Efficacy of continuous topical oxygen therapy in hard-to-heal wounds in Colombia: a retrospective analysis

Objective: To evaluate the use of continuous topical oxygen therapy (cTOT) in hard-to-heal or chronic wounds in Colombia, South America.
Method: This multicentre, retrospective analysis studied the efficacy of treating hard-to-heal wounds using a cTOT device in patients over a 3-6-month period. Data were collected retrospectively from patient records. Descriptive statistics were used to summarise the characteristics of the patient population, types of wounds and treatment outcomes. Patients were divided into two groups: a continuous cTOT-treated group (n=47) and a discontinuous cTOT-treated group (n=22). The duration of treatment and wound size reduction were compared. Changes in pain medication usage and the incidence of infections were also analysed.
Results: A total of 69 patients were included in the analysis. Complete healing was achieved in 64% of the continuous cTOT-treated group and 36% of the discontinuous cTOT-treated group, with most patients being pain-free and not requiring medication after treatment.
Conclusion: The results of this study suggest the benefits of cTOT over traditional treatments in accelerating wound healing and reducing pain, medication necessity and wound infection.
Declaration of interest: SM is an employee and WC is part of the Clinical Advisory Board of NATROX Wound Care (Inotec AMD Ltd., UK). WXM is Scientific Director at Cure Latam, the distributor of NATROX in Colombia. EW has received consultancy payments from NATROX Wound Care (Inotec AMD Ltd.). All other authors have no conflict of interest to declare.

hard-to-heal wounds • continuous topical oxygen therapy • pain reduction • wound healing • global medical resources • wound • wound care

Chronic or hard-to-heal wounds present a substantial challenge in healthcare, significantly impacting the quality of life of patients and placing a considerable burden on medical resources worldwide.[1,2] In 2019, the estimated global spend on wound care was roughly $299.482 billion USD, including $11.162 billion USD in South America alone.[3] Hard-to-heal wounds affect an estimated 40 million people worldwide, with 1–2% of the population in developed countries experiencing them at any given time.[2,4–6] In emerging economies, particularly in regions of South America, the challenge of hard-to-heal wounds is exacerbated by factors such as low levels of literacy, limited access to high-quality healthcare, reliance on imported medical devices, cost barriers, and absence of universal health insurance coverage,[6] resulting in a notably high rate of amputations due to complications.[7]

Unlike acute wounds, which typically heal within a predictable timeframe,[8] hard-to-heal wounds persist, despite conventional treatments.[9,10] They are often described as challenging to manage[10,11] and present with inadequate tissue oxygenation and nutrient supply,[12,13] frequently worsening due to underlying conditions, such as diabetes, hypertension and venous insufficiency.[9,10] These comorbidities can disrupt the normal healing process, resulting in wounds that are difficult to close and prone to complications. Such wounds often require prolonged treatment, cause pain, reduce mobility and, in severe cases, lead to infection, sepsis or limb amputation.[2]

Traditional treatments, also referred to as standard of care (SoC), may not always provide complete healing outcomes.[14] A study conducted by Snyder et al.[15] showed the relationship between percentage wound area reduction (PWAR) and healing outcomes in diabetic foot ulcers (DFUs). The findings revealed that DFUs exhibiting <50% PWAR at the four-week timepoint demonstrated a significantly reduced likelihood of healing by 12 weeks compared with those achieving a PWAR of ≥50% (p≤0.001). Furthermore, the analysis indicated that PWAR values during the initial weeks (1–3) also varied between ulcers that ultimately healed and those that did not after the 12-week period; however, the sensitivity and specificity of PWAR as a predictive measure were optimised at week 4. These findings underscore the importance of PWAR as an early prognostic indicator of treatment efficacy, warranting a re-evaluation of clinical management protocols when a 50% PWAR threshold is not met.[15] Thus, there remains

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a need for alternative therapies that offer more effective solutions to SoC, should wounds not achieve a PWAR of >50% after four weeks of therapy.

Continuous topical oxygen therapy (cTOT) supplies oxygen 24 hours a day, seven days a week, to a moist wound bed, at a rate of 11ml/hour (regardless of the size of the wound bed) under normobaric pressures, significantly increasing the partial pressure of oxygen (pO_2) in the superficial wound tissue.[16] Preclinical studies indicate that topical application of pure oxygen significantly increases pO_2 in open wounds. In this research, pO_2 was measured at a depth of 2mm in the wound bed using an implanted probe. Initial pO_2 was <10mmHg with air (21% oxygen), but application of pure oxygen raised it over fourfold to 40mmHg within four minutes. This suggests potential therapeutic benefits for pure oxygen in wound management.[17]

cTOT is a medical treatment designed to enhance the healing of hard-to-heal wounds by providing a controlled supply of oxygen directly to the wound site.[16] Oxygen is critical for various cellular processes essential for tissue repair, including collagen synthesis, cell proliferation and angiogenesis (the formation of new blood vessels).[13,18] Adequate oxygenation can enhance the immune response[19,20] and reduce the risk of infection by inhibiting the growth of harmful anaerobic bacteria.[21] Increasing the local oxygen concentration at the wound site can thus be a key factor in promoting faster wound closure and reducing inflammation.[13,22] Histological and gene expression analyses performed by Keller et al.[23] on skin subjected to TOT indicated a notable reduction in inflammatory response markers and transcription products, including interleukin (IL)-6, IL-8, tumour necrosis factor (TNF)-alpha, matrix metalloproteinase (MMP)-1 and MMP-12. Furthermore, there was a significant increase in structural skin proteins, such as collagen I, elastin and filaggrin.[23]

This retrospective analysis aimed to gain a comprehensive understanding of the real-world impact of cTOT on various types of hard-to-heal wounds in a population of patients in Colombia, South America.

