

Successful Treatment of Moderately Ischemic DFUs using Intermittent Topical Oxygen

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AIM: This study evaluated intermittent topical oxygen therapy (**TWO2**) in the treatment of moderately ischemic DFUs.

METHOD: In the published article in Diabetes Care in 2020, the RCT titled “A Multinational, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy of Cyclical Topical Wound Oxygen Therapy (**TWO2**) in the treatment of Chronic Diabetic Foot Ulcers:

The **TWO2** Study,” it was established that using this therapy produced wounds that were 6 times more likely to heal in 12 weeks and that they had a 6 times lower recurrence rate at 12 months. A post hoc analysis of this study revealed that even moderately ischemic wounds as assessed according to IWGDF criteria, which is defined as any one, or combination, of the following; ABI ≥ 0.7 , TBI < 0.75 , monophasic biphasic Doppler waves below the knee, TCPO2

< 60 , great toe pressure < 60 , or skin perfusion pressure < 60 ., can be successfully treated using this technology.

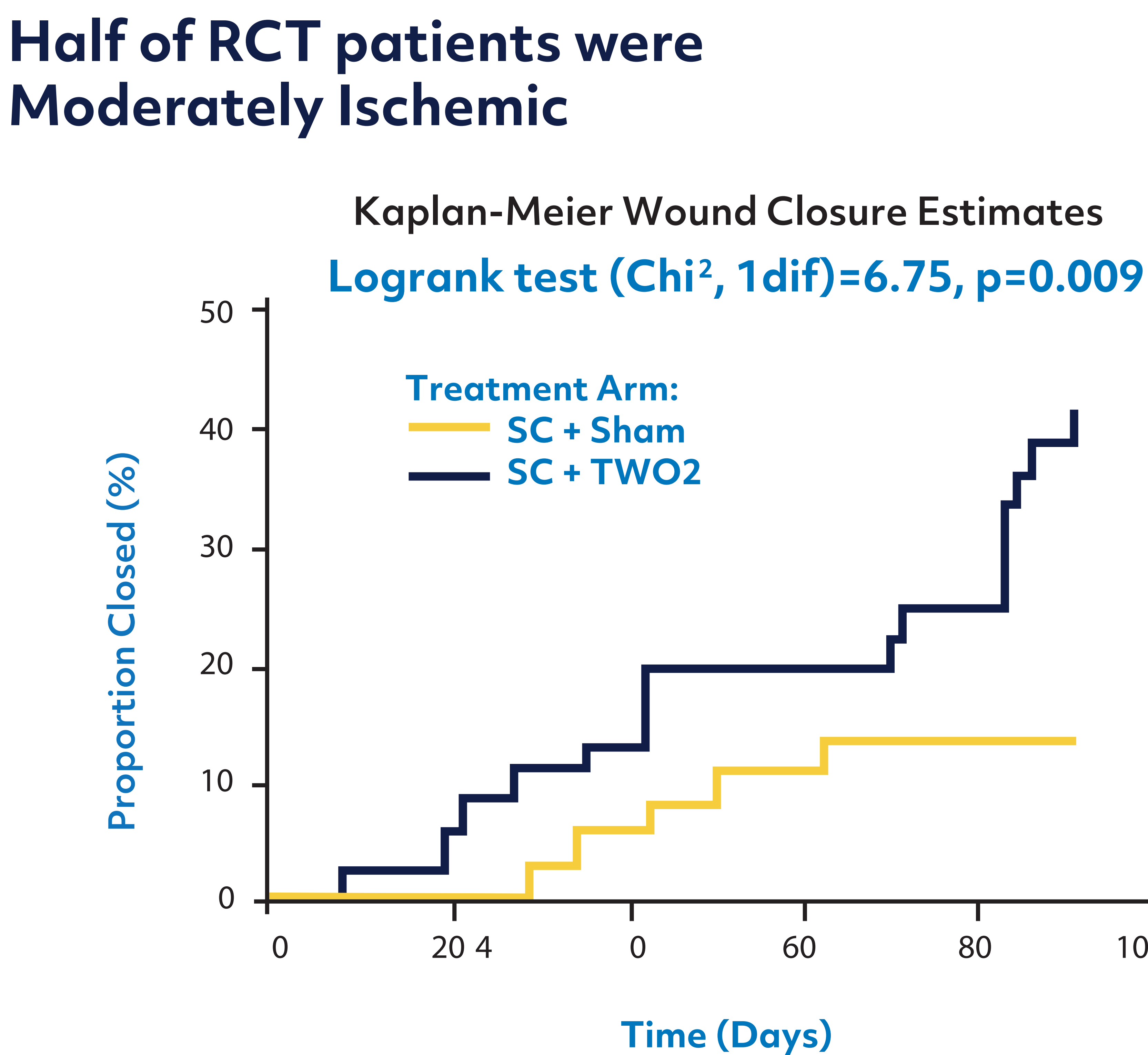
The study inclusion criteria were as follows: diabetic patients with non healing, full-thickness DFUs measuring between $1\text{cm}^2 < \text{UT grade 1 or 2}$ DFU $< 20\text{cm}^2$ post debridement. The duration of the DFU was between 4 weeks and 1 year and all had received standard care for at least 4 weeks.

