



diabetic Foot Italy
Gruppo Interassociativo AMD - SID
podopatia diabetica



6° Congresso Nazionale del Gruppo di Studio della Podopatia Diabetica

La Sindrome del Piede Diabetico in Italia nel terzo millennio:
un approccio globale, discipline diverse, professionalità integrate
in un percorso unitario con "il paziente diabetico al centro"

Presidente del Congresso: Dr. Roberto Da Ros
Responsabile Scientifico: Dr. Roberto Anichini



Starhotels Savoia Excelsior Palace
Trieste, 31 gennaio / 2 febbraio 2019

GESTIONE DELLE LESIONI ED UTILIZZO NUOVE TECNOLOGIE

TUTOR: Vincenzo Stoico

REGISTA: Enrico Brocco

- Preparazione ferita, triage, stadiazione - Francesco Petrella
- Approccio alle lesioni - Katja Speese
- Nuove tecnologie - Marco Meloni

RIUNIONE GRUPPI DI STUDIO

DEFINIZIONE FINALE DEGLI ELABORATI DEI LAVORI DEI GRUPPI DI
STUDIO

Riunione: Carlo Maria Caravaggi, Enrico Brocco, Gianluca Faggioli,
Giovanni Federici, Paolo Galenda, Renato Giordano, Laura Giurato,
Ornella Ludovico, Lorena Mancini, Alberto Piaggese, Vincenzo Stoico,
Luigi Uccioli

Wound Care - Vincenzo Stoico

Il /la dr./sa Vincenzo Stoico dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).



IWGDF Guida sull'uso di procedure per migliorare la guarigione delle ulcere croniche del piede nel paziente diabetico

Redatto da the IWGDF Working Group on Wound Healing

RACCOMANDAZIONI

- 1) Detergere regolarmente le ulcere con acqua pulita o soluzione salina, debridement quando possibile al fine di rimuovere i detriti dalla superficie della ferita e coprirle con medicazione sterile ed inerte al fine di controllare essudato eccessivo e mantenere un ambiente caldo-umido per promuovere la guarigione (Grado di raccomandazione: Forte – Qualità delle prove: Bassa)**
- 2) In generale rimuovere slough, tessuto necrotico ed ipercheratosi circostante con il tagliente, preferendolo ad altre metodiche, valutare le relative controindicazioni come una grave ischemia (Forte – Bassa)**
- 3) Selezionare principalmente le medicazioni sulla base del controllo dell'essudato, comfort e costo (Forte – Bassa)**
- 4) Non utilizzare medicazioni antimicrobiche con l'obiettivo di migliorare la guarigione delle ferite e prevenire infezioni secondarie (Forte – Bassa)**

**IWGDF Guida sull'uso di procedure per migliorare la
guarigione delle ulcere croniche del piede nel paziente
diabetico**