Methods

Study design

This was a multicentre (30 municipalities in 12 departments of Colombia), retrospective analysis of real-world use of cTOT to treat hard-to-heal wound aetiologies in Colombia.

Ethical considerations and patient consent

The study was conducted in accordance with Health Portability and Accountability Act guidelines, and in adherence to the tenets of the International Conference on Harmonization E6 Good Clinical Practice (ICH GCP) and the Declaration of Helsinki. The analysis was performed in accordance with Act No. 003-30AGO2024 and approved by the Research Ethics Committee of Misericordia Clinical International. Since this was a retrospective clinical trial with no additional intervention, an ethics committee approval number was not required, in accordance with Resolution 8430 of 1993 of the Colombian Ministry of Health. However, as an institutional measure, a standard informed consent form was used. All patients provided written, informed consent to publish the anonymised case details and associated deidentified images. No compensation was provided.

Selection criteria

To better reflect real-world use, the study employed few inclusion and exclusion criteria. Patients were eligible if they were ≥18 years of age, had been diagnosed with hard-to-heal wounds, such as DFUs and venous leg ulcers (VLUs), regardless of underlying conditions (e.g., diabetes, hypertension or venous insufficiency), and had received cTOT (NATROX O_2, NATROX Wound Care, UK). Patients <18 years of age or with incomplete medical records were excluded.

Data collection

Data were collected retrospectively from patient records. The following variables were recorded:

- Demographic information: age, sex and comorbidities (e.g., type 2 diabetes, hypertension and chronic renal failure)
- Wound characteristics: type and duration of the wound
- Treatment details: duration of cTOT, use of antimicrobial agents before and after cTOT, frequency of treatments, and additional wound care interventions
- Primary outcomes: duration of treatment, reduction in wound size, PWAR and time to complete healing
- Secondary outcomes: changes in pain medication use and incidence of wound infection.

Statistical analysis

Descriptive statistics were used to summarise the characteristics of the patient population, types of wounds and treatment outcomes. Continuous variables were expressed as mean±standard deviation or median, depending on their distribution. Categorical variables were presented as frequencies and percentages. Comparative analyses were performed using t-tests (two-sample unequal variance) to assess differences in treatment outcomes between the continuous and discontinuous therapy groups. A p-value of <0.05 was considered statistically significant.

Primary outcomes analysis

The duration of treatment and wound size reduction were compared between the two groups, with the PWAR per week calculated to assess the rate of wound healing.

Secondary outcomes analysis

Changes in pain medication use and the incidence of infections were analysed to evaluate the broader impact of cTOT.

Results

A total of 69 patients with DFUs, VLUs, pressure ulcers (PUs), arterial ulcers (AUs), post-traumatic wounds, post-surgical wounds, Fournier's gangrene and burns met the criteria and were divided into two groups: a continuous (uninterrupted) cTOT-treated group (n=47) and a discontinuous (interrupted) cTOT-treated group (n=22), as per Table 1. It should be noted that the cohort receiving interrupted cTOT did so because of delayed insurance authorisations. For the purposes of this study, the authors used the terms 'continuous cTOT' and 'discontinuous cTOT' to denote such interruptions in the supply of cTOT. The highest proportion of wounds were DFUs (44.7%; 36.4% for continuous and discontinuous cTOT-treated cohorts, respectively) followed by VLUs (19.1% and 31.8% in the continuous and discontinuous cTOT-treated cohorts, respectively) (Fig 1).

Table 1. Patient demographics overall (n=69) and per continuous (uninterrupted) cTOT (n=47) and discontinuous (interrupted) cTOT-treated groups (n=22). *Prior to cTOT treatment

Demographic		Overall (n=69)	Continuous cTOT (n=47)	Discontinuous cTOT (n=22)	p-value
Mean age, years		59.7	58.1	63.3	0.10
Sex, n	Female	30	18	12	0.22
	Male	39	29	10	
Mean wound duration,* months		16.7	14.1	19.2	0.52
Wound type, n	DFU	29	21	8	
	VLU	16	9	7	
	AU	2	1	1	
	PU	9	6	3	
	Post-traumatic	7	6	1	
	Post-surgical	2	1	1	
	Fournier's gangrene	2	2	0	
	Burn	2	1	1	

cTOT—continuous topical oxygen therapy; AU—arterial ulcer; DFU—diabetic foot ulcer; PU—pressure ulcer; VLU—venous leg ulcer

Fig 1. Wound aetiologies from the two cohorts: continuous cTOT (n=47) **(a)**; discontinuous cTOT (n=22) **(b).** cTOT—continuous topical oxygen therapy; DFU—diabetic foot ulcer; VLU—venous leg ulcer; AU—arterial ulcer; PU—pressure ulcer

