

Supplementary Table S3. Outcomes and time-point of cytokine collection.

First author, year	Outcomes	Definition of outcome	Follow-up	Time-point of sampling	Paired data
Beidler 2009 [1]	a. Rapid vs delayed healer b. Before vs after compression	a. Rapid healing: >40% wound size reduction after 4 w of compression Delayed healing: <40% reduction after 4 w of compression b. Before and after 4 w of compression with Profore/Profore lite	4 w	Baseline and 4 w	a. No b. Yes
Charles 2008 [2]	Healing vs non-healing	Non-healing: >5 cm ² and present >6 mo Healing: <5cm ² and present for <6 mo	NA	Baseline	No
Drinkwater 2003 [3]	Healing vs non-healing	Nonhealing: Ulcer healing within 1 year of treatment Healing: Unhealed ulcers at 1 year of treatment	At least 1 year, or until healed	Baseline*	No
Escandon 2012 [4]	Correlation to healing	Correlation between cytokine change and healing (change in wound area)	4 w	Baseline and 4 w	Likely
Filkor 2016 [5]	Responder vs non-responder	Responder: ≥20% area reduction in 4 w Non-responder: <20% area reduction in 4 w	4 w	Unclear	No
Fivenson 1997 [6]	Correlation to healing	The individual samples correlated to the percentage healing (change in surface area)	8 w	Baseline and weekly for 8 w	No, repeated measures
Gohel 2008 [7]	Correlation to a. Ulcer size change b. Baseline levels and ulcer size change	a. Correlation between cytokine change and ulcer size change, baseline vs 5 w later b. Correlation between baseline levels and ulcer size change at the end of the study, baseline vs 5 w later Median ulcer size reduced from 4.4 to 2.2 cm ² after 5 weeks, although 17 of 80 ulcers increased in size.	5 w	Baseline and 5 w	Yes
Grandi 2018 [8]	Correlation to wound mean volume reduction	Unclear	Unclear, around 3 w	Baseline and repeated after 1h after irradiation	Yes
Harris 1995 [9]	Healing vs non-healing	Non-healing: NR Healing: Ulcer epithelializing and granulating	NA	Baseline	No
He 1997 [10]	Correlation to healing	NR	3h 20 min	Baseline after 1 h of leg dependency	Yes
Hodde 2020 [11]	Healed vs non-healed	Healed vs non-healed at 12 w Healed ulcer not defined	Up to 12 w	Weekly up to 12 w	Assumed
Krejner 2017 [12]	Poor, moderate, good and fast healing (per week)	Percent reduction from initial wound area, mean wound healing/w. Wound area performed within at least 1 mo preceding the assessment. Poor: <5% per week, Moderate: 5-10%, Good: 11-15%, Fast: >15%.	NA	Baseline*	No
Lagatolla 1995 [13]	a. Healed vs non-healed b. Correlation to time to healing	Healed: Complete healing within 6 mo Nonhealed: No healing within 6 mo	6 mo	Unclear	No
Ligi 2016 [14]	Inflammatory vs granulating	Clinical evaluation	NR but during admission	Baseline, repeated in some after surgical debridement	No

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Ligi 2017 [15]	Inflammatory vs granulating	Clinical evaluation by medical doctors with expertise	NA	Baseline	No
McQuilling 2021 [16]	a. Healing vs non-healing b. Correlation between cytokine level and percentage area change	a. Non-healing: Wounds that did not achieve >85% closure by 12 w Healing: Wounds that achieved >85% closure visit 12 or were healed b. Cytokine levels correlated to percent wound size reduction (wounds healing between -50 to 50%).	12 w	1, 2, 3, 4, 12 w	No, repeated measurements
Murphy 2002 [17]	Healing vs non-healing (=before & after compression)	Non-healing: NR. Compression not received. Healing: Reduction in the ulcer size 4-6 w from baseline on compression. Median size reduced from 2.9 to 1.4 cm ² .	12 w	Baseline and 4-6 w	Yes
Mwaura 2006 [18]	Healing vs non-healing	Non-healing: Not fulfilling the criteria of "healing". Healing: >20% decrease in ulcer area after 8 w of compression, decrease in slough and increase of healthy granulation tissue.	8 w	Baseline	No
Pukstad 2010 [19]	Healing vs non-healing	NR	8 w, or healing	Baseline, 4 and 8 w	No, repeated measurements
Sadler 2012 [20]	Percentage reduction in ulcer area	Percentage reduction in ulcer area over 4 w (linear regression)	4 w	Baseline and 4 w (4 w for analysis)	No
Senet 2003 [21]	Healing vs non-healing	NR (linear healing of the wound edge calculated)	12 w	Baseline, 4, 8, 12 w	Uncertain
Serra 2013 [22]	High-healing vs slow-healing	High-healing: ≥1 cm ² /week Slow-healing: <1 cm ² /week Calculated by subtracting the final ulcer area at the end of the study from the initial area, and divided by no of observations.	Median follow-up time 13 mo	Baseline, w 4, 3 mo and 5 mo	Unclear, repeated measurements
Serra 2015 [23]	High-healing vs slow-healing	High-healing: ≥1 cm ² /week Slow-healing: <1 cm ² /week See Serra 2013 for definition of healing	Median follow-up time 13 mo	Baseline, 4 w, 3 mo, 5 mo	Unclear, repeated measurements
Stacey 2019 [24]	Healing vs non-healing (and indeterminate)	Area change over 3 w determined if the wound was healing or not healing. Non-healing: Area increase for two consecutive weeks (two measurements). The area at the middle time point of the 3 w was classified as non-healing. Healing: Area reduction over two weekly segments. Indeterminate: Wound showing no consistency in area reduction/increase.	Up to 13 w	Baseline and weekly up to 13 w	No, repeated measurements
Tian 2003 [25]	Healing vs non-healing	Non-healing: Chronic VLU failing outpatient treatment with compression. Pt admitted for split skin grafting. No reduction in size over >3 mo or rapid increase in size. Healing: After 2 w of bed resting, formation of granulation tissue, epithelialization and reduction in size. Median size reduction: 20%.	2 w	Baseline and 2 w	Yes
Trengove 2000 [26]	a. Healing vs non-healing b. Ulcer size change	a. Non-healing: No ulcer size reduction in 3 mo on compression, or increase in size at inclusion. Pt admitted for split skin grafting. Healing: Increased granulation, epithelialization, reduction of slough and ulcer area after 2 w. Median size reduction: 12%. b. Percentage change in wound size after 2 w.	2 w	Baseline and 2 w	Yes
Wallace 1998 [27]	Healing vs non-healing	Non-healing: No ulcer size reduction >3 mo on compression, or increase in size at inclusion.	2 w	Baseline and 2 w	Yes

Healing: NR (2 w of regular saline dressings and bed rest: median size reduction: 8%).					
Wiegand 2017 [28]	a. Correlation to wound size reduction b. Responder vs non-responder	a. Cytokine changes from baseline to w 2 correlated to percentage reduction of wound size at w 4 (prediction of healing) b. Responder: >40% area reduction w 4 Non-responder: ≤40% area reduction w 4	4 w	Baseline, 2, 4 w	No

*Assumed

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