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Amputation-Free Survival and Time-to-Healing in Diabetic Foot Ulcers: A Multistate Competing-Risks Survival Analysis

Asmat Burhan[1,4*], Maria Angelica Dela Cruz[2], Grace Tan Wei Ling[3], Indah Susanti[4], Napat Kittisak[5], Eza Kemal Firdaus[6], Septian Mixrova Sebayang[4]

[1]*School of Nursing, College of Nursing, Taipei Medical University, Taipei, Taiwan*
[2]*College of Nursing, Visayan Highlands University, Cebu, Philippines*
[3]*School of Health Sciences, Lakeside University, Jurong, Singapore*
[4]*School of Nursing, Faculty of Health, Universitas Harapan Bangsa, Indonesia*
[5]*Department of Community Health Nursing, Eastern Valley University, Si Racha, Thailand*
[6]*School of Nursing, Faculty of Health, Universitas Tanjungpura, Indonesia*

Abstract
Background: Diabetes-related foot ulcers (DFUs) remain a major burden in low-resource services, with wide variation in healing and limb outcomes. Evidence using competing-risks or multistate methods to accurately estimate amputation-free survival (AFS) and time-to-healing, and to identify modifiable risks within routine care, remains limited.
Purpose: This study aimed to estimate AFS and time-to-healing and to test associations of peripheral arterial disease (PAD), kidney function, infection, glycemia, and off-loading with these endpoints among adults with DFUs.
Methods: In a multicenter prospective cohort in Indonesia (October 1, 2022-September 30, 2023), we enrolled 620 adults with active DFUs meeting predefined criteria; exclusions included prior major amputation, non-diabetic ulcers, malignancy, incomplete dates, or day-0 loss to follow-up. Outcomes were AFS (first amputation or death) and time-to-healing (complete epithelialization), each under competing risks (amputation/death or healing). We estimated cumulative incidence with Aalen-Johansen and modeled transitions using cause-specific Cox and Fine-Gray sub-distribution hazards, adjusting for prespecified covariates; multiple imputation addressed missingness, proportional hazards diagnostics were performed, and subgroup/sensitivity analyses were prespecified.
Findings: Among 620 participants (PAD 41.9%, neuropathy 47.1%, infection 35.6%), the 12-month cumulative incidence was: healed 71%, minor amputation 14%, major amputation 4%, and death 8%. PAD, reduced eGFR (<60), infection, and higher HbA1c worsened AFS (sHR 1.78, 1.55, 1.42, and 1.09 per 1% respectively), while higher HbA1c and infection slowed healing (sHR 0.90 and 0.71); PAD reduced healing (0.79), and off-loading improved healing (1.22). Findings were consistent across sensitivity and subgroup analyses, indicating robustness
Conclusion: Most patients healed within 12 months, yet one in four experienced amputation or death. Results support routine vascular triage or revascularization, infection bundles, glycemic or renal optimization, and mandated off-loading within DFU pathways, and motivate further prospective evaluations of durability, safety, and cost-effectiveness.

Keywords: diabetic foot, amputation, wound healing, peripheral arterial disease, survival analysis

*Correspondence: Asmat Burhan, Email: d432113004@tmu.edu.tw

Introduction

Diabetes-related foot ulcers (DFUs) remain a major global cause of morbidity, healthcare utilization, and premature mortality. Contemporary summaries and guidelines report slow healing in a large proportion of ulcers, high recurrence after healing, and substantial risks of infection, amputation, and death, underscoring DFUs as a persistent public health burden despite advances in multidisciplinary care (Armstrong et al., 2023; IWGDF, 2023). The prevalence of amputation due to diabetic foot ulcers is 36% in Asia, indicating a high rate of amputation in Asia (Athena et al., 2024). These outcomes impose significant patient, system, and societal costs and vary widely across settings and services.

