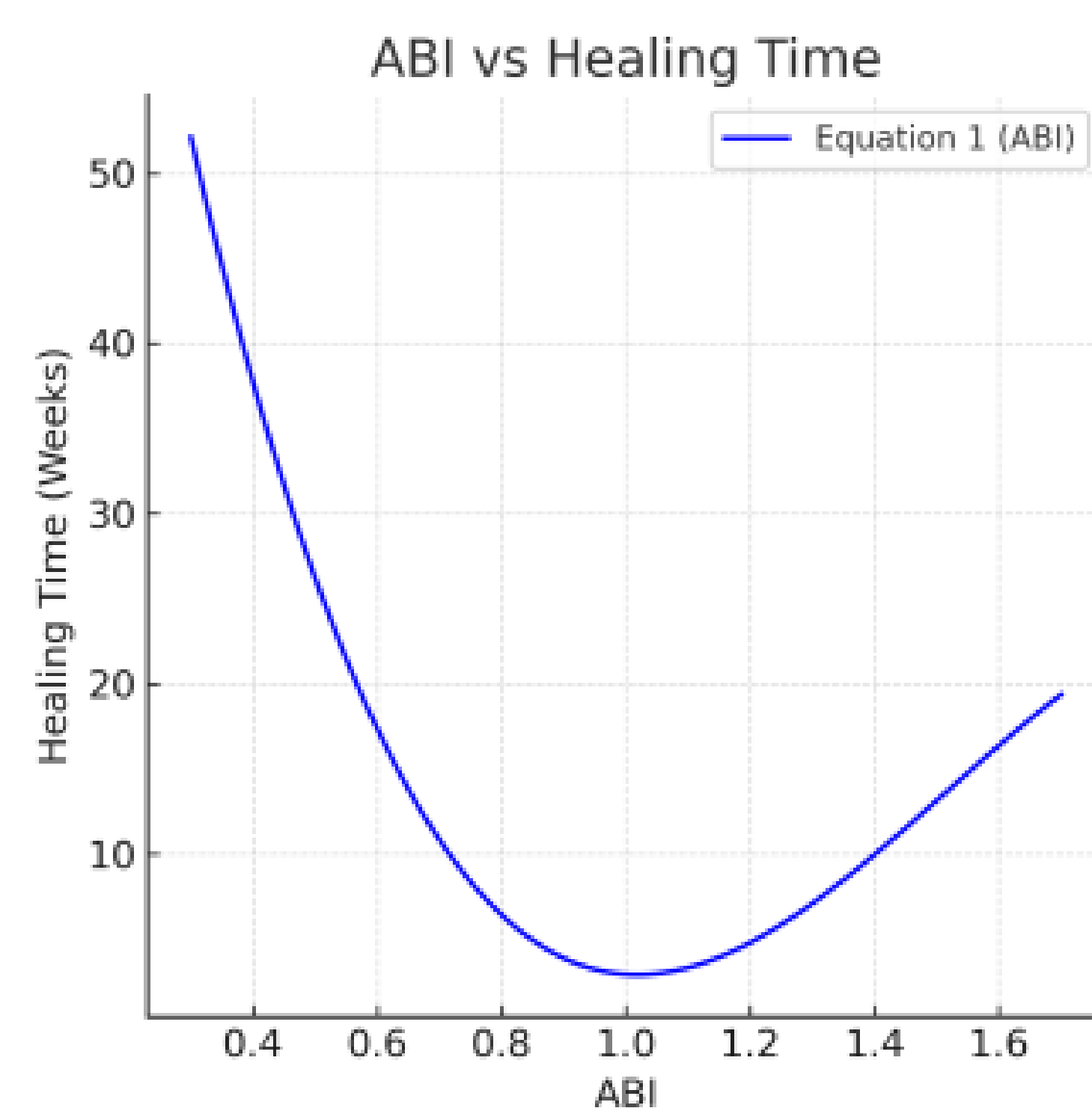


Fig A

Healing Time Prediction Equations

Equation Number	Equation
1	$T(ABI) = -42.93 * (ABI)^3 + 195.75 * (ABI)^2 - 265.05 * (ABI) + 115.16$
2	$R(A1c) = 0.3$ if $A1c \leq 7$, else decreasing linearly to 0.005 for $A1c > 11.1$
3	$\Delta T(ABI) = [-42.93 * (ABI)^3 + 195.75 * (ABI)^2 - 265.05 * (ABI) + 115.16] - T_ABI$ Baseline
4	$\Delta T(A1c) = A / R(A1c) - A / 0.3$
5	$\Delta T = \Delta T(ABI) + \Delta T(A1c)$
8	$T = 1.25 * (A / R_total + \Delta T(ABI) + 0.5 * ESR + 0.1 * CRP)$ if smoker else unchanged

