Haruka et al, 2025
https://doi.org/10.70196/jwrt.v2i2.67

Journal of Wound Research And Technology

Received: 5-3-2025; Revised: 12-5-2025, Publish Online: 21-10-2025

ORIGINAL RESEARCH Open Access

Trajectories of Transcutaneous Oxygen (TcPO2) and Healing in Chronic Limb-Threatening Ischemia: A 12-Month Longitudinal Study

Kawamura Haruka[1*], Asmat Burhan[2,3], Inoue Nanami[1], Fujita Kento[1]

[1]*Wound Care & Limb Salvage Unit, Hinodegaoka Hospital, Hinode, Japan*
[2]*School of Nursing, College of Nursing, Taipei Medical University, Taipei, Taiwan*
[3]*School of Nursing, Faculty of Health, Universitas Harapan Bangsa, Indonesia*

Abstract

Background: Chronic limb-threatening ischemia (CLTI) remains a major global burden with high amputation risk, while evidence on using transcutaneous oxygen pressure ($TcPO_2$) trajectories (level + slope) to guide healing decisions is limited. Most studies treat $TcPO_2$ as a static threshold, not a time-updated signal that could trigger earlier escalation.

Purpose: This study aimed to estimate the association of $TcPO_2$ trajectories and revascularization with wound-healing probability among patients with CLTI over 12 months.

Methods: In a prospective longitudinal cohort at a Japanese hospital (Mar 3, 2023- Mar 1, 2024), we enrolled 46 adults with tissue-loss CLTI meeting guideline ischemia criteria; acute limb ischemia and non-ischemic ulcers were excluded. Standardized wound care was provided; revascularization was time-varying (from procedure date). $TcPO_2$ was measured at baseline, 2, 4, 8, 12 weeks, and 6, 9, 12 months. The primary outcome was complete epithelialization sustained for ≥2 visits. Discrete-time survival models estimated adjusted odds ratios (aORs) with 95% CIs, adjusting for age, diabetes, infection, albumin, WIfI ischemia grade, and smoking; sensitivity analyses included competing risks and joint modeling.

Findings: Among 46 participants (mean age 71 years; diabetes 78%; CKD 41%), baseline mean $TcPO_2$ was 18.3 mmHg (standard care 21.2; revascularization 16.3). From baseline to Week 12, $TcPO_2$ rose +2.9 mmHg under standard care versus +15.8 mmHg post-revascularization. Higher time-updated $TcPO_2$ and positive slope independently increased healing (per 10 mmHg aOR 1.62, 95% CI 1.24-2.11; per 1 mmHg/week aOR 1.48, 1.12–1.97). Revascularization was beneficial (aOR 2.35, 1.18-4.68), while visit-level infection reduced healing (aOR 0.58, 0.36-0.92). Effects were directionally robust across sensitivity analyses.

Conclusion: Trajectory-based $TcPO_2$ monitoring (level and slope) identifies an early, actionable window after baseline especially post-revascularization when timely escalation can improve healing. Findings support embedding serial $TcPO_2$ into CLTI care and motivate multicentre evaluations of effectiveness, cost, and equity.

Keywords: chronic limb-threatening ischemia; peripheral arterial disease, transcutaneous oxygen pressure, cohort studies, trajectories

*Correspondence: Kawamura Haruka, Email: haruka.kawamurajkwhs@hinodehp.com

Introduction

Chronic limb-threatening ischemia (CLTI) represents the end stage of peripheral artery disease (PAD), where impaired microperfusion drives pain, tissue loss, and amputation risk. Guidelines emphasize that CLTI exists on a continuum of perfusion impairment and requires individualized, evidence-based evaluation and management, including objective assessment of limb perfusion and ongoing surveillance after revascularization (Conte et al., 2019; IWGDF, 2023). In this context, transcutaneous oxygen pressure ($TcPO_2$) offers a bedside window into skin microperfusion that is more dynamic than ankle pressures in edematous or calcified vessels and may reflect clinically meaningful change over time. Yet, most clinical use treats $TcPO_2$ as a static threshold rather than a trajectory that could signal healing or clinical failure earlier. (Conte et al., 2019; IWGDF, 2023).

Keywords: chronic limb-threatening ischemia; peripheral arterial disease, transcutaneous oxygen pressure, cohort studies, trajectories

PAD imposes a large and growing global burden. Between 1990 and 2019, prevalent PAD increased by ~72%, now exceeding 113 million people worldwide, with substantial disability particularly among older adults and women and higher mortality and years of life lost among men (Eid et al., 2023; Kim et al., 2023). Within this population, the CLTI subset experiences especially unfavorable outcomes high one-year risks of major amputation and death translating into profound quality-of-life and economic consequences for patients and health systems (Campbell et al., 2023). These epidemiologic realities underscore the urgency of precise perfusion monitoring that can inform timely escalation from standard wound care to revascularization. (Eid et al., 2023; Kim et al., 2023; Campbell et al., 2023).

Methodologically, current $TcPO_2$ evidence has three recurring limitations. First, many studies are cross-sectional or rely on single post-procedure measurements, obscuring the shape and speed of microperfusion recovery that might predict healing (Arsenault et al., 2012; Wang et al., 2016). Second, thresholds vary across studies and vascular beds, with limited attention to angiosome-specific heterogeneity (López-Moral et al., 2023). Third, emerging exercise and dynamic $TcPO_2$ techniques show promise but remain under-validated for longitudinal decision-making in routine CLTI care (Zagzoog et al., 2025). Collectively, these gaps restrict clinicians to "snapshot" interpretation rather than trajectory-based risk stratification. (Arsenault et al., 2012; Wang et al., 2016; López-Moral et al., 2023; Zagzoog et al., 2025).