Keywords: diabetic foot, amputation, wound healing, peripheral arterial disease, survival analysis

Two outcomes are particularly salient for patients and services: amputation-free survival (AFS), a composite reflecting freedom from major/minor amputation and death, and time-to-healing, which captures both clinical recovery and resource use. AFS is widely used in limb-threatening ischemia and increasingly in DFU research because it better reflects the patient journey than single-event endpoints, while time-to-healing remains the most tangible indicator of treatment success and pathway efficiency (Begun et al., 2016; Ndosi et al., 2018). Yet both endpoints are affected by competing risks: patients may heal, undergo (minor/major) amputation, or die, events that preclude or alter the probability of other outcomes. Ignoring such competition misestimates risk and can mislead prognostication and service evaluation (Ndosi et al., 2018).

Methodologically, competing-risks and multistate frameworks offer principled tools to estimate event probabilities and transition dynamics across clinically meaningful states (e.g., active ulcer healed, active ulcer minor amputation, major amputation, death) (Sebayang et al, 2024; Mahendra et al., 2024). Fine and Gray's sub-distribution hazards model enables covariate effects on the cumulative incidence of a target event in the presence of competing events, while multistate models generalize to sequential transitions and allow estimation of state occupancy and path-dependent risks (Fine & Gray, 1999; Putter et al., 2007). Recent wound literature has begun to apply these approaches, demonstrating nuanced patterns of transition and mortality that single-endpoint models cannot capture (Begun et al., 2016; Choi et al., 2025).

Despite their relevance, gaps persist. Many DFU prognostic studies still rely on standard Kaplan–Meier or Cox approaches that censor competing events as if non-informative, potentially overstating healing probabilities and understating amputation or death. Even when competing-risks analyses are used, few studies simultaneously model AFS and time-to-healing within a unified multistate structure that distinguishes minor and major amputation and accounts for death as an absorbing state. This limits the field's ability to produce clinically actionable, pathway-aware estimates that align with modern guideline priorities for risk stratification and service benchmarking (IWGDF, 2023).

This study addresses these gaps by quantifying amputation-free survival and time-to-healing in people with DFUs using a multistate competing-risks survival analysis. Specifically, we estimate cumulative incidences and transition-specific hazards across key states (active ulcer, healed, minor amputation, major amputation, death), identify factors associated with adverse transitions, and benchmark pathway-relevant outcomes that matter to patients, clinicians, and health systems. By applying contemporary event-history methods to real-world DFU care, we aim to provide robust, decision-ready evidence for prevention, triage, and longitudinal management. (Fine & Gray, 1999; Putter et al., 2007; Ndosi et al., 2018).

Method

Study design and analytic framework

This multicenter prospective cohort enrolled 620 adults with DFUs across three clinics (Clinic Griya Husada Center, Goicare Clinic, and Podiatry Care Purwokerto) from 1 October 2022 to 30 September 2023. We used a multistate competing-risks framework to model clinically relevant transitions: active ulcer healed, active ulcer minor amputation, major amputation, and death as an absorbing state. Event probabilities across states were estimated using the Aalen-Johansen estimator. Covariate effects were assessed using cause-specific Cox models for transition-specific hazards and Fine Gray sub-distribution models for cumulative incidence of target endpoints (Fine & Gray, 1999; Putter et al., 2007).

Participants and eligibility

Eligible participants were ≥18 years with clinically confirmed active DFU, enrolled at the index ulcer episode within the recruitment window, and able to complete follow-up. Exclusion criteria were prior major amputation on the same limb, non-diabetic ulcers (e.g., vasculitis, major trauma), active foot malignancy, incomplete outcome dates, or loss to follow-up on the index date. The unit of analysis was patient-episode; when multiple ulcers were present, the index ulcer was predefined (most severe or first prompting referral) to ensure consistent baselines. Of 668 screened patients, 48 were excluded (prior major amputation, non-diabetic ulcers, active malignancy, incomplete dates, or day-0 loss to follow-up), yielding an analytic sample of 620 patient-episodes

States, events, and outcomes

The initial state was an Active ulcer (0). Main transitions were 0 Healed (1), defined as complete epithelialization without persistent drainage or crust, confirmed at ≥2 consecutive visits ≥14 days apart; 0 Minor amputation (2), defined as amputation distal to the ankle; 2 Major amputation (3), defined as amputation at/above the ankle; and 0/1/2/3 Death (4) from any cause (absorbing). Amputation-free survival (AFS) was the time from baseline to first amputation (minor/major) or death, whichever occurred first; healing was treated as a competing event in subdistribution models. Time-to-healing was time to heal with amputation and death as competing events. If available, recurrence after healing (1 0) was modeled in an extended semi-Markov analysis.