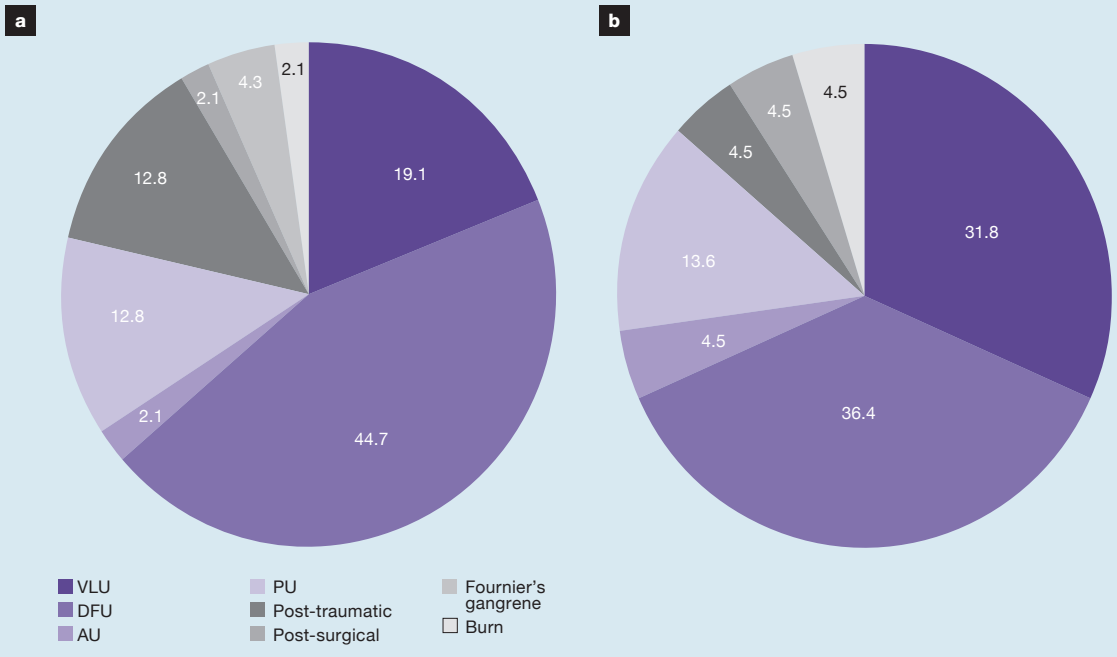


Fig 2. Treatment duration in weeks (mean and median treatment durations) for continuous and discontinuous cTOT across the overall dataset (mean=cross within box, median=line within box). Treatment durations with outliers **(a)**; treatment durations without outliers **(b)**. A significant difference was observed between continuous and discontinuous cTOT, with and without outliers (p=0.006 and p<0.001, respectively)

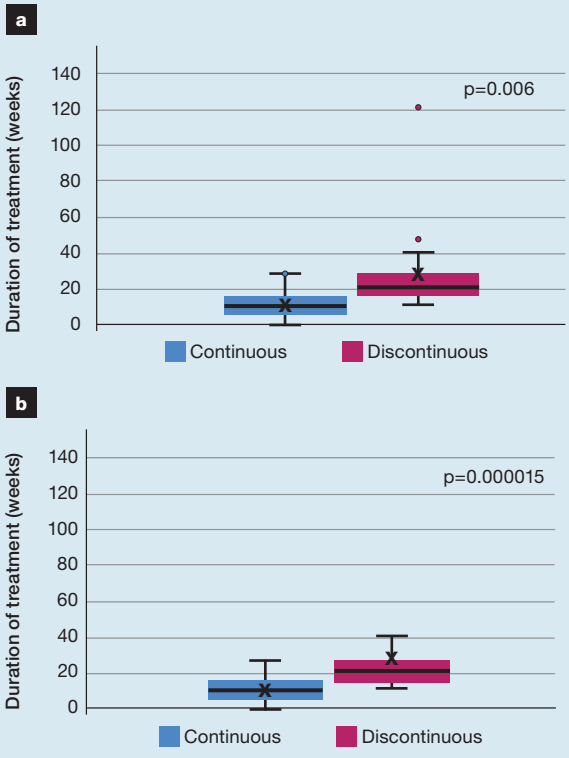


Fig 3. Comparison of continuous topical oxygen therapy (cTOT) treatment durations for diabetic foot ulcers (DFU) (mean, weeks) for both continuous and discontinuous cTOT across the dataset of patients with DFUs while comparing the results between male and female patients

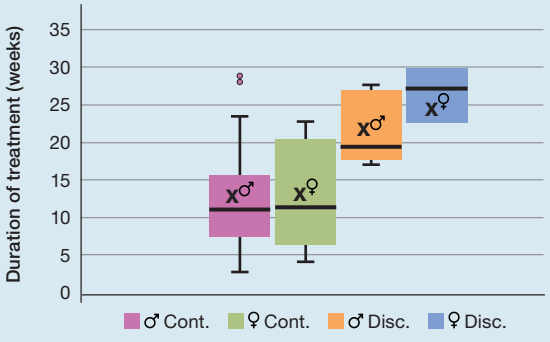
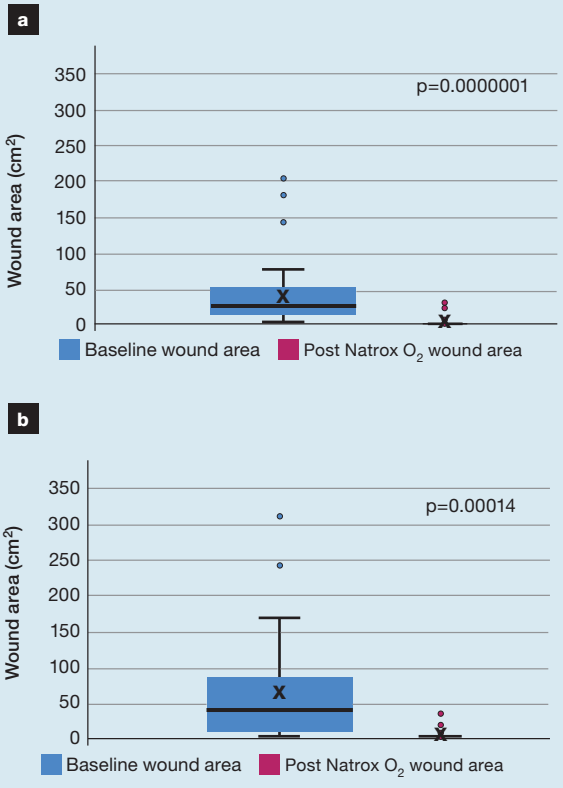


Fig 4. Reduction in wound size by area for continuous **(a)** and discontinuous cTOT treatments **(b)**. Box plots illustrate the reduction in wound area from baseline (blue) to post-treatment (red). A significant reduction in wound area was observed for continuous and discontinuous cTOT treatments (both p<0.001)



Treatment durations

Significant differences in treatment durations between continuous (uninterrupted) cTOT and discontinuous (interrupted) cTOT were observed. The mean duration for continuous cTOT treatment was 12.2±7.4 weeks, while discontinuous cTOT treatment had a considerably longer mean duration of 27.4±23.0 weeks (p=0.006) (Fig 2). After removing outliers, the mean duration for continuous cTOT treatment slightly decreased to 11.0±6.1 weeks (median=10.3 weeks), and the discontinuous cTOT treatment mean duration reduced to 21.7±7.8 weeks (median=20.0 weeks) (Fig 2). The significance between the means persisted (p<0.001).