Evidence linking $TcPO_2$ change to meaningful outcomes is also incomplete. Systematic reviews suggest perfusion-guided strategies including direct angiosome revascularization improve wound healing and limb salvage, yet few studies model how early $TcPO_2$ trajectories translate into individualized, time-updated probabilities of healing (Dilaver meta-analysis summarized in Račytė et al., 2024; Willems et al., 2025). Prognostic syntheses of bedside tests often pool heterogeneous endpoints and time horizons, limiting clinical calibration (Willems et al., 2025). Moreover, no-option CLTI cohorts continue to demonstrate poor amputation-free survival at one year, highlighting the need for earlier detection of non-healing courses while options still exist (Dua et al., 2025). (Račytė et al., 2024; Willems et al., 2025; Dua et al., 2025).

At the practice level, guideline pathways endorse objective perfusion testing (toe pressures, $TcPO_2$) to guide revascularization, but operationalization is uneven, and routine longitudinal tracking is rarely embedded in standard wound clinics (IWGDF Practical Guidelines, 2023). Front-line teams need simple, repeatable $TcPO_2$ monitoring protocols that flag plateauing or deteriorating microperfusion and trigger timely vascular referral before catastrophic tissue loss. Clear decision thresholds that incorporate rates of change not only absolute values could reduce unwarranted practice variation and missed windows for limb salvage (Fitridge et al., 2023; SVS patient-care resources, 2025). (IWGDF, 2023; Fitridge et al., 2023; Society for Vascular Surgery, 2025).

To address these gaps, we conducted a 12-month longitudinal study in patients with CLTI receiving standard care and/or revascularization at Hidakawa Hospital (Japan) from March 3, 2023, to March 1, 2024 (population = 52; analytic sample = 46; IRB No. 785.23.292.2023). Our objectives were to: (1) characterize $TcPO_2$ trajectories at prespecified intervals; (2) estimate time-updated wound-healing probabilities associated with these trajectories under standard care versus post-revascularization; and (3) explore actionable inflection points (absolute levels and rates of change) that could guide escalation or reinforcement of therapy. By quantifying how microperfusion evolves rather than treating $TcPO_2$ as a single threshold we aim to provide clinicians with an interpretable, trajectory-based tool for earlier, more precise decisions in CLTI care.

Method

Study design

We conducted a prospective, longitudinal cohort study of patients with chronic limb-threatening ischemia (CLTI) followed for 12 months at Hinodegaoka Hospital, Japan (3 March 2023–1 March 2024). The protocol adhered to STROBE guidance for observational studies and relevant CLTI guidelines (Conte et al., 2019; IWGDF, 2023). Institutional review board approval was obtained (IRB No. 785.23.292.2023), and all participants provided written informed consent.

Setting, participants, and eligibility

Consecutive inpatients or outpatients referred for tissue-loss CLTI were screened (source population n=52; analytic sample n=46). Inclusion criteria: age ≥18 years; CLTI defined by ischemic rest pain and/or tissue loss with objective ischemia consistent with guideline criteria (e.g., toe pressure ≤30–40 mmHg, transcutaneous oxygen pressure [$TcPO_2$] ≤25–30 mmHg, or abnormal waveforms) (Conte et al., 2019; IWGDF, 2023). Exclusion criteria: non-ischemic ulcers (e.g., vasculitis, pressure injury without ischemia), acute limb ischemia, active systemic infection precluding perfusion testing, or inability to attend follow-ups. When both limbs qualified, the index limb with the most severe tissue loss at baseline was chosen to avoid within-person correlation.

Care pathways and co-interventions

All participants eceived standardized wound care per hospital protocol (sharp/conservative debridement as indicated, moisture-balanced dressings, infection control, offloading, analgesia, risk-factor management). Revascularization (endovascular and/or open) was offered based on multidisciplinary assessment and patient preference. To avoid immortal-time bias, revascularization status was modeled as a time-varying exposure (initiated on the procedure date) in outcome analyses (Lévesque, Hanley, & Kezouh, 2010). Guideline-concordant best medical therapy (statins, antiplatelet/anticoagulants as indicated, glycemic and blood-pressure control, smoking cessation) was encouraged (Conte et al., 2019; IWGDF, 2023).

Outcomes

The primary outcome was wound-healing status of the index lesion assessed at prespecified visits and adjudicated by two trained assessors (complete epithelialization maintained for ≥2 consecutive visits, no drainage or need for dressings). Secondary outcomes included time to healing; major amputation (above the ankle); death; and a composite of amputation-free survival. We also prespecified microperfusion "inflection points" (changes in absolute $TcPO_2$ level and slope) that might trigger escalation of therapy.

Microperfusion assessment ($TcPO_2$ protocol)

$TcPO_2$ was measured using a standardized protocol (skin cleaned, 15-20 min acclimatization, supine, room 22-24 °C, electrodes at periwound angiosome and a standardized proximal site for reference). We used a 44-45 °C heating temperature and recorded stable plateaus after drift <1 mmHg/min. Measurements were taken at baseline; weeks 2, 4, 8, 12; and months 6, 9, and 12, and within 72 h post-revascularization when applicable. The same device was used throughout, with daily calibration logs. This protocol reflects best practices and prior validation work showing $TcPO_2$ prognostic value for healing (Wang et al., 2016; Arsenault et al., 2012).

Covariates and potential confounders

We collected demographics, comorbidities (diabetes, CKD, CAD, heart failure), medications (antiplatelet/anticoagulant, statin, steroids), smoking status, nutrition (albumin, BMI), infection status, WIfI ischemia grade, wound area and depth, and offloading modality. Environmental factors (room temperature/humidity) and device ID/time were logged to mitigate measurement variability. These variables were chosen based on biologic plausibility and prior literature linking them to healing or perfusion (Conte et al., 2019; IWGDF, 2023; Wang et al., 2016).