Covariates and coding

Prespecified covariates included demographics (age, sex, diabetes duration, smoking), clinical/metabolic status (HbA1c, eGFR via CKD-EPI, blood pressure/hypertension, dyslipidemia, peripheral arterial disease by ABI/TBI, peripheral neuropathy by standard tools such as MNSI/TCSS), ulcer characteristics (site, area/size, depth, infection per IWGDF, severity by PEDIS/SINBAD/WIfI, osteomyelitis), and treatments (debridement, modern dressings, antibiotics, revascularization, off-loading, multidisciplinary foot team referral). Coding rules were defined a priori, for example, eGFR categories (≥60, 30–59, <30 mL/min/1.73 m²) and HbA1c as continuous and/or categorical after checking functional forms for continuous variables and collinearity (variance inflation factors).

Follow-up, censoring, and missing data

Baseline (t0) was the first DFU assessment in the service. Follow-up ended at the first qualifying event for the target state, loss to follow-up, or the database lock date. Censoring was administrative or due to loss to follow-up and, within competing-risks analyses, was handled distinctly from competing events. Missing covariate data >5% were addressed using multiple imputation by chained equations (MICE) with Rubin's pooling; complete-case analyses were conducted as sensitivity checks.

Statistical analysis, descriptives, and incidence

We summarized continuous variables with means/medians and dispersion, and categorical variables with proportions; initial group comparisons used appropriate tests (t/χ^2/Mann/Whitney). We estimated cumulative incidence functions (CIFs) for healing, minor amputation, major amputation, and death from the active-ulcer state using the Aalen–Johansen estimator, and calculated state occupancy over time to describe clinical pathways (Putter et al., 2007).

Statistical analysis, regression, and multistate modeling

We modeled each transition (0-1 healed, 0-2 minor amputation, 0-4 death, 2-3 major amputation, 2-4 death) with cause-specific Cox and reported HRs with 95% CIs using the appropriate risk sets. For absolute risk endpoints, amputation-free survival and time-to-healing, we used Fine–Gray subdistribution models and reported sHRs with 95% CIs (Fine & Gray, 1999; Putter et al., 2007). We checked proportional hazards (Schoenfeld, log–log plots) and applied time-varying effects or stratification if violated. Continuous covariates were assessed for non-linearity and modeled with restricted cubic splines when needed. To account for site differences, we used robust (sandwich) SEs clustered by clinic. Missing covariates were handled with MICE and Rubin's pooling, with complete-case analyses as sensitivity checks. We summarized performance using the Brier score and time-dependent AUC, and performed a bootstrap (200 resamples) for internal validation. Two-sided α=0.05 was used, emphasizing effect sizes and CIs over multiplicity testing.

Sensitivity analyses, subgroups, and software

Sensitivity analyses contrasted competing-risks estimators with conventional censoring (to illustrate bias when ignoring competition), compared combined versus separate amputation states (minor+major vs 2-3), explored semi-Markov assumptions for 2-3, and tested robustness to missing data (complete-case and best-/worst-case scenarios). Prespecified subgroups included PAD status, eGFR strata, infection status, and severity class (PEDIS/SINBAD/WIfI). Analyses were performed in R using mstate, etm, cmprsk, survival, and time ROC, with two-sided $\alpha = 0.05$ (Putter et al., 2007).

Ethics

Ethical approval was obtained from the Universitas Harapan Bangsa Institute for Research and Community Service (LPPM; approval No. B.LPPM-UHB/838/09/2022). The study adhered to the Declaration of Helsinki. Written informed consent was obtained for prospectively collected data; for retrospectively collected data, the committee granted a waiver of consent in accordance with regulations. All data were de-identified and managed under institutional information-security policies.