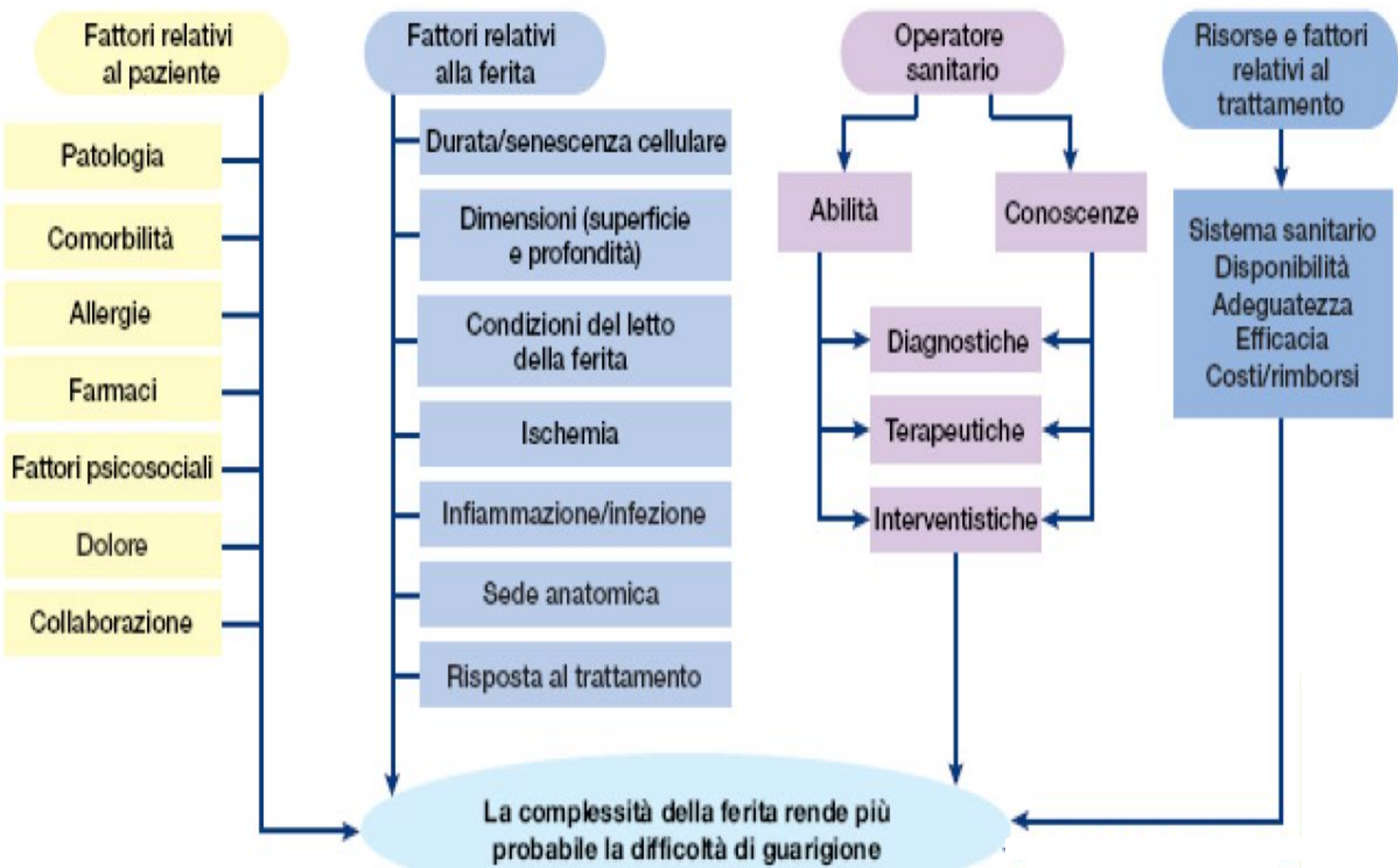
Redatto da the IWGDF Working Group on Wound Healing

RACCOMANDAZIONI

7) Non scegliere agenti per migliorare la guarigione delle ulcere che alterano la biologia della ferita, compresi i fattori di crescita e i prodotti per la pelle di bioingegneria al posto dei trattamenti standard accettati per un'assistenza di buona qualità (Forte – Bassa)

8) Non scegliere agenti per avere un impatto sulla guarigione delle ulcere, attraverso l'alterazione dell'ambiente fisico, ad esempio attraverso l'uso di elettricità, magnetismo, ultrasuoni e onde d'urto, al posto dei trattamenti standard accettati per un'assistenza di buona qualità (Forte – Bassa)

9) Non scegliere trattamenti sistemici per migliorare la guarigione delle ulcere, compresi i farmaci e terapie a base di erbe, al posto dei trattamenti standard accettati per un'assistenza di buona qualità (Forte – Bassa)



Fattori che possono influenzare il trattamento delle ferite

HbA_{1c} and Lower-Extremity Amputation Risk in Low-Income Patients With Diabetes