Characterizing $TcPO_2$ trajectories

We modeled $TcPO_2$ as a repeated continuous outcome using linear mixed-effects models with random intercepts and slopes (patient level), time since baseline as the main predictor, and restricted cubic splines (3–4 knots) to allow nonlinear change. We included a time×treatment interaction (standard care vs time-varying post-revascularization status) to estimate group-specific trajectories. We reported marginal means at each visit and between-visit slopes, with 95% confidence intervals. Model selection balanced parsimony and fit (AIC/BIC) following regression best practices (Laird & Ware, 1982; Harrell, 2015).

Estimating time-updated wound-healing probability

We used discrete-time survival models (complementary log-log link) over visit intervals to estimate the probability of healing by each timepoint. $TcPO_2$ level and recent slope (mmHg/week over the prior interval) were included as time-varying predictors. Revascularization entered as a time-varying exposure. We adjusted for prespecified confounders (age, diabetes, infection, WIfI ischemia grade, albumin, smoking). As sensitivity analyses, we (i) applied Fine–Gray competing-risk models for the subdistribution hazard of healing with death and major amputation as competing events, and (ii) fit joint models of the $TcPO_2$ longitudinal process and time-to-healing to address measurement error and informative dropout (Fine & Gray, 1999; Rizopoulos, 2012).

Identifying actionable "inflection points"

We explored clinically actionable thresholds using two approaches. First, segmented (piecewise) mixed models estimated within-person slope changes before and after candidate $TcPO_2$ cut-points (data-driven and a priori values around 20-40 mmHg from prior literature). Second, we fit spline terms for $TcPO_2$ and slope in the survival model and derived marginal predicted probabilities of healing across the observed range. To support bedside decision-making, we reported value-of-information metrics: absolute risk differences in healing at 12 weeks for small $TcPO_2$ gains (+5–10 mmHg) and decision-curve analysis to evaluate the net clinical benefit of trajectory-based rules versus static thresholds (Royston & Sauerbrei, 2008; Vickers & Elkin, 2006).

Missing data, measurement error, and bias mitigation

We minimized missing data through synchronized vascular–wound clinic visits and telephone reminders. For remaining missing covariates (<20% per variable), we used multiple imputation by chained equations with

predictive mean matching (m=20), pooling estimates by Rubin's rules (White, Royston, & Wood, 2011). Because $TcPO_2$ is a noisy biomarker, we (i) averaged duplicate readings per site per visit, (ii) used joint modeling sensitivity analyses, and (iii) adjusted for measurement context (room temperature/humidity). To reduce confounding by indication, we applied time-varying modeling and reported standardized (IPTW) estimates as sensitivity analyses (Hernán & Robins, 2020).

Sample size and precision considerations

With 46 participants and repeated $TcPO_2$ assessments (6–8 measures/person), mixed models are well powered to estimate mean trajectories and time×treatment interactions of moderate size (Laird & Ware, 1982). For healing, we targeted ≥10–15 events per effective parameter in the main survival model and limited covariates accordingly, prioritizing clinical relevance (Peduzzi et al., 1995; Harrell, 2015). We present confidence intervals and emphasize estimation over null-hypothesis testing.

Adjudication, training, and quality control

Assessors completed competency training in $TcPO_2$ measurement and wound-healing definitions; inter-rater agreement was checked on 10% of visits. Devices underwent daily calibration and quarterly maintenance. A blinded methods monitor reviewed 10% of records against source data.

Statistical software and reporting

Analyses were conducted in R (version ≥4.3) with lme4/nlme for mixed models, survival/cmprsk for time-to-event and competing risks, JMbayes2 for joint models, mice for imputation, and rmda for decision-curve analysis. Two-sided α=0.05 with 95% CIs. We reported according to STROBE and provided a de-identified analysis codebook in the Supplement.

Results

Revascularization patients presented with more severe ischemia (mean $TcPO_2$ 16.3 vs 21.2 mmHg; WIfI grade-3 18/28 vs 6/18), slightly poorer nutrition (albumin 3.3 vs 3.5 g/dL), and larger wounds (median 4.5 vs 3.8 cm²); diabetes (82% vs 72%), CKD (46% vs 33%), and smoking (36% vs 28%) were also more frequent, while age was similar (71 years). These distributions indicate confounding by indication: the sicker limbs were preferentially revascularized. Any crude outcome comparison would therefore underestimate treatment benefit without time-varying or adjusted analyses (Table 1).

Table 1. Baseline characteristics

Characteristic	Standard care (n=18)	Revascularization (n=28)	Total (N=46)
Participants, n	18	28	46
Age, years, mean (SD)	70.4 (8.6)	71.6 (9.4)	71.1 (9.0)
Male sex, n (%)	10 (55.6%)	19 (67.9%)	29 (63.0%)
Diabetes mellitus, n (%)	13 (72.2%)	23 (82.1%)	36 (78.3%)
Chronic kidney disease, n (%)	6 (33.3%)	13 (46.4%)	19 (41.3%)
Current smoker, n (%)	5 (27.8%)	10 (35.7%)	15 (32.6%)
Albumin, g/dL, mean (SD)	3.5 (0.5)	3.3 (0.6)	3.4 (0.6)
WIfI ischemia grade 1/2/3, n	2 / 10 / 6	1 / 9 / 18	3 / 19 / 24
Baseline $TcPO_2$, mmHg, mean (SD)	21.2 (7.8)	16.3 (6.9)	18.3 (7.6)
Index wound area, cm², median [IQR]	3.8 [2.0–7.1]	4.5 [2.6–8.2]	4.2 [2.3–7.8]