Diabetic foot ulcers (DFUs)

DFUs were the only wound aetiology with sufficient numbers for a sub-population analysis. For those patients with DFUs, the mean duration of continuous cTOT treatment was 13.2 weeks (all patients), with male patients (mean=13.3 weeks, median=11.5 weeks) and female patients (mean=13.1 weeks, median=11.8 weeks) showing similar durations. In contrast, discontinuous cTOT treatment had a mean duration of 23.9 weeks (all patients), with male patients (mean=22.1 weeks, median=19.7 weeks) and female patients (mean=27.0 weeks, median=27.6 weeks) showing longer durations (Fig 3). The t-test indicated statistically significant

Fig 5. Comparison of percentage wound area reduction (PWAR) **(a)** and PWAR per week **(b)** between continuous cTOT (blue) and discontinuous cTOT (red) treatments. A non-significant difference in PWAR between the two treatment groups was observed (p=0.33) and a significant difference in PWAR/week between the two treatment groups was observed (p<0.001), with continuous cTOT treatment showing a higher reduction rate

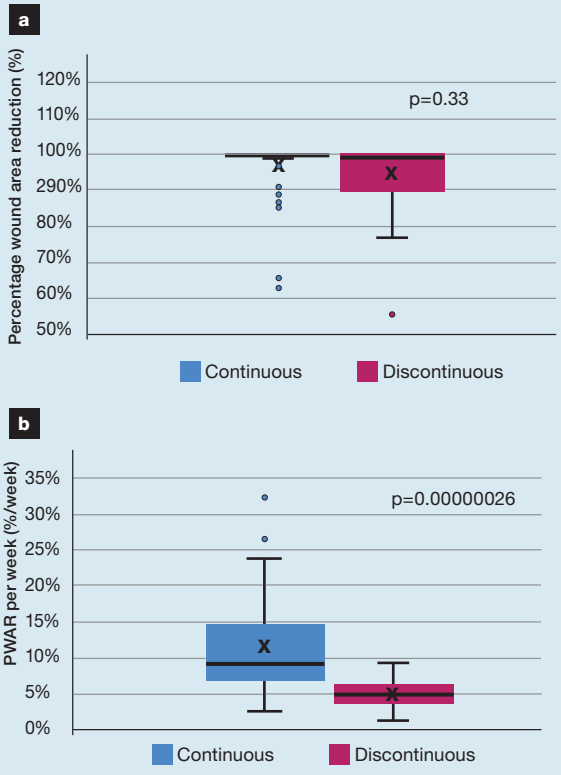
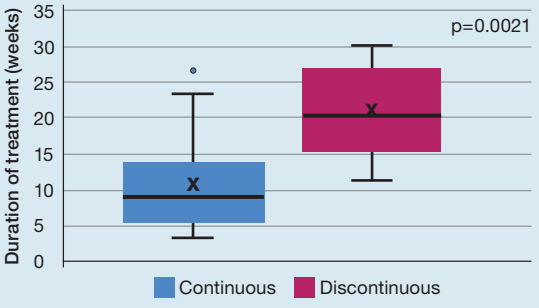


Fig 6. Time to complete healing in weeks between continuous (blue) and discontinuous cTOT (red) treatments. A significant difference in healing time between the two treatment groups was observed (p=0.0021), with continuous cTOT treatment having a faster healing time



differences between continuous and discontinuous cTOT treatments, with a p-value of p<0.001.

Wound size reduction

Both treatment modalities resulted in significant reductions in wound size. Continuous cTOT treatment reduced mean wound size from 42.5cm² to 1.6cm², with a median decrease from 27.0cm² to 0.0cm² (p<0.001). Discontinuous cTOT treatment had a mean reduction in wound area from 67.6cm² to 4.9cm², with a median decrease from 40.1cm² to 0.2cm² (p<0.001) (Fig 4).

Fig 7. Change in pain status before and after treatment in the continuous and discontinuous cTOT treatment groups. Significant reduction from baseline: *p<0.001 continuous cTOT; †p<0.001 discontinuous cTOT

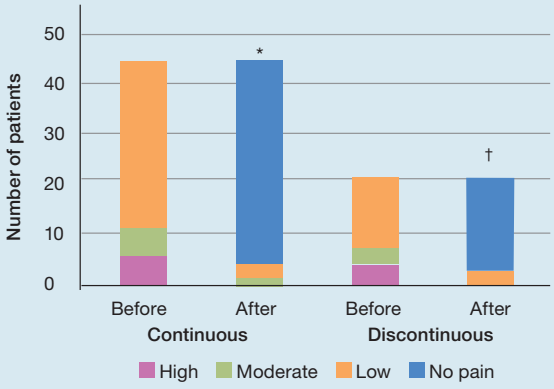
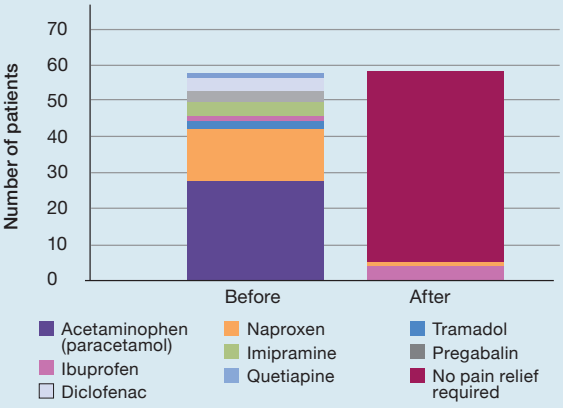