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 GANG HU, MD, PHD¹

DIABETES CARE, VOLUME 36, NOVEMBER 2013

Table 2—Hazard ratio (HR) (95% CI) of LEA according to different levels of HbA_{1c} at baseline and during follow-up among African American and white patients with diabetes

	HbA _{1c} , % (mmol/mol)						P for trend	Each 1% increase (continuous variable)
	<6.0 (42)	6.0–6.9 (42–52)	7.0–7.9 (53–63)	8.0–8.9 (64–74)	9.0–9.9 (75–85)	≥10.0 (86)		
Baseline								
African American	5,121	4,938	2,613	1,713	1,327	4,096		
Cases	27	51	38	32	45	143		
Person-years	32,733	35,317	20,075	13,736	10,347	29,693		
Age-adjusted HR	1.00	1.84 (1.15–2.93)	2.40 (1.47–3.94)	2.95 (1.76–4.93)	5.09 (3.15–8.24)	5.50 (3.62–8.35)	<0.001	1.18 (1.14–1.22)
Multivariable-adjusted HR ^a	1.00	1.95 (1.21–3.14)	2.07 (1.25–3.44)	2.47 (1.45–4.20)	3.82 (2.32–6.30)	4.09 (2.62–6.38)	<0.001	1.14 (1.10–1.19)
Multivariable-adjusted HR ^b	1.00	1.73 (1.07–2.80)	1.65 (0.99–2.77)	1.96 (1.14–3.36)	3.02 (1.81–5.04)	3.30 (2.10–5.20)	<0.001	1.12 (1.08–1.17)
White	5,536	3,770	2,044	1,317	987	1,906		
Cases	27	29	42	32	32	80		
Person-years	32,427	24,760	14,432	9,138	6,663	12,168		
Age-adjusted HR	1.00	1.38 (0.82–2.34)	3.35 (2.07–5.45)	3.88 (2.31–6.50)	5.22 (3.10–8.76)	6.98 (4.46–10.9)	<0.001	1.29 (1.23–1.35)
Multivariable-adjusted HR ^a	1.00	1.30 (0.76–2.23)	2.62 (1.58–4.34)	2.66 (1.54–4.60)	3.28 (1.92–5.61)	3.71 (2.31–5.96)	<0.001	1.17 (1.11–1.23)
Multivariable-adjusted HR ^b	1.00	1.16 (0.66–2.02)	2.28 (1.35–3.85)	2.38 (1.36–4.18)	2.99 (1.71–5.22)	3.25 (1.98–5.33)	<0.001	1.15 (1.09–1.21)

HbA_{1c} and Lower-Extremity Amputation Risk in Low-Income Patients With Diabetes

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	<6.0 (42)	6.0–6.9 (42–52)	7.0–7.9 (53–63)	8.0–8.9 (64–74)	9.0–9.9 (75–85)	≥10.0 (86)	P for trend	
Follow-up								
African American	4,212	5,094	3,570	2,419	1,748	2,765		
Cases	22	46	62	56	50	100		
Person-years	25,216	35,125	27,580	19,319	14,188	20,473		
Age-adjusted HR	1.00	1.55 (0.93–2.57)	2.51 (1.54–4.08)	3.24 (1.97–5.33)	4.08 (2.45–6.77)	5.51 (3.43–8.86)	<0.001	1.17 (1.12–1.22)
Multivariable-adjusted HR ^a	1.00	1.89 (1.12–3.19)	2.57 (1.55–4.26)	3.05 (1.82–5.12)	4.00 (2.35–6.80)	4.25 (2.56–7.05)	<0.001	1.10 (1.05–1.15)
Multivariable-adjusted HR ^b	1.00	1.51 (0.87–2.63)	1.95 (1.13–3.38)	2.27 (1.29–3.98)	2.96 (1.66–5.27)	3.14 (1.81–5.45)	<0.001	1.07 (1.02–1.12)
White	4,483	4,345	2,824	1,735	1,082	1,091		
Cases	18	33	53	45	42	51		
Person-years	24,270	28,248	20,227	12,190	7,674	6,978		
Age-adjusted HR	1.00	1.55 (0.87–2.75)	3.37 (1.97–5.76)	4.66 (2.68–8.11)	6.71 (3.81–11.8)	9.32 (5.35–16.2)	<0.001	1.29 (1.22–1.36)
Multivariable-adjusted HR ^a	1.00	1.63 (0.90–2.96)	3.06 (1.73–5.40)	3.55 (1.98–6.37)	4.13 (2.26–7.57)	4.62 (2.54–8.39)	<0.001	1.15 (1.08–1.23)
Multivariable-adjusted HR ^b	1.00	1.40 (0.74–2.65)	2.70 (1.46–5.01)	3.12 (1.67–5.84)	3.70 (1.93–7.10)	3.96 (2.08–7.53)	<0.001	1.13 (1.06–1.21)

