



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



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Abstract

Background: Chronic limb-threatening ischemia (CLTI) remains a major global burden with high amputation risk, while evidence on using transcutaneous oxygen pressure (TcPO₂) trajectories (level + slope) to guide healing decisions is limited. Most studies treat TcPO₂ as a static threshold, not a time-updated signal that could trigger earlier escalation.

Purpose: This study aimed to estimate the association of TcPO₂ 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). TcPO₂ 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, Wfl 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 TcPO₂ was 18.3 mmHg (standard care 21.2; revascularization 16.3). From baseline to Week 12, TcPO₂ rose +2.9 mmHg under standard care versus +15.8 mmHg post-revascularization. Higher time-updated TcPO₂ 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 TcPO₂ monitoring (level and slope) identifies an early, actionable window after baseline especially post-revascularization when timely escalation can improve healing. Findings support embedding serial TcPO₂ 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

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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 (TcPO₂) 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 TcPO₂ as a static threshold rather than a trajectory that could signal healing or clinical failure earlier. (Conte et al., 2019; IWGDF, 2023).

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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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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, TcPO₂) 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 [TcPO₂] ≤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 received 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 TcPO₂ level and slope) that might trigger escalation of therapy.

Microperfusion assessment (TcPO₂ protocol)

TcPO₂ 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 TcPO₂ 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 TcPO₂ trajectories

We modeled TcPO₂ 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 \times 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. TcPO₂ 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 TcPO₂ 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 TcPO₂ cut-points (data-driven and a priori values around 20–40 mmHg from prior literature). Second, we fit spline terms for TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 16.3 vs 21.2 mmHg; Wifl 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)
Wifl 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, cm ² , 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; TcPO₂ = transcutaneous oxygen pressure; mmHg = millimeters of mercury; SVS Wifl = 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 TcPO₂ (+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)



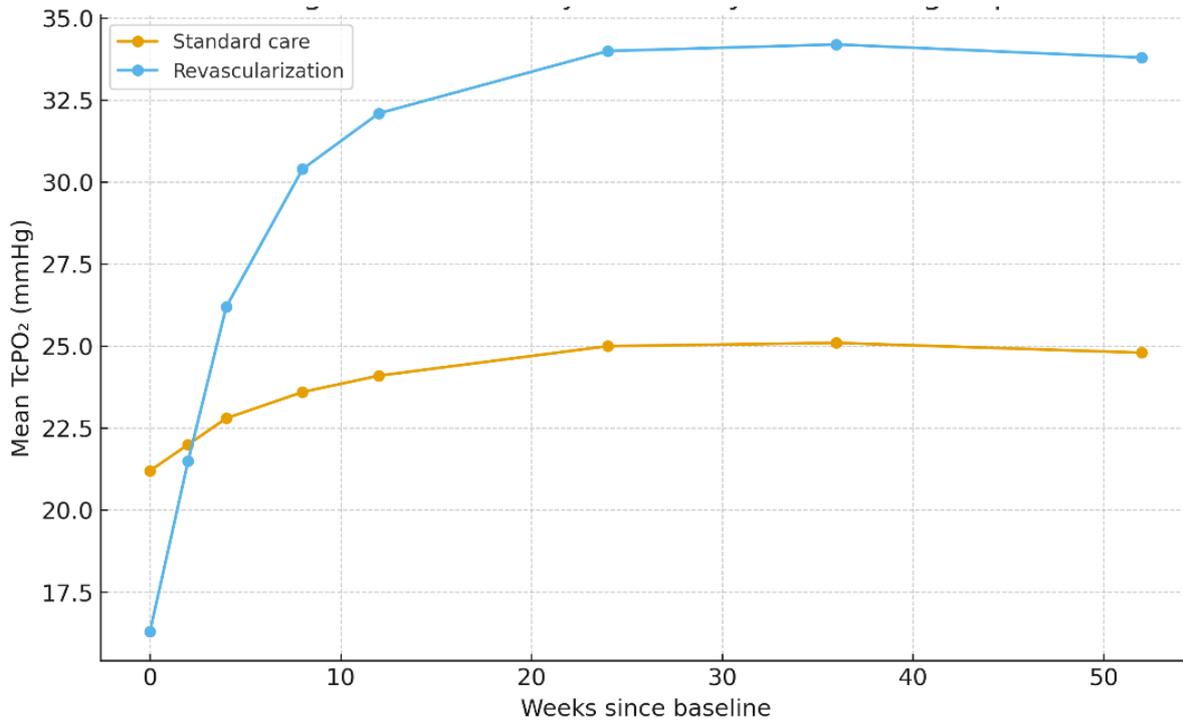


Figure 1. TcPO₂ trajectories by treatment group

TcPO₂ 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. TcPO₂ 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; TcPO₂ = transcutaneous oxygen pressure; mmHg = millimeters of mercury; mean TcPO₂ = average tissue oxygen at each visit; slope (mmHg/wk) = week-over-week rate of change in TcPO₂; wk = week; mo = month

Higher time-updated TcPO₂ level (aOR per 10 mmHg 1.62, 95% CI 1.24–2.11) and positive TcPO₂ 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; Wfl 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
Wifl 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; TcPO₂ = transcutaneous oxygen pressure; mmHg = millimeters of mercury; SVS Wifl 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 TcPO₂ 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).