Fig 8. Changes in prescribed pain medication use, before and after cTOT treatment



Percentage wound area reduction (PWAR)

Continuous cTOT treatment achieved a mean PWAR of 97±8% (median=100%). Discontinuous cTOT treatment had a mean PWAR of 94±11% (median=99%). The differences in overall PWAR between treatments were not statistically significant (p=0.33). However, the weekly PWAR showed a higher reduction rate with continuous cTOT treatment (mean=11±7% per week) than with discontinuous cTOT treatment (mean=5±2% per week). These differences were statistically significant (p<0.001) (Fig 5).

Fig 9. Impact of continuous or discontinuous cTOT treatment on pain medication use. Change in the number of pain medications used **(a)**; change in the frequency of daily medications used **(b)**. Significant reduction between number of patients pre- and post-treatment requiring ≥1 pain medications: *p<0.001 (continuous cTOT), ‡p<0.001 (discontinuous cTOT). Significant reduction in pain medication use: $p<0.001 (continuous cTOT), #p<0.001 (discontinuous cTOT)

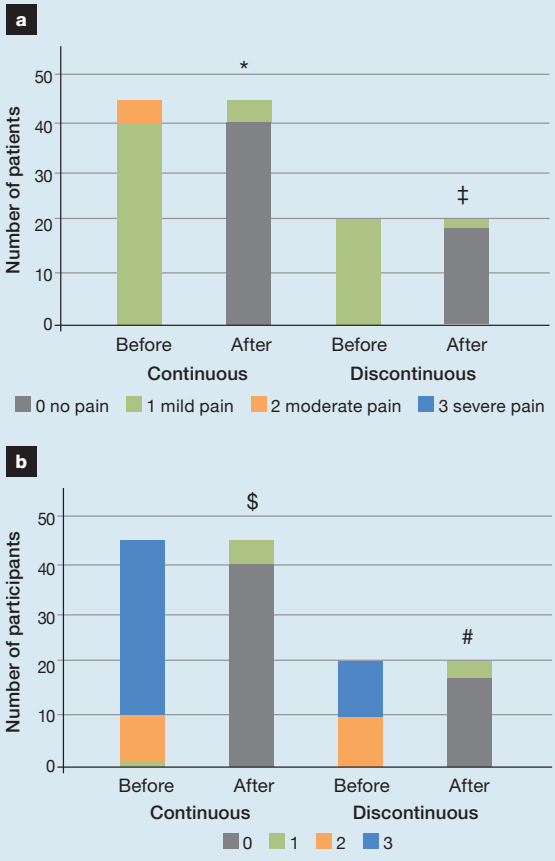
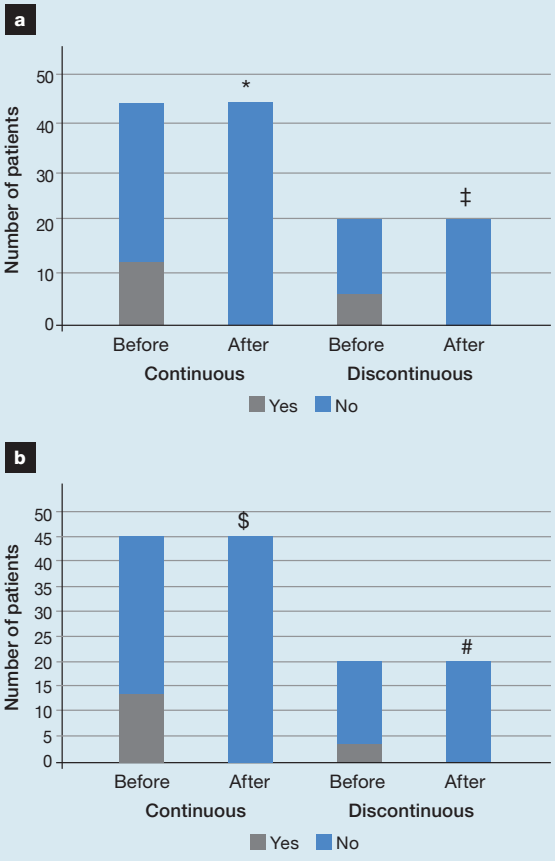


Fig 10. Effects of cTOT in continuous and discontinuous treatment groups on the number of patients with infected wounds before and after cTOT treatment **(a)**, and antibiotic prescription rates pre- and post-treatment **(b)**. Significant difference between number of patients with an infection pre- and post-treatment: *p<0.001 (continuous cTOT), ‡p=0.005 (discontinuous cTOT). Significant difference between patients requiring antibiotic prescriptions pre- and post-treatment: $p<0.001 (continuous cTOT), #p=0.011 (discontinuous cTOT)



Time to complete healing

The mean time to complete healing was significantly shorter for continuous cTOT treatment (mean=10.5±5.7 weeks, median=9.0 weeks) compared with discontinuous cTOT treatment (mean=20.7±6.4 weeks, median=20.3 weeks), indicating that continuous cTOT treatment led to faster healing times (p=0.0021) (Fig 6). Also, the percentage of completely healed patients was greater in the continuous cTOT group (30 of 49 patients (64%)), compared with the discontinuous cTOT group (8 of 22 patients (36%)).