Data are n unless otherwise indicated. ^aAdjusted for age, sex, type of insurance, income, smoking, peripheral arterial disease, ulcer, and foot deformity at baseline and during follow-up and for baseline (in the baseline analyses) and updated mean (in the follow-up analyses) of BMI, LDL cholesterol, systolic blood pressure, and glomerular filtration rate. ^bAdjusted for age, sex, type of insurance, income, smoking, peripheral arterial disease, ulcer, and foot deformity at baseline and during follow-up; for baseline (in the baseline analyses) and updated mean (in the follow-up analyses) of BMI, LDL cholesterol, systolic blood pressure, and glomerular filtration rate; and for use of antihypertensive drugs, glucose-lowering agents, and cholesterol-lowering agents.

✓ **Alginati, schiume e idrocolloidi** non hanno evidenziato nessun vantaggio in termini di efficacia

✓ **Idrogel** probabilmente più efficaci della **garza salina sterile** nelle ulcere del piede diabetico

✓ **Debridement** chirurgico più efficace del trattamento standard

✓ Trials condotti su **pochi pazienti**

✓ Molti potenziali errori (**bias**)

✓ Follow up **brevi**

✓ Nessuna evidenza, si scelga in base al rapporto costo/beneficio

✓ **Better quality research is needed**



Nuove tecnologie

- Campi elettromagnetici
 - Fotobiomodulazione
 - Medicazioni topiche
- Modulatori di metalloproteasi
 - Terapia rigenerativa

**Treatment of diabetic foot
ulcers with Therapeutic
Magnetic Resonance (TMR®)
improves the quality
of granulation tissue**

Letizia Ferroni,¹ Chiara Gardin,¹
Andrea De Pieri,¹ Maria Sambataro,²
Elena Segnanfreddo,² Elisabetta Iacopi,³
Chiara Goretti,³ Barbara Zavan,¹
Alberto Piaggese³

- ✓ During the follow-up, significantly more lesions healed in the Active Group (14/20 in Group B vs 4/20 in Group A, $P < 0.05$). Moreover, the healing time was faster in Active Group than in Sham group (44.8 ± 12.1 vs 96.7 ± 23.5 days, respectively, $P < 0.05$).
- ✓ In conclusion, our data suggest that TMR ®magnetic fields may act reducing the inflammatory state, triggering a chain of events that promotes the shifting of the lesion towards the proliferative phase. The clinical correlates of the activity of TMR® demonstrated a more frequent and faster healing of DFUs; while the absence of side effects confirms the very positive safety profile of this approach to wound healing.

LIMITATIONS: cost-effectiveness, duration of ulcers, size, localization

Evaluation of fluorescence biomodulation in the real-life management of chronic wounds: the EUREKA trial

JOURNAL OF WOUND CARE VOL 27, NO 11, NOVEMBER 2018

Marco Romanelli,¹ MD, PhD; Alberto Piaggese,² MD; Giovanni Scapagnini,³ MD, PhD; Valentina Dini,¹ MD, PhD; Agata Janowska,¹ MD; Elisabetta Iacopi,² MD; Carlotta Scarpa,⁴ MD; Stéphane Fauvergne,⁵ MD; Franco Bassetto,⁴ MD; EUREKA Study Group

Overall, the system was considered as very easy to use, and 92.4% of the questionnaires reported that investigators would recommend the system to their colleagues. Mean reasons given to investigators to explain this high level of satisfaction were the ease of use and the efficacy of the treatment.