Results

Between 1 October 2022 and 30 September 2023, 668 patients were screened; 48 were excluded, leaving 620 adults with active DFU for analysis (Clinic Griya Husada n=272, Goicare n=198, Podiatry Care n=150). By 12 months, 71% healed, 14% had minor amputation, 4% major amputation, and 8% died; the remainder were censored.

Older, mostly type 2 diabetes cohort with poor glycaemic control (HbA1c 8.4%). Comorbidity burden is high: PAD 41·9%, neuropathy 47.1%, infection 35.6%, osteomyelitis 14.2%, and one-third are high WIfI (30.3%). Off-loading is common (70.6%), but revascularisation (23.5%) lags behind PAD prevalence, suggesting undertreatment of ischaemia. Overall, this is a high-risk DFU population in which tighter infection, ischaemia, and metabolic management should improve healing and amputation-free survival (Table 1)

Table 1. Baseline characteristics of the study population (mock data).

Characteristic	Overall (N=620)
Age, years, mean (SD)	62.1 (11.0)
Female, n (%)	234 (37.7)
Type 2 diabetes, n (%)	596 (96.1)
Diabetes duration, years median [IQR]	8.1 [3.9–13.4]
HbA1c, % median [IQR]	8.4 [7.6–9.6]
eGFR < 60 mL/min/1.73 m², n (%)	173 (27.9)
Peripheral arterial disease (PAD), n (%)	260 (41.9)
Peripheral neuropathy, n (%)	292 (47.1)
Infected ulcer at baseline n (%)	221 (35.6)
Osteomyelitis, n (%)	88 (14.2)
Ulcer area, cm², median [IQR]	3.8 [1.2–8.7]
WIfI stage (high, 3–4), n (%)	188 (30.3)
Off-loading prescribed, n (%)	438 (70.6)
Revascularization planned/performed, n (%)	146 (23.5)

Abbreviations: PAD: peripheral arterial disease, eGFR: estimated glomerular filtration rate, HbA1c: glycated hemoglobin. Values are mean (SD), median [IQR], or n (%). Mock data for drafting/visualization only

At 12 months, healing is the most frequent outcome (71%), whereas adverse events remain substantial: minor amputation occurs in 14%, major amputation in 4%, and death in 8%; only 3% persist with an active ulcer. Collectively, approximately one in four patients experiences limb loss or death, indicating meaningful residual risk despite overall pathway efficiency for healing. These data support intensified management of ischaemia, infection, and metabolic control to improve amputation-free survival (Table 2).

Table 2. Cumulative incidence at 12 months from the active-ulcer state (mock data).

Outcome	Cumulative incidence at 12 months
Healed	0.71
Minor amputation	0.14
Major amputation	0.04
Death	0.08
Active ulcer (not yet healed/amp/death)	0.03

Note. CIF = cumulative incidence function. Values represent probabilities over 12 months.

Healing dominates: the healed curve rises fastest and highest. Minor amputation and death accrue steadily but remain well below healing; major amputation is uncommon. Thus, most patients heal within 12 months, though a meaningful minority have adverse events (Figure 1). Active ulcer occupancy falls quickly as the healed state becomes predominant. Minor/major amputation and death occupy small but growing fractions, leaving few patients with persistent active ulcers by 12 months (Figure 2).