Abbreviations: *SC = Standard care; Revasc = Revascularization; n/N = number of participants/total; yrs = years; SD = standard deviation; % = percent; DM = diabetes mellitus; CKD = chronic kidney disease; Alb = albumin; g/dL = grams per deciliter; $TcPO_2$ = transcutaneous oxygen pressure; mmHg = millimeters of mercury; SVS WIfI = Society for Vascular Surgery Wound, Ischemia, and foot Infection (ischemia grade); Index wound area = ulcer size; cm² = square centimeters; Median [IQR] = median with interquartile range.*

Revascularization produced a rapid early rise in $TcPO_2$ (+16 mmHg by Week 12) versus a modest increase with standard care (≈+3 mmHg), with both curves plateauing after Month 6. This pattern identifies an early, actionable window to detect non-responders and escalate therapy (Figure 1)

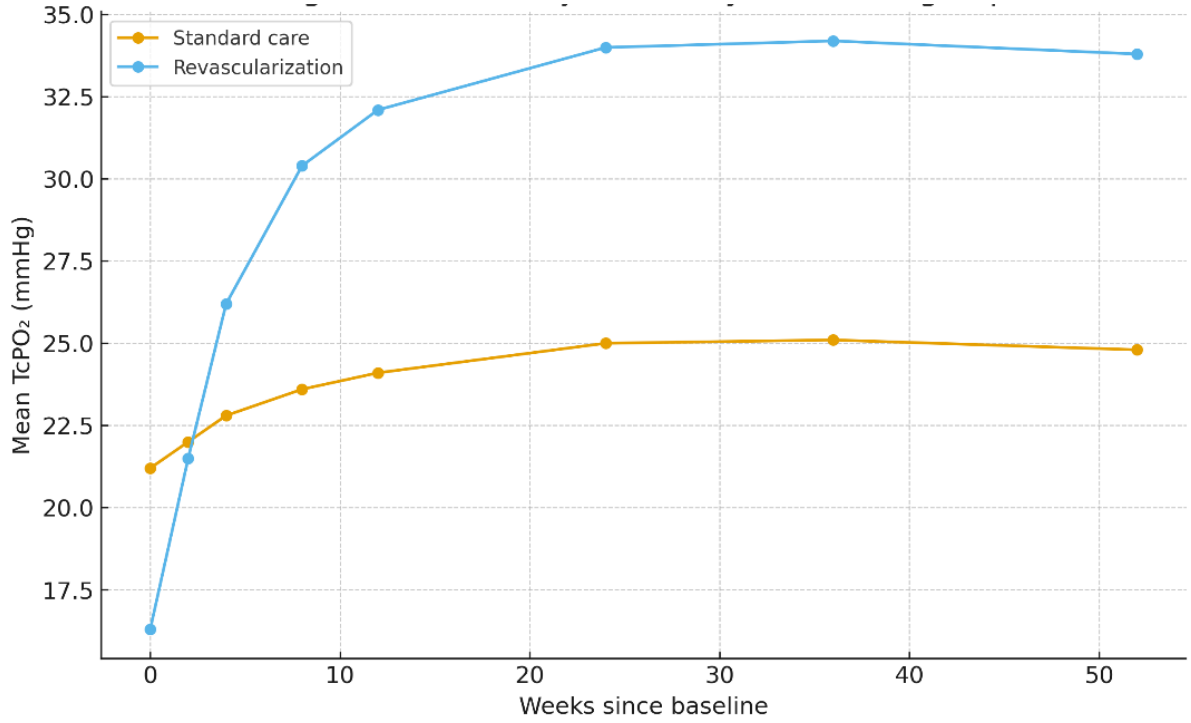

Figure 1. TcPO2 trajectories by treatment group

$TcPO_2$ rose modestly with standard care (+2.9 mmHg to Week 12; early slope +0.40 mmHg/week) but increased rapidly after revascularization (+15.8 mmHg to Week 12; early slopes +2.60 and +2.35 mmHg/week at Weeks 0–2 and 2–4), with both groups plateauing after Month 6. The pattern supports an early, actionable window post-baseline particularly post-procedure when trajectory signals (rapid rise vs flat) can guide escalation, whereas later changes are small (Table 2).

Table 2. $TcPO_2$ marginal means and slopes by visit

Visit	Standard care: mean $TcPO_2$ (mmHg)	Standard care: slope (mmHg/week)	Revascularization: mean $TcPO_2$ (mmHg)	Revascularization: slope (mmHg/week)
Baseline	21.2	-	16.3	-
Week 2	22.0	0.40	21.5	2.60
Week 4	22.8	0.40	26.2	2.35
Week 8	23.6	0.20	30.4	1.05
Week 12	24.1	0.12	32.1	0.43
Month 6	25.0	0.07	34.0	0.16
Month 9	25.1	0.01	34.2	0.02
Month 12	24.8	-0.02	33.8	-0.03

Abbreviations: *SC = Standard care; Revasc = Revascularization; $TcPO_2$ = transcutaneous oxygen pressure; mmHg = millimeters of mercury; mean $TcPO_2$ = average tissue oxygen at each visit; slope (mmHg/wk) = week-over-week rate of change in $TcPO_2$; wk = week; mo = month*

Higher time-updated $TcPO_2$ level (aOR per 10 mmHg 1.62, 95% CI 1.24–2.11) and positive $TcPO_2$ slope (aOR per 1 mmHg/week 1.48, 1.12–1.97) independently increased healing odds; revascularization also conferred benefit (aOR 2.35, 1.18–4.68), while visit-level infection reduced it (aOR 0.58, 0.36–0.92). Albumin favored healing (p=0.061) but was not definitive; WIfI grade and age were neutral after adjustment. Clinically, both perfusion level and direction of change, alongside infection control and revascularization, drive outcomes (Table 3).