Despite the chronicity and heterogeneity of the different wounds treated in this study, the overall clinical profile is considered promising. The study results revealed the interesting clinical potential of the system in terms of rate of wound closure, mean time to reach wound closure, extremely low rate of wound breakdown and mean RWAR

LIMITATIONS: there was no formal sample size calculation for each group, no randomisation and no control group. There was also a limited number of inclusion and exclusion criteria...different grade of DFUs

CONCLUSIONS: These results confirm that the studied system based on FB offers an important and innovative approach in the management of chronic hard-to-heal wounds

The Use of a Novel Super-Oxidized Solution on Top of Standard Treatment in the Home Care Management of Postsurgical Lesions of the Diabetic Foot Reduces Reinfections and Shortens Healing Time

The International Journal of Lower
Extremity Wounds

1-7

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DOI: 10.1177/1534734618795593

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The chemical reasons...: the creation of a microenvironment unfavorable to bacterial proliferation with consequent reduction of inflammatory pattern and the creation of an ideal pabulum for the development of the healing process.

Despite our study not taking into account the role of systemic antibiotic therapy, we expect that the adoption of super-oxidized solution will associate with a reduction of antibiotic use and a positive effect on antibiotic resistance.

Despite our study representing a single-center pilot experience, the data derived allows to consider this novel solution as an effective part of the integrated therapeutic approach in all diabetic foot cases, alongside surgery, systemic antibiotics treatment, and revascularization if necessary

LIMITATIONS: wound location, depth, absence of comparison with other anti-septic agent, ability to walk

Others new dressings/devices

Topical haemoglobin spray for diabetic foot ulceration

Bateman SD, Br J Nurse, 2015

Effect of low-level light therapy on diabetic foot ulcers: a near-infrared spectroscopy study

Salvi M et al, J. Biomed Opt, 2017

Honey dressing on a leg ulcer with tendon exposure in a patient with type 2 diabetes

Teobaldi I et al, Endocrinol Metabolism Diab Case Rep, 2018

Potential cost-effectiveness of using a collagen-containing dressing in managing diabetic footulcers in the UK

Guest JF et al, J Wound Care, 2018

The LeucoPatch® system in the management of hard-to-heal diabetic foot ulcers: study protocol for a randomised controlled trial

Game F, Trials., 2017

The role of chloramines in treatment of diabetic foot ulcers: an exploratory multicentre randomised controlled trial

Berggvist K et al, Clin Diabetes Endocrinol, 2016

Sucrose octasulfate dressing versus control dressing in patients with neuroischaemic diabetic foot ulcers (Explorer): an international, multicentre, double-blind, randomised, controlled trial

Michael Edmonds, José Luis Lázaro-Martínez, Jesus Manuel Alfayate-García, Jacques Martini, Jean-Michel Petit, Gerry Rayman, Ralf Lobmann, Luigi Uccioli, Anne Sauvadet, Serge Bohbot, Jean-Charles Kerihuel, Alberto Piaggese

Summary

Background Diabetic foot ulcers are serious and challenging wounds associated with high risk of infection and lower-limb amputation. Ulcers are deemed neuroischaemic if peripheral neuropathy and peripheral artery disease are both present. No satisfactory treatment for neuroischaemic ulcers currently exists, and no evidence supports one particular dressing. We aimed to assess the effect of a sucrose octasulfate dressing versus a control dressing on wound closure in patients with neuroischaemic diabetic foot ulcers.