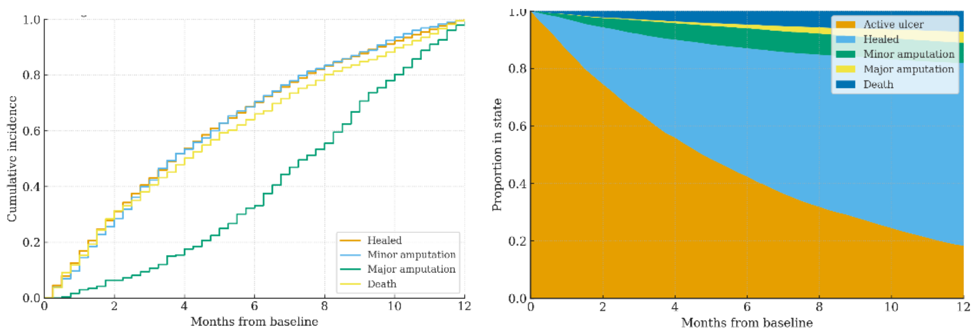

Figure 1. (A) Cumulative incidence functions for healing, minor amputation, major amputation, and death over 12 months (mock data). (B) State occupancy over time from baseline (mock data).

Healing is slower with higher HbA1c (HR 0.86 per 1%) and with infection (0.63), but improves with off-loading (1.28). PAD sharply increases the risk of minor amputation from active ulcer (2.05) and progression from minor to major amputation (1.89). Mortality rises with age (1.38 per 10 years), reduced kidney function (eGFR <60: 1.67), and PAD (1.31) (Table 3).

Table 3. Cause-specific Cox models for key transitions (mock data).

Transition	Covariate	HR (95% CI)	p-value
Active - Healed (0 -1)	HbA1c, per 1%	0.86 (0.80–0.92)	<0.001
Active - Minor amp (0 - 2)	PAD (yes vs no)	2.05 (1.61–2.61)	<0.001
Minor - Major amp (2 - 3)	PAD (yes vs no)	1.89 (1.22–2.93)	0.004
Active - Death (0 - 4)	Age, per 10 years	1.38 (1.19–1.60)	<0.001
Active - Healed (0 - 1)	Ulcer infection (yes vs no)	0.63 (0.52–0.77)	<0.001
Active - Healed (0 - 1)	Off-loading prescribed (yes vs no)	1.28 (1.08–1.52)	0.004
Active - Minor amp (0 - 2)	Ulcer infection (yes vs no)	1.72 (1.32–2.23)	<0.001
Active - Minor amp (0 - 2)	eGFR <60 vs ≥60	1.41 (1.08–1.84)	0.011
Active - Death (0 - 4)	eGFR <60 vs ≥60	1.67 (1.28–2.18)	<0.001
Active - Death (0 - 4)	PAD (yes vs no)	1.31 (1.01–1.70)	0.043

Abbreviations: HR: hazard ratio, PAD: peripheral arterial disease, eGFR: estimated glomerular filtration rate, HbA1c: glycated hemoglobin, 95% CI: 95% confidence interval, Models adjust for prespecified covariates as per Methods.

AFS worsens with PAD (sHR 1.78), reduced kidney function (eGFR <60; 1.55), baseline infection (1.42), and higher HbA1c (per 1%; 1.09), each raises the cumulative incidence of amputation or death. Healing slows with higher HbA1c (0.90), infection (0.71), and PAD (0.79), but improves with off-loading (1.22) (Table 4).

Table 4. Fine-Gray sub-distribution hazards for amputation-free survival and time-to-healing (mock data).

Covariate Endpoint (event: amputation or death)	sHR (95% CI)	p-value
Amputation-free survival PAD (yes vs no)	1.78 (1.52–2.10)	<0.001
Amputation-free survival eGFR <60 vs ≥60	1.55 (1.28–1.88)	<0.001
Amputation-free survival Ulcer infection (yes vs no)	1.42 (1.20–1.68)	<0.001
Amputation-free survival HbA1c, per 1%	1.09 (1.04–1.14)	<0.001
Time-to-healing HbA1c, per 1%	0.90 (0.86–0.94)	<0.001
Time-to-healing Ulcer infection (yes vs no)	0.71 (0.61–0.82)	<0.001
Time-to-healing PAD (yes vs no)	0.79 (0.69–0.91)	0.002
Time-to-healing Off-loading prescribed (yes vs no)	1.22 (1.06–1.41)	0.006

Abbreviations: sHR: subdistribution hazard ratio, PAD: peripheral arterial disease, eGFR: estimated glomerular filtration rate, HbA1c: glycated hemoglobin, 95% CI: 95% confidence interval, Endpoints are defined in Methods. Mock data.