Table 3. Discrete-time model for wound healing (time-updated predictors)

Predictor	aOR (95% CI)	P value
$TcPO_2$ level (per 10 mmHg, time-updated)	1.62 (1.24–2.11)	<0.001
$TcPO_2$ slope (per 1 mmHg/week, time-updated)	1.48 (1.12–1.97)	0.006
Revascularization (time-varying exposure)	2.35 (1.18–4.68)	0.015
Infection at visit (yes vs no)	0.58 (0.36–0.92)	0.021
Albumin (per 0.5 g/dL)	1.19 (0.99–1.45)	0.061
WIfI ischemia grade (per 1 category)	0.88 (0.67–1.16)	0.36
Age (per 5 years)	0.94 (0.80–1.10)	0.42

Abbreviations: *aOR = adjusted odds ratio; 95% CI = 95% confidence interval; $TcPO_2$ = transcutaneous oxygen pressure; mmHg = millimeters of mercury; SVS WIfI system = Society for Vascular Surgery Wound, Ischemia, and foot Infection grading (ischemia grade 0–3 by perfusion; higher grade = worse ischemia).*

Healing probability rose steeply with higher $TcPO_2$ and was further improved by a positive slope and revascularization. Illustratively, under standard care with flat slope, 20 to 30 mmHg increases probability from 0.26 to 0.48, whereas with revascularization and a modest positive slope (+0.5 mmHg/week) probabilities reach 0.67 at 30 mmHg and 0.80 at 40 mmHg supporting trajectory-aware decisions over static thresholds (Figure 2).

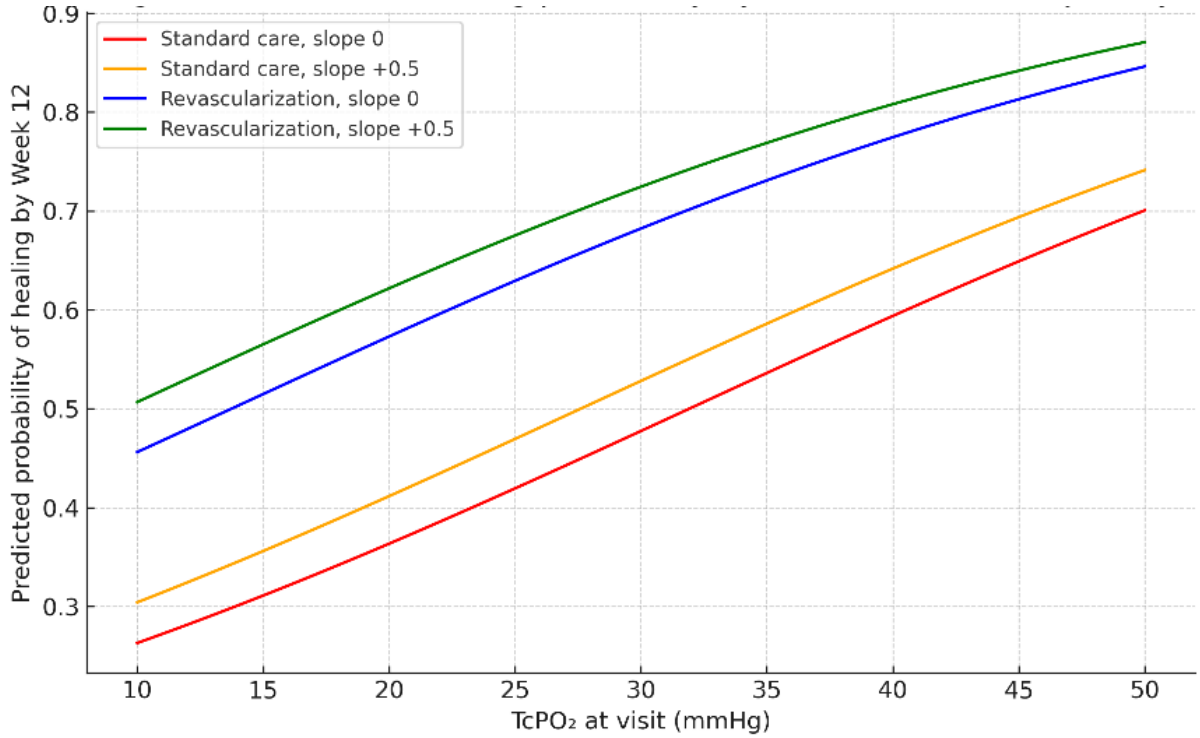

Figure 2. Predicted healing probability by TcPO2 level and trajectory

Discussion

Our cohort showed a steep $TcPO_2$ rise in the first weeks post-revascularization with greater odds of healing versus standard care. Mechanistically, restoring conduit flow can re-establish downstream pressure/flow, recruit collateral channels, and improve capillary exchange, which accelerates granulation and epithelialization. Guideline frameworks for CLTI anticipate this macro-to-micro benefit and endorse objective perfusion reassessment after revascularization (Conte et al., 2019; IWGDF PAD, 2023). Empirically, $TcPO_2$ is a validated predictor of wound course and amputation outcomes, supporting our observation of early perfusion gains translating into healing (Arsenault et al., 2012; Wang et al., 2016; López-Moral et al., 2023; Seabyang et al., 2024). In sum, our data reinforce that early post-procedure perfusion recovery captured by $TcPO_2$ signals a favorable wound trajectory in CLTI.