Pain management

Pain levels

All 69 patients reported pain prior to initiating cTOT treatment. A substantial reduction in pain levels was observed, with 91% of all patients in the study with pain initially reporting no pain post-treatment. Continuous cTOT treatment reduced the number of patients with 'high' and 'moderate' pain from 12 to 1 and those with low pain from 35 to 3. Discontinuous cTOT treatment reduced 'high' and 'moderate' pain cases from 8 to 0 and 'low' pain cases from 14 to 2. The reductions were statistically significant in both groups (p<0.001 for both) (Fig 7).

Medication use and frequency

The reduction in pain levels also correlated with a reduced requirement for pain medication. A reduction in the number of different types of pain medication was reported, with the majority of patients (91% overall) no longer needing any pain medication by the end of treatment, as shown in Fig 8. Acetaminophen remained the most used painkiller but patients using this medication reduced from 63% to 6% and from 50% to 9% for continuous and discontinuous cTOT groups, respectively.

Continuous cTOT treatment led to a significant reduction in the number of patients requiring pain

Fig 11. Case study 1 (patient 1). Continuous (uninterrupted) cTOT. A 53-year-old male patient with a history of type 2 diabetes, hypertension, chronic renal failure and venous insufficiency presented with a diabetic foot ulcer (DFU) on the dorsal part of the left foot. The patient received negative pressure wound therapy, conventional dressings and surgical cleansing before cTOT. The patient was taking quetiapine 25mg and acetaminophen 500mg for pain control prior to cTOT treatment but discontinued the use of both medications after starting cTOT. Initially measuring 65.0cm² (13cm in length and 5cm in width), the wound reduced to 0.5cm² after 29.1 weeks of cTOT, representing a 99.23% decrease in wound size. Microbiological assessments before treatment revealed *Pseudomonas aeruginosa* and *Escherichia coli*. Following the initiation of cTOT, no infection was reported and post-treatment microbiology results were negative. Hard-to-heal DFU dorsal surface: beginning of cTOT treatment **(a)**; seven weeks into treatment **(b)**; and at the end of treatment at 29 weeks **(c)**

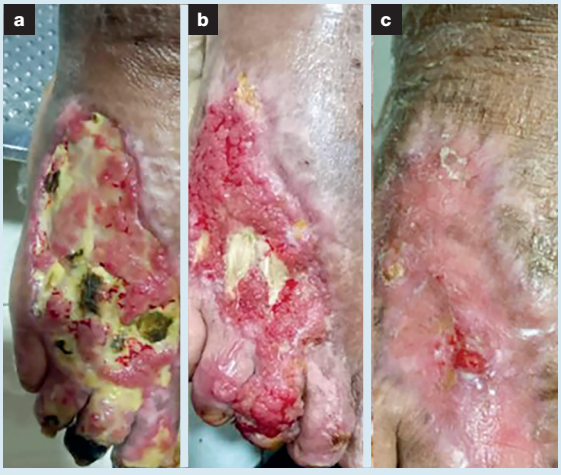
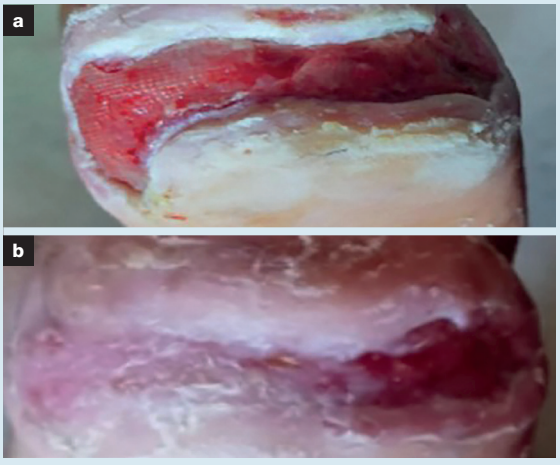


Fig 12. Case study 2 (patient 2). Continuous (uninterrupted) cTOT. A 54-year-old male patient with a history of type 2 diabetes and hypertension presented with a diabetic foot ulcer (DFU) on the plantar surface of the right foot. The ulcer had been stagnant for over three months. Previous treatments included conventional wound dressings, offloading, debridement and topical antimicrobial therapy, but no surgical interventions, cellular, acellular and matrix-like products (CAMPs) or other advanced therapies had been used. The patient was on acetaminophen for pain management, with a low pain level reported before cTOT treatment. Initially measuring 16.0cm² (2.0cm in length and 8.0cm in width), the wound size reduced to 0.0cm², indicating complete healing over 10.7 weeks of cTOT. After cTOT, no pain was experienced, and pain medication was not required. No microbial infections were detected before or after the treatment. Hard-to-heal DFU plantar surface, right foot: baseline **(a)** and after cTOT treatment (10.7 weeks) **(b)**



medication overall (p<0.001). For those patients (n=43) needing one pain medication before continuous cTOT, only four patients needed one medication after continuous cTOT. For those patients requiring two pain medications, this was reduced to zero following cTOT use. Discontinuous cTOT treatment showed a similar reduction, with medication instances dropping from 22 to 2 (p<0.001) (Fig 9a).

Wound infection status

No clinical signs and symptoms of wound infection were noted in either cohort following cTOT treatment. The incidence of infections in wounds significantly reduced from 14 to zero following continuous cTOT therapy, whereas in the discontinuous cTOT cohort, the number of infected wounds declined from seven to zero. The t-test p-values were <0.001 for continuous cTOT treatment and 0.005 for discontinuous cTOT treatment (Fig 10a). A corresponding cessation of antibiotic use for all patients in both patient groups was observed as shown in Fig 10b. Some of the results are illustrated as case studies in Figs 11–15, in order to provide an overview of the types of wound treated.