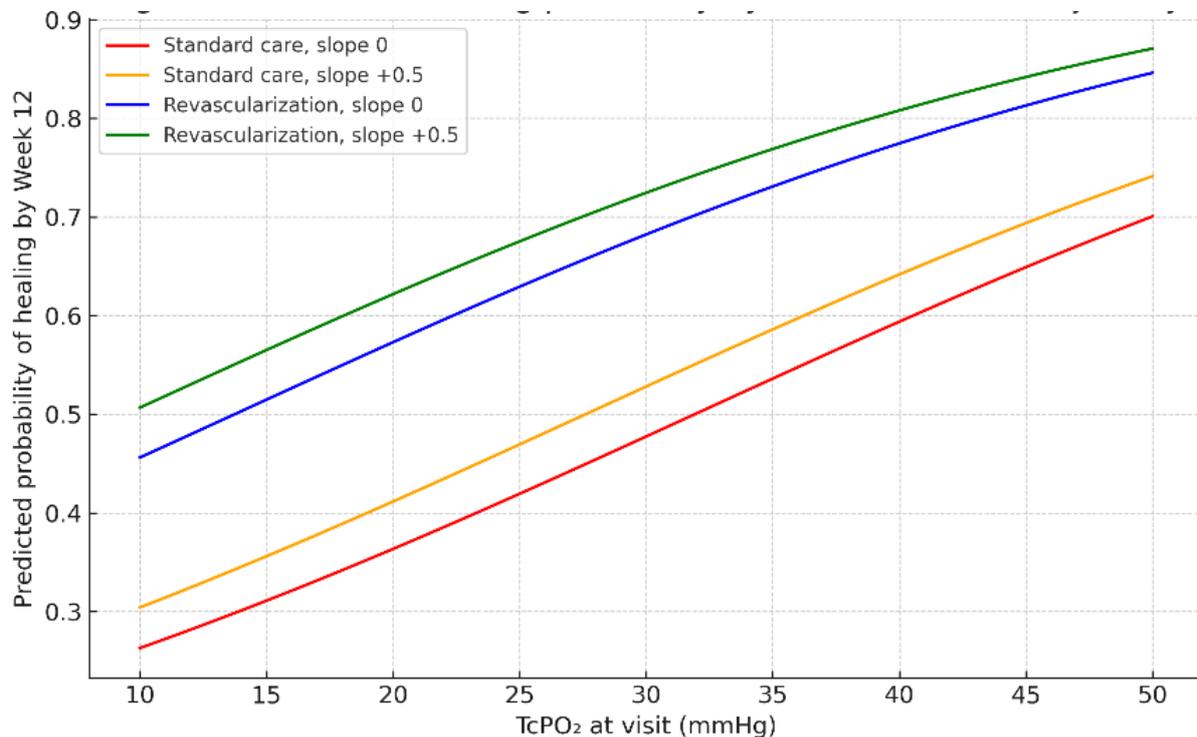


Figure 2. Predicted healing probability by TcPO₂ level and trajectory

Discussion

Our cohort showed a steep TcPO₂ 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, TcPO₂ 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 TcPO₂ signals a favorable wound trajectory in CLTI.

Higher contemporaneous TcPO₂ and rising TcPO₂ 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 TcPO₂ 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 TcPO₂, 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 TcPO₂ 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 TcPO₂ is <30 mmHg or slopes are flat could reduce missed windows for limb salvage.

Beyond Month 6, mean TcPO₂ 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 TcPO₂ with patient-centered outcomes.

Our prediction curves and discrete-time models showed that incorporating TcPO₂ *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, TcPO₂ 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 TcPO₂ 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 TcPO₂ 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., $\geq 80\%$ of CLTI patients have TcPO₂ re-measured by Week 4; $\geq 90\%$ with TcPO₂ < 30 mmHg or zero slope receive escalation"). Payers and hospital administrators should reimburse serial TcPO₂ 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 TcPO₂ gains and higher adjusted odds of healing, while higher time-updated TcPO₂ 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 TcPO₂ monitoring into routine care, trigger vascular review when TcPO₂ 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.

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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, TcPO₂ 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.

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