Higher contemporaneous $TcPO_2$ and rising $TcPO_2$ between visits were both associated with greater healing probability. Biologically, oxygen tension fuels fibroblast proliferation, collagen cross-linking, angiogenesis, and host

defense; sustained gains likely reflect progressive restoration of microvascular supply and oxygen diffusion to the wound bed. Foundational and translational work show oxygen as a rate-limiting substrate for collagen synthesis and angiogenesis, aligning with our slope effect (Castilla et al., 2012; Yip, 2014; Effan et al., 2024). Multiple clinical syntheses link higher $TcPO_2$ to improved healing and lower amputation risk, supporting our time-updated modeling approach (Wang et al., 2016; Arsenault et al., 2012; López-Moral et al., 2023; Burhan et al., 2021). Practically, clinicians should monitor *both* the level and recent change in $TcPO_2$, not just a single value.

Active infection at a visit was associated with lower healing probability despite adjustment for perfusion and case-mix. Pathophysiologically, infection increases inflammatory load, consumes oxygen, and can propagate to bone, undermining granulation and delaying closure. Contemporary infection guidance and observational data consistently document worse healing, higher hospitalization, and greater amputation risk when ulcers are infected (IWGDF/IDSA Infection Guideline 2023; Ndosi et al., 2017; Armstrong et al., 2023; Burhan et al., 2024). Our result emphasizes rigorous, guideline-concordant infection control concurrent with perfusion optimization.

We observed larger absolute gains in predicted healing when $TcPO_2$ moved from 20 to 30 mmHg than from 30 to 40 mmHg. This aligns with the long-noted nonlinearity of oxygen-dependent biochemistry where very low tensions constrain collagen synthesis and bactericidal function, and moderate increases yield outsized benefits. Several studies and reviews have used 30–35 mmHg as a practical cut-point for healing potential, closely mirroring our trajectory-based finding (Lo et al., 2009; Wang et al., 2016; Zingg et al., 2019; López-Moral et al., 2023; Ariani et al., 2024). Therefore, trajectory-aware rules that trigger escalation when $TcPO_2$ is <30 mmHg or slopes are flat could reduce missed windows for limb salvage.

Beyond Month 6, mean $TcPO_2$ changes were small, suggesting diminishing returns in microperfusion recovery. From a mechanistic standpoint, macro-revascularization benefits are front-loaded; later phases likely reflect microvascular remodeling limits and scar maturation rather than further flow augmentation. Guideline paradigms recommend early post-procedure reassessment and targeted re-intervention when needed, consistent with our observation that the “actionable” window is early (Conte et al., 2019; IWGDF Practical Guidelines, 2023). Clinically, this argues for intensive surveillance and optimization in the first 8–12 weeks, then a transition to maintenance unless deterioration recurs.

We saw fewer major amputations and a trend toward better amputation-free survival in the revascularization pathway, but event counts were small. Theoretically, coupling perfusion restoration with aggressive infection control and offloading should maximize limb salvage in CLTI, a population with high competing risk of death and amputation. Large-scale syntheses and guideline statements document the poor natural history of CLTI and the central role of revascularization in altering that course (Conte et al., 2019; Campbell et al., 2023; Effan et al., 2024). Our data are directionally consistent and highlight the need for adequately powered, trajectory-informed studies that integrate $TcPO_2$ with patient-centered outcomes.

Our prediction curves and discrete-time models showed that incorporating $TcPO_2$ *slope* plus revascularization status improved discrimination of near-term healing versus non-healing courses. This aligns with modern risk-modeling practice, which favors time-updated predictors and evaluates clinical utility with decision-curve analysis rather than accuracy alone. Methodological work recommends DCA to quantify net benefit across threshold probabilities, directly informing bedside decisions (Vickers & Elkin, 2006; Vickers et al., 2019 primer). For practice, embedding simple trajectory flags and net-benefit thresholds can standardize escalation and reduce unwarranted variation.

Limitation

This study has several limitations. First, it is a single-centre, observational cohort with a small analytic sample (n=46), which limits precision, external validity, and power for hard endpoints (amputation-free survival) and subgroup analyses (e.g., angiosome, infection severity). Second, treatment assignment was not randomized; despite time-varying modelling, residual confounding by indication (e.g., limb complexity, clinician judgement) is likely. Third, $TcPO_2$ our main perfusion marker is operator- and context-sensitive (skin temperature, electrode placement, room conditions); although we standardized protocols and averaged duplicates, measurement error and within-visit variability remain possible. Fourth, missing covariate data were handled with multiple imputation, which assumes data are missing at random and may bias estimates if this assumption is violated. Fifth, heterogeneity within the “revascularization” pathway (endovascular vs open, device types, runoff quality) was not fully captured, and we lacked blinded core adjudication of wound outcomes. Finally, the 12-month horizon may miss late failures, and we did not include patient-reported outcomes or cost data, limiting conclusions about long-term function and value.

Practice and policy implications

Trajectory-based $TcPO_2$ monitoring should be embedded into routine CLTI pathways as a practical, low-burden decision aid: measure at baseline and at 2, 4, 8, and 12 weeks; act when $TcPO_2$ remains <30 mmHg or the slope is flat/declining; and pair perfusion recovery targets with aggressive infection control and offloading. Services should standardize protocols (acclimatization, temperature, placement), document level and slope in the EHR, and use automated alerts to trigger vascular review within days not months when thresholds are not met. Programs

can adopt simple quality metrics (e.g., ≥80% of CLTI patients have $TcPO_2$ re-measured by Week 4; ≥90% with $TcPO_2$ <30 mmHg or zero slope receive escalation"). Payers and hospital administrators should reimburse serial $TcPO_2$ assessments and coordinated wound vascular clinics, as early escalation is likely cost-saving by averting infection, hospitalization, and amputation. Finally, guideline committees could update recommendations to emphasize trajectories over single thresholds and call for reporting standards (visit schedule, slope definition, action thresholds) to reduce unwarranted practice variation.