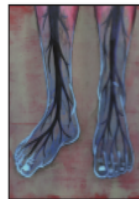
Treatment strategies for neuroischaemic diabetic foot ulcers

The presence of diabetes increases the risk of an amputation of a leg, foot, or toe by approximately 23 times that of a person without diabetes. Most amputations in people with diabetes are preceded by ulceration of the foot, and it is estimated that around 7000 people with diabetes are affected by ulceration of the foot at any one time in England. Caring for people with ulcers and trying to improve healing to avoid amputations is hugely expensive to the UK National Health Service, with costs estimated to be approximately £1 billion per year.¹ In *The Lancet Diabetes & Endocrinology*,² Michael Edmonds and colleagues report the results of a large, multicentre, double-blind, randomised, controlled trial of a sucrose octasulfate dressing versus a control dressing (without sucrose octasulfate) for treatment of neuroischaemic diabetic foot ulcers. The dressings were administered for 20 weeks, and the primary outcome was the number of patients with

a control dressing, and masking to treatment allocation for the measurements of wound size. In particular, an attempt was made to standardise offloading across several countries, and although only half the participants had devices that immobilised the ankle, there was no difference in offloading between the two treatment groups.

But, should clinicians be leaping to adopt this new therapy option, in view of the size of the effect reported? The results are certainly more encouraging than findings for most interventions that have been reported to date. Additionally, although the results of a full health economic analysis are awaited, it is evident that the sucrose octasulfate dressing is easy to apply, and therefore, apart from the dressing itself, there should be no additional costs in a treated patient's clinical pathway.

However, the generalisability of the use of this dressing remains to be confirmed. Although reportedly more than



Lancet Diabetes Endocrinol 2017

Published Online:
December 20, 2017
[http://dx.doi.org/10.1016/S2213-8588\(17\)30439-4](http://dx.doi.org/10.1016/S2213-8588(17)30439-4)

See Online/Articles
[http://dx.doi.org/10.1016/S2213-8588\(17\)30438-2](http://dx.doi.org/10.1016/S2213-8588(17)30438-2)



Lipido-colloid technology

- A jellified matrix of hydrocolloid (CMC) and fatty substances



NanoOligosaccharide – Factor

- A known MMP Modulator (action on MMP2 and MMP9, notably)
- MMP2 and MMP9 are the most involved in DFU
- Interacts with growth factors and cell proliferation

The EXPLORER RCT

Objective

To demonstrate that TLC-NOSF wound dressing is superior to the same dressing without TLC-NOSF, in the local treatment of neuro-ischemic DFU

Design

Randomised, double-blind, controlled trial in two parallel groups

Treatment arms

2 treatment arms with a total of 240 patients

Indication

Neuro-ischemic DFU

Primary endpoint

Complete wound closure* rate after 20 weeks of treatment with the studied wound dressings

Investigation center

43 centres in France, Germany, Italy, Spain and the UK

Duration

20 weeks treatment with 12 weeks follow-up

Etiological treatment

Both arms were treated with standard of care, including off-loading

*Complete wound closure is defined as 100% reduction in DFU surface area with full epithelialization of the target DFU, without exudates and has to be confirmed 2 weeks later (Wx+2) by the investigator

The EXPLORER RCT - Primary Endpoint

Primary Endpoint

To demonstrate that TLC-NOSF wound dressing is superior to the same dressing without NOSF, in the local treatment of neuro-ischemic DFU