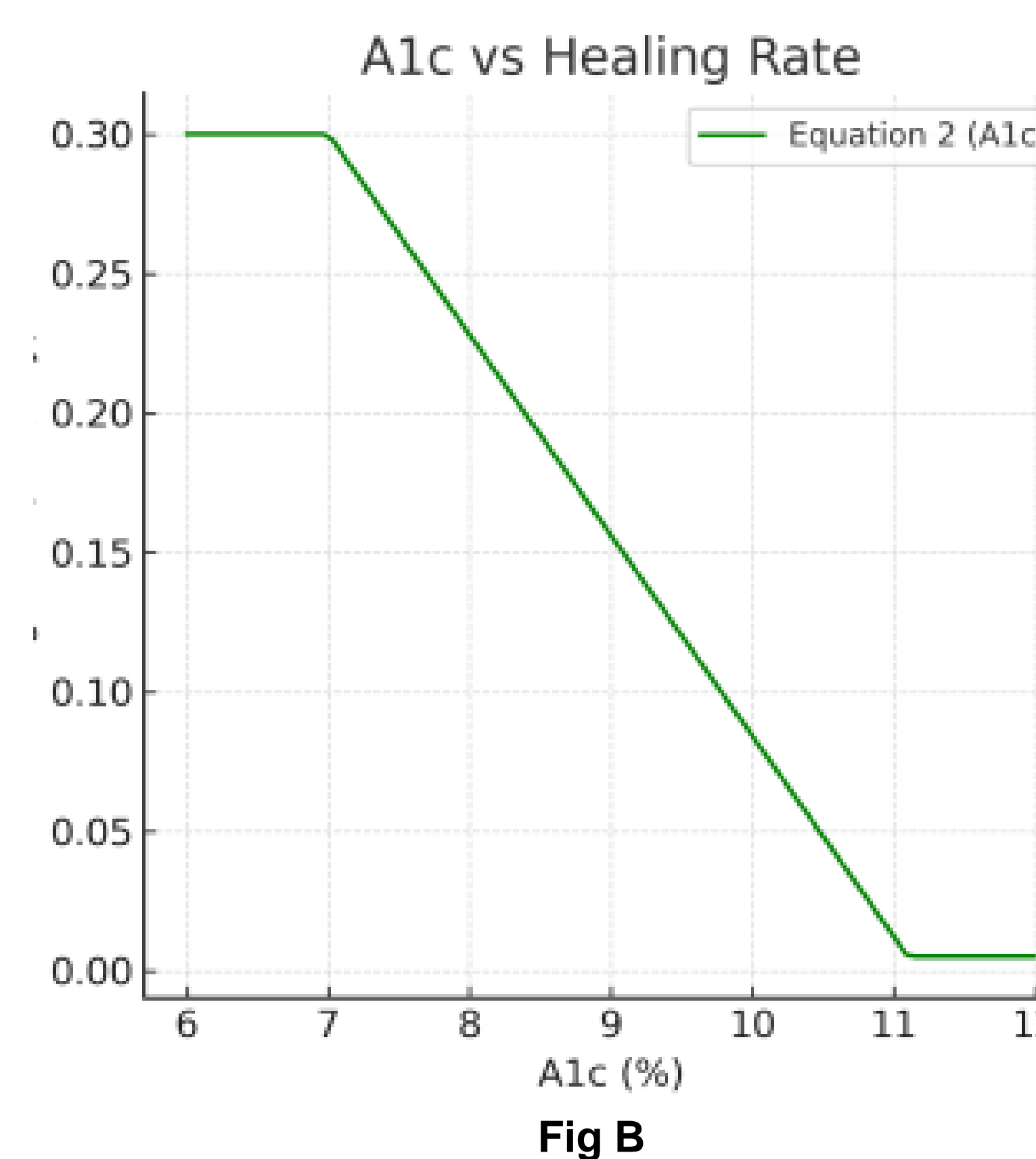


Fig B

Fig C.

Figure A demonstrates the graphical visualization of the equation used to adjust healing times. Figure B shows the rapid decline in wound healing in sq. cm as A1c increases. Figure C provides the equations used to produce the final predicted healing time.

Analysis and Discussion

Model Performance and Clinical Relevance
 The artificial intelligence (AI) model developed for predicting diabetic foot ulcer (DFU) healing times integrates key patient-specific factors, including: Ankle-Brachial Index (ABI), Hemoglobin A1c (A1c), wound size (A), inflammatory markers (ESR, CRP), and smoking status. These variables were selected based on their known impact on wound healing and incorporated into a set of equations to quantify their influence. The core model, expressed as a series of mathematical equations, leverages ABI-based polynomial regression (Equation 1) to estimate baseline healing time and a dynamically adjusted healing rate (Equation 2) to account for glycemic control. The model then computes individual contributions to delayed healing due to ABI deviations (Equation 3) and hyperglycemia (Equation 4), summing these delays into a final time adjustment (Equation 5). A final correction (Equation 8) integrates systemic inflammation (via ESR and CRP) and applies a smoking penalty (25% delay), reflecting well-documented delays in smokers. A prospective study is needed to further generalize these findings.

References

- Zhang, Yuqi. "Factors Associated with Healing of Diabetes-Related Foot Ulcers: Observations from a Large Prospective Real-World Cohort | Diabetes Care | American Diabetes Association." *American Diabetes Association*, diabetesjournals.org. 21 June 2021. diabetesjournals.org/doi/10.2337/143.138821/Factors-Associated-With-Healing-of-Diabetes.
- Tehan, Peta. "Wiley Online Library | Scientific Research Articles, Journals, ..." *OnlineLibrary.Wiley.Com*, Diabetic Medicine. 1 Sept. 2022. onlinelibrary.wiley.com/doi/10.1111/j.1945-5100.1994.tb01092.x.