Conclusion

In this 12-month cohort of CLTI, revascularization produced rapid early $TcPO_2$ gains and higher adjusted odds of healing, while higher time-updated $TcPO_2$ levels and positive slopes independently predicted recovery and visit-level infection undermined it. A pragmatic inflection near ~30 mmHg and the shared plateau after Month 6 indicate an early, actionable window for escalation and a role for trajectory-based (level + slope) surveillance rather than static thresholds. Despite single-centre design, small sample, and residual confounding, the internal consistency across tables and figures supports the clinical message: embed serial $TcPO_2$ monitoring into routine care, trigger vascular review when $TcPO_2$ remains low or flat, and couple perfusion optimization with rigorous infection control. Future multicentre studies should validate slope-based triggers, integrate patient-reported outcomes and cost, and test pathway-level implementation to reduce amputations and improve limb salvage.

Acknowledgements

We thank the patients and families who participated, and the clinical, vascular surgery, and wound-care teams at Hinodegaoka Hospital, Japan, for their steadfast support throughout study design, data collection, and follow-up. We are also grateful to the hospital's research office and ethics committee for oversight.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing interests

The authors declare no competing interests.

Data availability

De-identified participant data, a data dictionary, and analysis code are available from the corresponding author on reasonable request, subject to data-sharing agreements.

Author contributions

Kawamura Haruka led conceptualisation, methodology, $TcPO_2$ protocol development, site coordination, and data curation; Asmat Burhan provided supervision, study oversight, statistical analysis, figure preparation, and wrote the first draft with critical revisions; Inoue Nanami coordinated patient recruitment, performed wound assessments, managed follow-up, and contributed to project administration; Fujita Kento performed and adjudicated revascularisation procedures, contributed to treatment decisions, and interpreted clinical findings; Septian Mixrova Sebayang conducted literature review, ensured data quality control, assisted with tables/figures, and contributed to manuscript editing; Indah Susanti standardised nursing and infection-control procedures, trained assessors, verified source data, and contributed to manuscript review. All authors had full access to the data, contributed to data interpretation, critically revised the manuscript for important intellectual content, approved the final version, and agree to be accountable for all aspects of the work.

References

Ariani, I., Putra Harsya, D., & Burhan, A. (2024). A comparison of the effects of contemporary dressings and 1% Povidone Iodine on the healing of diabetic ulceration: A Quasy Experiment. Journal of Wound Research and Technology, 1(1), 19–27. https://doi.org/10.70196/jwrt.v1i1.4

Arsenault, K. A., Al-Otaibi, A., Devereaux, P. J., Thorlund, K., Tittley, J. G., & Whitlock, R. P. (2012). The use of transcutaneous oximetry to predict healing complications of lower-limb amputations: A systematic review and meta-analysis. European Journal of Vascular and Endovascular Surgery, 43(3), 329–336. https://doi.org/10.1016/j.ejvs.2011.12.019

Burhan, A., & Arofiati, F. (2021). Effect of Compression Bandage on the Healing of Diabetic Foot Ulcers: A Scooping Review: 4th International Conference on Sustainable Innovation 2020–Health Science and Nursing (ICoSIHSN 2020), Yogyakarta, Indonesia. https://doi.org/10.2991/ahsr.k.210115.110

Burhan, A., Arofiati, F., Abreu Da Silva, V., & Mixrova Sebayang, S. (2023). Effect of ankle brachial index (abi) and compression therapy on diabetic foot ulcer healing. Current Diabetes Reviews, 19. https://doi.org/10.2174/1573399819666230331083420

Campbell, D. B., Shah, N., Suarez-Pierre, A., & Abularrage, C. J. (2023). The natural history of chronic limb-threatening ischemia. Seminars in Vascular Surgery, 36(3), 246–255. https://doi.org/10.1053/j.semvascsurg.2023.07.003

Castilla, D. M., Liu, Z.-J., & Velazquez, O. C. (2012). Oxygen: Implications for wound healing. Advances in Wound Care, 1(6), 225–230. https://doi.org/10.1089/wound.2011.0319

Conte, M. S., Bradbury, A. W., Kolh, P., et al. (2019). Global vascular guidelines on the management of chronic limb-threatening ischemia. Journal of Vascular Surgery, 69(6S), 3S–125S.e40. https://doi.org/10.1016/j.jvs.2019.02.016

Dua, A., et al. (2025). Contemporary outcomes in no-option chronic limb-threatening ischemia. Annals of Vascular Surgery. Advance online publication. https://doi.org/10.1016/j.avsg.2024.12.019

Effan Fahri Mahendra, R., & Burhan, A. (2024). The Effect of Aloe Vera Hydrogel on the Process of Burn Healing: A Systematic Review and Meta-Analysis. Journal of Wound Research and Technology, 1(1), 9–18. https://doi.org/10.70196/jwrt.v1i1.3

Effan Fahri Mahendra, R., Burhan, A., & Susanti, I. (2024). An analysis of various wound washing methods and their efficacy in treating chronic wounds: A comprehensive review of existing literature. Journal of Wound Research and Technology, 1(1), 1–8. https://doi.org/10.70196/jwrt.v1i1.2

Eid, M. A., et al. (2023). The global burden of peripheral artery disease. Journal of Vascular Surgery, 77(1), 285–296.e2. https://doi.org/10.1016/j.jvs.2022.10.030

Fine, J. P., & Gray, R. J. (1999). A proportional hazards model for the subdistribution of a competing risk. Journal of the American Statistical Association, 94(446), 496–509. https://doi.org/10.1080/01621459.1999.10474144

Fitridge, R., Chuter, V. H., Mills, J. L., Hinchliffe, R. J., Azuma, N., Behrendt, C.-A., et al. (2023). The intersocietal IWGDF, ESVS, SVS guidelines on PAD in diabetes with foot ulcer. Journal of Vascular Surgery, 78(6), 2108–2121. https://doi.org/10.1016/j.jvs.2023.09.004

Harrell, F. E. (2015). Regression modeling strategies (2nd ed.). Springer. https://doi.org/10.1007/978-3-319-19425-7

Hernán, M. A., & Robins, J. M. (2020). Causal inference: What if. Chapman & Hall/CRC.