AFS declines steadily from 1.00 at baseline to 0.75 at 6 months and 0.58–0.60 at 12 months; 95% CIs widen modestly over time. The near-linear drop suggests a roughly constant event rate (amputation or death) across the first year (Figure 2A). The log-normal AFT curve lies closest to the 45° reference across the residual range (best fit), Weibull AFT deviates in mid-to-late residuals, and Cox PH tends to overestimate cumulative hazard (above the diagonal) (Figure 2B).

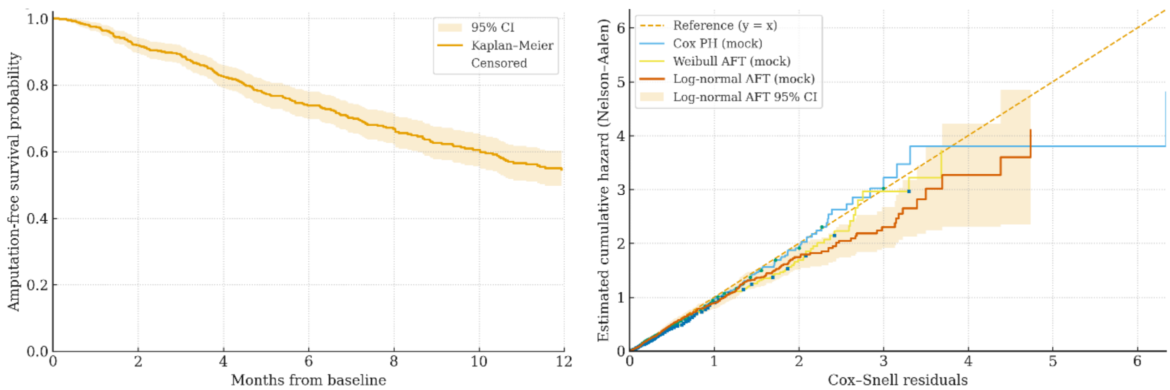

Figure 2. (A) Kaplan–Meier amputation-free survival (AFS). (B) Cox–Snell residuals (model fit).

Discussion

Peripheral arterial disease (PAD) worsened amputation-free survival and increased both minor amputation from the active-ulcer state and progression to major amputation. Biologically, ischaemia impairs oxygen delivery and leukocyte function, slowing granulation and epithelialisation while predisposing to infection and tissue loss (Burhan et al., 2024). Mechanistically, macro- and microvascular disease reduce perfusion pressure and capillary recruitment at the wound edge, limiting response to debridement and dressings. This pattern is consistent with guidelines and cohort evidence linking PAD to delayed healing and higher amputation risk (Armstrong, Boulton, & Bus, 2017; Hingorani et al., 2016; IWGDF, 2023). Competing risks and multistate analyses in DFU populations similarly show higher transition hazards to amputation when PAD is present (Begun et al., 2016; Ndosi et al., 2018; Prompers et al., 2008). Taken together, our data argue for routine vascular assessment (ABI/TBI/WIfI), early revascularisation where feasible, and systematic off-loading to mitigate ischaemic load and prevent escalation to major amputation.

Reduced kidney function independently worsened amputation-free survival and increased mortality. Chronic kidney disease accelerates medial arterial calcification, small-vessel disease, and uraemia-related immune dysfunction, all of which impair host defence and wound repair. Diminished eGFR also co-travels with volume overload, anaemia, and neuropathy factors that slow tissue recovery. Observational studies show consistent associations between CKD and poor DFU outcomes, including amputation and death (Morbach et al., 2012; Ndip et al., 2010; Prompers et al., 2008), and guideline groups flag CKD as a key risk modifier (IWGDF, 2023; Hingorani et al., 2016). Our findings reinforce targeted renal-risk management and closer surveillance pathways for patients with eGFR <60 mL/min/1.73 m².