Discussion

Hard-to-heal wounds do not progress through the healing cascade in a timely manner, making it difficult to achieve complete wound closure.[10,11] Thus, management of hard-to-heal wounds often requires long treatment durations including hospital care and systemic treatment with antibiotics.[3,11] The morbidity, associated costs and access to treatment of hard-to-heal wounds highlight the need for adoption of effective and easy-to-apply wound treatments.[24] In South America, the varied geographic location, social factors, religious beliefs and economic influences affect how medical conditions are treated, in our experience. While hard-to-heal wounds are prevalent in South America, advanced treatment options are limited and many patients do not have access to specialised wound care. Epidemiological and health economic data by country are scarce; however, there have been an increasing number of studies illustrating the toll that hard-to-heal wounds take on the healthcare system in various regions. A study from Brazil estimated the total annual medical costs for the treatment of DFUs was Int$ 27.7 million for inpatient care and Int$ 333.5 million for outpatient care (1 Int$=1.748 BRL), resulting in a total economic burden of Int$ 361 million in 2014.[25]

Fig 13. Case study 3 (patient 23). Continuous (uninterrupted) cTOT. A 67-year-old male patient with a history of type 2 diabetes and hypertension presented with a diabetic foot ulcer (DFU) on the right foot between the first and the fourth toe. Previous treatments included conventional wound dressings and negative pressure wound therapy. The patient was experiencing low levels of pain, managed with acetaminophen before cTOT. Initially measured at 10.0cm² (4.0cm in length and 2.5cm in width), the wound size reduced to 0.0cm², indicating complete healing over 4.7 weeks of cTOT. After cTOT, no pain was experienced and pain medication was not required. No microbial infections were detected before or after the treatment. Hard-to-heal DFU, right foot between first and fourth toe: baseline **(a)** and at the end of cTOT treatment at 4.7 weeks **(b)**

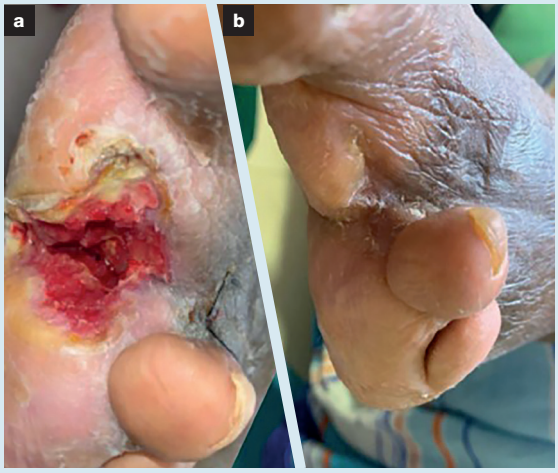
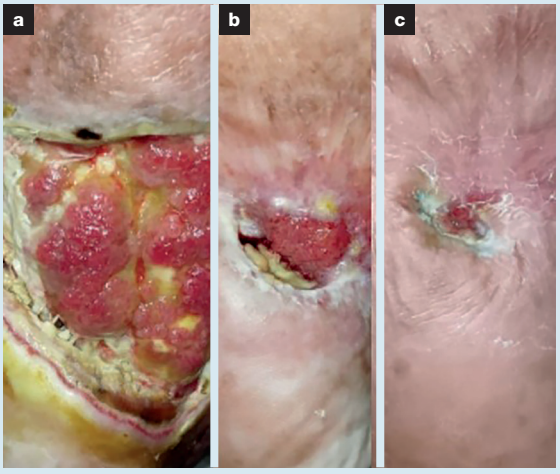


Fig 14. Case study 4 (patient 48). Continuous (uninterrupted) cTOT. A 58-year-old male patient with a history of type 2 diabetes and hypertension presented with a hard-to-heal ulcer on the plantar area of the foot. Despite previous treatments, including partial amputation, the ulcer persisted. The patient experienced low levels of pain, managed with acetaminophen before starting cTOT. Initially measuring 45.5cm² (7.0cm in length and 6.5cm in width), the wound size decreased significantly to 0.5cm², indicating a 98.9% reduction in wound area after 28.4 weeks of cTOT. After cTOT, no pain was experienced and pain medication was not required. No microbial infections were detected before or after the treatment. Hard-to-heal DFU, plantar surface: at baseline **(a)**; after 19.5 weeks in treatment **(b)** and at the end of the treatment at 28.4 weeks **(c)**



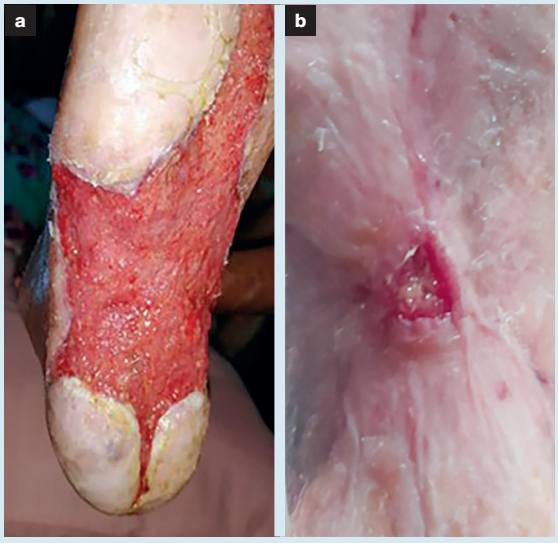
Meanwhile, in Peru, the annual cost of DFU management with SoC was noted to be roughly $2.7 million.[26]

The population of Colombia was estimated to be 52 million in 2023.[27] Some 95% of Colombians are cared for in the country's public–private healthcare system.[24] While this figure is impressive, barriers to care in rural and remote areas remain. Healthcare access can be difficult in rural areas as there are only 2.4 doctors per 1000 residents.[28] Most healthcare delivery is concentrated in urban areas where hospitals and clinics may have long wait times for appointments. Additionally, healthcare coverage is extended to a small number of routine clinical services with residents still facing out-of-pocket expenses for many advanced therapies.[27] This is especially problematic for the 37% of the population living in poverty.[27] There is a demand in Colombia for innovative and effective therapies to enhance healthcare access and improve patient outcomes.