Patients received optimal standard care, including sharp debridement, the same foam dressings, and a below knee offloading device, equivalent to TCC. Patients who then failed a 2-week run-in period with the study standard care received either a **TWO2**, or sham device, both devices looked and operated identically. Moderate ischemia, according to IWGDF criteria, was defined as anyone or combination of the following ABI ≥ 0.7 , TBI < 0.75 , monophasic biphasic Doppler waves below the knee, TCPO2 < 60 , great toe pressure < 60 or skin perfusion pressure < 60 .

RESULTS: 18 patients each were included in the study group and sham group. At 12 weeks, 7 of 18 patients (39%) in the **TWO2** healed completely compared to 0 of 18 patients (0%) in the sham group ($p < 0.0076$).

CONCLUSIONS: This randomized study demonstrated that moderately ischemic diabetic foot ulcers had significantly higher healing rates using **TWO2** than the sham treatment. **TWO2** provides a multimodal approach to achieve higher healing rates by increasing oxygenation, providing non-contact compression and humidification.

REFERENCE: Frykberg R, Franks P, et al. A multinational, multicenter, randomized, double-blinded, placebo-controlled trial to evaluate the efficacy of cyclical Topical Wound Oxygen (**TWO2**) therapy in the treatment of chronic diabetic foot ulcers: the **TWO2** study. Diabetes Care, 2020.



IWGDF Ischemia Key			
NORMAL	ABI > 0.9 and TBI ≥ 0.75, Full BDBK, TCPO2/GTP/SPP ≥ 60		
MODERATE	ABI ≥ 0.7 and TBI < 0.75, Monophasic BDBK, TCPO2/GTP/SPP < 60		
SEVERE	TCPO2/GTP/SPP < 30		

Active TWO2			
Ischemia Level	n	Healed (n) at 12 Weeks	Healed %
NORMAL	17	8	53.00%
MODERATE	18	7	47.00%
SEVERE	1	0	0%
TOTAL	36	15	41.70%

Odds Ratio: Likely Healing Outcome at 12 Weeks

Produced an odds ratio (OR) of 4.57 (97.8% CI 1.19, 17.57), $P=0.010$ After adjustment for University of Texas Classification (UTC) ulcer grade, the OR increased to 6.00 (97.8% CI 1.44, 24.93), $P=0.004$.

By chance significantly more Severe Ulcers randomized by chance into the Active study arm:

	SHAM TWO2	ACTIVE TWO2	TOTAL
	n=37	n=36	n=73
UTC grade IB	2 (5.4)	1 (2.8)	3 (4.1)
UTC grade IC	2 (5.4)	1 (2.8)	3 (4.1)
UTC grade IIA	4 (10.8)	9 (25)	13 (17.8)
UTC grade IIB	0 (0)	1 (2.8)	1 (1.4)
UTC grade IIC	2 (5.4)	4 (11.1)	6 (8.2)