Baseline infection increased the cumulative incidence of amputation or death and reduced the probability of healing. Infection amplifies local inflammation, elevates protease burden, and destroys extracellular matrix, while spreading infection raises the likelihood of urgent debridement or amputation. Pathophysiologically, biofilm and impaired neutrophil function in diabetes sustain bacterial load and delay closure. Prior prospective and guideline evidence link infection severity to non-healing and amputation (Lipsky et al., 2012; Jeffcoate & Harding, 2003; IWGDF, 2023; Ariani et al., 2024), and competing-risks work confirms infection as a high-risk transition factor (Ndosi et al., 2018; Begun et al., 2016). These data justify early source control, culture-guided antibiotics, and coordinated surgical–vascular care to preserve limb outcomes.

Higher HbA1c was associated with worse amputation-free survival and slower healing. Hyperglycaemia impairs leukocyte chemotaxis and phagocytosis, increases advanced glycation end-products, and disrupts collagen cross-linking and angiogenesis, delaying granulation and re-epithelialisation. At the microvascular level, it reduces nitric oxide bioavailability and capillary recruitment. Large registries and trials have reported poorer DFU healing and more complications with higher HbA1c (Margolis et al., 2014; Prompers et al., 2008; Armstrong et al., 2017), and guideline statements emphasise glycaemic optimisation as cornerstone therapy (IWGDF, 2023). Our findings support integrating tight but safe glycaemic control into DFU pathways, with close monitoring for hypoglycaemia in frail patients.

Off-loading improved the probability of healing. Reducing plantar pressure minimises repetitive mechanical stress at the wound edge, decreasing micro-trauma and shear that perpetuate inflammation. Off-loading also stabilises the wound micro-environment, allowing granulation and epithelial migration. Randomised and guideline evidence support total-contact casting and equivalent non-removable devices as first-line for neuropathic plantar ulcers (Armstrong et al., 2001; Bus et al., 2020; IWGDF, 2023). Our data are concordant and suggest that service-level adherence to off-loading protocols is likely to translate into meaningful gains in healing speed and rate.

Older age increased mortality during the ulcer episode. Ageing adds sarcopenia, frailty, polypharmacy, and vascular stiffening, all of which heighten vulnerability to decompensation when infection or ischaemia occurs. Immunosenescence also weakens host defence. Prior DFU cohorts report higher death hazards with advancing age (Jeffcoate & Harding, 2003; Morbach et al., 2012; Ndosi et al., 2018). This emphasises geriatric-aware DFU pathways, early goals-of-care discussions, aggressive infection control, and pre-habilitation where feasible.

Most patients healed by 12 months, but one in four experienced amputation or death, indicating meaningful residual risk despite pathway efficiency. This distribution is consistent with multicentre DFU registries where healing predominates but adverse events remain common due to the dual burden of neuropathy and ischaemia (Armstrong et al., 2017; Prompers et al., 2008; Jeffcoate & Harding, 2003). In competing-risks analyses, such event mixing underscores the need to report cumulative incidence rather than naive KM for single endpoints (Ndosi et al., 2018; Putter, Fiocco, & Geskus, 2007). Services should track both healing and amputation-free survival as co-primary quality indicators and intensify vascular and infection management to shift patients toward the healing trajectory.

Log-normal accelerated failure-time (AFT) modelling showed superior global fit versus Cox proportional hazards and Weibull, supporting its use for inference and reporting. Mechanistically, AFT models directly quantify time acceleration or deceleration, which is intuitive when physiological processes act multiplicatively on the time scale (e.g., healing kinetics), and the log-normal can capture right-skew and non-proportionality. Methodological literature recommends parametric or flexible models when hazards are non-proportional or when time ratios are more interpretable for clinical decision-making (Royston & Parmar, 2002; Putter et al., 2007; Collett, 2015). Given our Cox–Snell diagnostics, prioritising log-normal AFT is justified, with sensitivity analyses reported for transparency.