A consensus group in Latin America recommended the use of TOT across all hard-to-heal wounds based on its high level of clinical evidence.[29] While cTOT has been proven to be effective in supporting rapid wound closure in a variety of wound types worldwide, the present study is the first cohort study, to the authors' knowledge, to examine the effects of cTOT on a population of patients in Colombia.

This present study assessed the efficacy of continuous and discontinuous cTOT, with both groups exhibiting more favourable wound outcomes than with previous SoC therapies. However, the patients receiving continuous cTOT showed faster healing, with a greater proportion of patients achieving complete wound closure compared with the discontinuous cTOT group (64% versus 36%, respectively). This concurs with previous studies on both DFUs and VLUs, where complete healing was achieved in 44.4% and 40% of wounds, respectively.[30,31] Additionally, in this study, treatment duration was significantly longer for patients in the discontinuous cTOT group ($p<0.001$). This trend was pronounced among patients with DFUs, although the sample size for other wound types was insufficient for a definitive comparison. Both treatment groups experienced significant wound size reductions, indicating the overall effectiveness of the cTOT therapy. However, patients who received continuous cTOT showed a significantly higher PWAR per week than those receiving discontinuous cTOT. This impact on healing concurs with previous data, including level 1 evidence from randomised controlled trials and meta-analyses,[22,30,32–36] and has been recognised by inclusion in various international guidance for treatment of hard-to-heal wounds.[37–41]

Fig 15. Case study 5 (Patient 20). Discontinuous (interrupted) cTOT. A 57-year-old male patient with type 2 diabetes and hypertension presented with a hard-to-heal DFU ulcer on the plantar aspect of the right foot. Previous treatments included conventional wound dressings. Before starting cTOT, the patient experienced low levels of pain managed with 550mg of naproxen taken twice daily. Initially, the wound measured 90cm² (12cm in length and 7.5cm in width). After 17.4 weeks of discontinuous cTOT, the wound reduced significantly to 1.2cm² (1cm in length and 1.2cm in width), achieving a 98.7% reduction in size. Following the treatment, the patient reported no pain and did not require further pain medication. No microbial infections or adverse events were observed before or after the treatment, underscoring the efficacy and safety of discontinuous cTOT for this patient's condition. Hard-to-heal DFU, plantar surface, right foot: at the beginning **(a)** and at the end of 17.4 weeks of discontinuous cTOT treatment **(b)**



Furthermore, continuous and discontinuous cTOT reduced medication use, frequency and pain levels, in agreement with similar data from a previous study showing 76% of patients experienced substantial, rapid pain relief while 53% became completely pain-free.[31]

Notably, no patient in either group in this present study had an infected wound or required antibiotics after treatment, emphasising the effectiveness of cTOT in supporting the immune response in managing wound infections. Interestingly, cTOT has previously been shown to shift bacterial population dynamics in a hard-to-heal wound away from harmful anaerobic bacteria linked with non-healing to more diverse aerobic and facultative populations.[21] Furthermore, cTOT has also been shown in vitro to enhance the sensitivity of organisms, particularly if in a biofilm, to antibiotics,[42] which may help to support the appropriate use of antimicrobials (antimicrobial stewardship) in the clinic.

Hard-to-heal wounds have a significant impact on patients' quality of life throughout the world.[2] The number of people with wounds is growing and this is likely to continue because of an ageing population. In resource-limited areas, controlling drivers of healthcare costs will make wound management more efficient. Embracing effective therapies, such as cTOT, will aid in mitigating deleterious downstream complications, including infection and amputation.

The complete eradication of wound infections and the cessation of antibiotic use in both groups further support the therapeutic benefits of cTOT. These findings are even more pronounced when patients are treated with cTOT continuously rather than intermittently, reinforcing evidence-based protocols for optimal care, improved wound progression and efficient resource use.

Limitations

The retrospective nature of this study limited the ability to establish causation and can introduce biases about how data were collected and recorded. Additionally, due to the real-world nature of these data, potential confounding factors, such as age, comorbidities and treatment adherence exist. Patient selection bias may also affect the results. The sample size may need to be larger to generalise findings across specific types of hard-to-heal wounds and patient demographics. The sample was drawn from patients in Colombia, therefore results might not reflect the broader Latin American population. This real-world analysis reflects that patients may have received treatments based on their specific conditions or preferences, potentially influencing outcomes. Additionally, the duration of cTOT treatment varied depending on the requirements of each wound. This heterogeneity can complicate comparisons and generalisations. Lastly, the lack of comprehensive health economics data poses a challenge to informed decision-making regarding resource allocation and treatment strategies.

Conclusion

The findings from this study of patients treated with the cTOT device indicate that, when used alongside good SoC, it can accelerate wound healing, shorten treatment duration, reduce pain levels and decrease the need for pain medication and its frequency of use. Furthermore, the results of this retrospective study underscore the potential of cTOT to expedite healing and reduce the burden of hard-to-heal wounds in patients, the Colombian healthcare system and healthcare systems worldwide.

The cTOT device used in this study proved to be an effective solution for delivering oxygen directly to the wound bed at a rate of 11ml/hour. The complete eradication of wound infection and the cessation of antibiotic use in both groups further support the therapeutic benefits of cTOT. These findings are more pronounced when patients are treated with cTOT continuously rather than intermittently. This also supports the case for consistent reimbursement and access to this therapy. JWC

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Reflective questions

- How might the findings of this study influence future treatment protocols for chronic or hard-to-heal wounds in Colombia and other regions?
- In what ways could patient education and support be enhanced to maximise the benefits of cTOT for those with hard-to-heal wounds?
- What considerations should healthcare providers take into account when deciding between the use of continuous and discontinuous cTOT?

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