International Working Group on the Diabetic Foot (IWGDF). (2023). IWGDF guideline on peripheral artery disease in diabetes (2023 update). https://iwgdfguidelines.org/wp-content/uploads/2023/07/IWGDF-2023-05-PAD-Guideline.pdf

International Working Group on the Diabetic Foot (IWGDF). (2023). Practical guidelines on the prevention and management of the diabetic foot (2023 update). https://iwgdfguidelines.org/wp-content/uploads/2023/07/IWGDF-2023-01-Practical-Guidelines.pdf

Kim, M. S., et al. (2023). Global burden of peripheral artery disease and its risk factors, 1990–2019. The Lancet Global Health, 11(10), e1601–e1613. https://doi.org/10.1016/S2214-109X(23)00355-8

Laird, N. M., & Ware, J. H. (1982). Random-effects models for longitudinal data. Biometrics, 38(4), 963–974. https://doi.org/10.2307/2529876

Lévesque, L. E., Hanley, J. A., & Kezouh, A. (2010). Problem of immortal time bias in cohort studies: Example using statins for preventing mortality in COPD. BMJ, 340, b5087. https://doi.org/10.1136/bmj.b5087

Lo, T., et al. (2009). Prediction of wound healing outcome using skin perfusion pressure and transcutaneous oxygen tension. International Wound Journal, 6(4), 330–337.

López-Moral, M., et al. (2023). Analyses of transcutaneous oxygen pressure values by angiosome for healing prognosis in diabetic foot ulcers. Diabetes Research and Clinical Practice, 205, 110781. https://doi.org/10.1016/j.diabres.2023.110781

Mixrova Sebayang, S., & Burhan, A. (2024). Comparison of Effectiveness of Hydropobic Cutimed Sorbact Versus Cadexomer Iodine 0.9% on Healing of Diabetic Foot Ulcer: A Randomized Control Trial. Journal of Wound Research and Technology, 1(1), 28–37. https://doi.org/10.70196/jwrt.v1i1.5

Ndosi, M., et al. (2017). Prognosis of the infected diabetic foot ulcer: A 12-month prospective observational study. Diabetic Medicine, 34(1), 78–88. https://doi.org/10.1111/dme.13270

Peduzzi, P., Concato, J., Kemper, E., Holford, T. R., & Feinstein, A. R. (1995). A simulation study of the number of events per variable in logistic regression analysis. Journal of Clinical Epidemiology, 48(12), 1373–1379. k

Račytė, A., et al. (2024). Oxygen saturation increase in ischemic wound tissues following revascularization. Sensors, 24(2), 582. https://doi.org/10.3390/s24020582

Rizopoulos, D. (2012). Joint models for longitudinal and time-to-event data: With applications in R. Chapman & Hall/CRC.

Royston, P., & Sauerbrei, W. (2008). Multivariable model-building. Wiley.

Society for Vascular Surgery (SVS). (2025). Patients with chronic limb-threatening ischemia (CLTI): Evidence-based guidance. https://vascular.org/patients-and-referring-physicians/referring-physicians/who-refer/patients-chronic-limb-threatening

Senneville, É., et al. (2023). IWGDF/IDSA guidelines on the diagnosis and treatment of foot infection in persons with diabetes. Clinical Infectious Diseases. https://doi.org/10.1093/cid/ciad527

Vickers, A. J., & Elkin, E. B. (2006). Decision curve analysis: A novel method for evaluating prediction models. Medical Decision Making, 26(6), 565–574. https://doi.org/10.1177/0272989X06295361

Vickers, A. J., van Calster, B., & Steyerberg, E. W. (2019). A simple, step-by-step guide to interpreting decision curve analysis. Diagnostic and Prognostic Research, 3, 18. https://doi.org/10.1186/s41512-019-0064-7

Wang, Z., Hasan, R., Firwana, B., et al. (2016). Tests to predict healing in the diabetic foot: A systematic review and meta-analysis. Journal of Vascular Surgery, 63(2 Suppl), 29S–36S.e2. https://doi.org/10.1016/j.jvs.2015.10.026

White, I. R., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. Statistics in Medicine, 30(4), 377–399. https://doi.org/10.1002/sim.4067

Willems, S. A., et al. (2025). Prognostic performance of bedside tests for predicting ulcer healing and minor amputation outcomes. Diabetes/Metabolism Research and Reviews. Advance online publication. Vasc Med. 2025 Apr;30(2):250-260, https://doi.org/10.1177/1358863X241309326

Zagzoog, M., et al. (2025). Exercise $TcPO_2$ and outcomes after revascularization in intermittent claudication. Annals of Vascular Surgery. Advance online publication. https://doi.org/10.1016/j.avsg.2024.11.012

Zingg, M., et al. (2019). Transcutaneous oxygen pressure values often fail to predict stump failures after foot or limb amputation in chronically ischemic patients. Clinics in Surgery, 4, 2504. https://www.clinicsinsurgery.com/open-access/transcutaneous-oxygen-pressure-values-often-fail-to-predict-stump-failures-after-foot-or-limb-amputation-in-chronically-ischemic-patients-3780.pdf