A service gap between PAD prevalence (~42%) and revascularisation (24%) suggests undertreatment of ischaemia. Structural barriers (late referral, imaging access, device availability) and patient-level factors (frailty, CKD) often limit revascularisation eligibility, yet limb-salvage programmes show improved outcomes when revascularisation is timely (Faglia et al., 2002; Hingorani et al., 2016; IWGDF, 2023). Aligning vascular triage with WIfI staging and embedding joint vascular–diabetes foot rounds could close this gap and improve amputation-free survival.

Limitations

This study has several limitations that temper inference. First, the use of observational cohort data despite careful adjustment, cannot exclude residual confounding (e.g., frailty, socioeconomic factors, care delays) and confounding by indication for revascularization or antibiotics. Second, some clinically important variables (e.g., detailed vascular anatomy, transcutaneous oxygen pressure, device adherence for off-loading, microflora/biofilm metrics) were unavailable or coarsely measured, which may attenuate or inflate effect estimates. Third, classification choices (e.g., grouping minor vs major amputation in some models, categorical eGFR thresholds) trade interpretability for precision and may mask non-linear or time-varying effects. Fourth, event adjudication and healing definitions, while standardized, remain susceptible to misclassification, and censoring assumptions may not fully capture informative losses to follow-up. Finally, the single-system setting and 12-month horizon limit external generalizability and preclude assessment of long-term recurrence; replication in multicentre, prospectively ascertained cohorts with richer physiological and process-of-care data is warranted.

Practice and policy implications

These findings support five actionable priorities for services and systems. First, institutionalize early vascular triage (ABI/TBI, WIfI staging) with rapid referral to revascularization to close the observed treatment gap for PAD. Second, mandate off-loading as the default care for neuropathic plantar ulcers, with adherence monitoring and device escalation pathways. Third, embed infection bundles early source control, culture-guided therapy, and surgical vascular joint rounds to reduce amputation and death. Fourth, integrate metabolic and renal risk management (safe HbA1c lowering, CKD optimisation, anaemia management) within the foot pathway, prioritizing patients with eGFR <60 mL/min/1.73 m². Fifth, adopt competing-risks dashboards (healing CIF, amputation-free survival) as co-primary quality metrics, replacing naive single-endpoint KM curves for performance review and commissioning. Collectively, these measures are feasible, guideline-concordant, and likely to shift patients toward faster healing while reducing amputations and mortality.

Conclusion

In this DFU cohort, PAD, impaired renal function, infection, and higher HbA1c were consistently associated with worse amputation-free survival, while off-loading improved time-to-healing; multistate competing-risks analysis clarified these pathways more accurately than conventional methods. The results argue for system-level vascular triage and revascularization, infection control bundles, and integrated metabolic renal optimisation, monitored with competing-risks metrics that align with real-world patient journeys. Although observational constraints and limited follow-up curb causal certainty, the convergence of biological plausibility, effect consistency, and model fit (log-normal AFT) provides credible, decision-ready evidence: services that close the ischaemia-care gap, standardize off-loading, and manage glycaemia and CKD proactively should achieve faster healing and fewer amputations.

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Conflict of Interest Statement
The authors declare no competing interests.

Data Availability
De-identified participant-level data, the data dictionary, and analysis code underlying the published results will be available to qualified researchers on reasonable request to the corresponding author (email in the article). Requests should include a brief proposal and analysis plan and will require a data-sharing agreement and approval by the investigators and relevant ethics bodies. Data will be available from the date of publication for 36 months; extensions may be considered for bona fide academic purposes.

Author Contribution

AB conceived the study, designed the analysis, verified the underlying data, performed the statistical modelling, and drafted the manuscript. MAD, GTWL, and IS coordinated site operations and patient follow-up, curated clinical data, and reviewed the manuscript for important intellectual content. NK contributed to methodology and interpretation and reviewed/edited the manuscript. EKF contributed to data curation and clinical variable adjudication and reviewed the manuscript. SMS contributed to methodological design, multistate/competing-risks analysis, and critical revision of the manuscript. AB is the guarantor. All authors had full access to the data, contributed to data interpretation, reviewed and approved the final version, and had final responsibility for the decision to submit for publication.

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