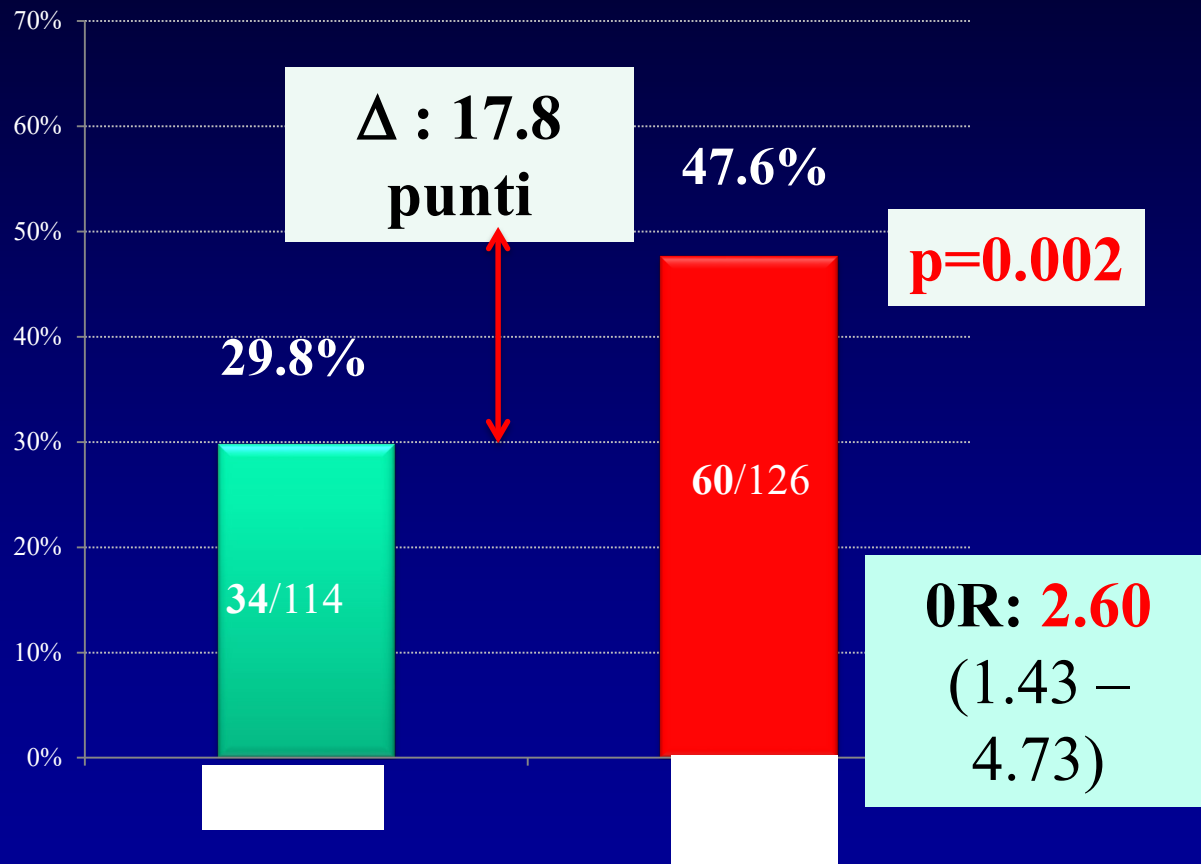
Judgment criteria

Complete Wound Closure* rate after 20 weeks of treatment with the tested wound dressings

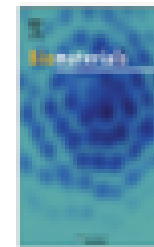
*Complete wound closure is defined as 100% reduction in DFU surface area with full epithelialization of the target DFU, without exudate and has to be confirmed 2 weeks later (Wx+2) by the investigator

Results – FIRST ENDPOINT

Wound closure at week 20



Higher rate of wound closure in the treatment-group (TLC-NOSF) with a chance of healing and wound closure > 260%



Leading opinion

Macrophage polarization: An opportunity for improved outcomes in biomaterials and regenerative medicine[☆]

Bryan N. Brown^{a,b}, Buddy D. Ratner^{c,d}, Stuart B. Goodman^{e,f}, Salomon Amar^g, Stephen F. Badylak^{a,b,h,*}

..... scaffold materials composed of extracellular matrix (ECM) have been shown to promote a switch from a predominantly M1 cell population immediately following implantation to a population enriched in M2 cells by 7e14 days post implantation

Diabetes Medications: Impact on Inflammation and Wound Healing

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Journal of Diabetes and Its Complications xxx (2015) xxx–xxx

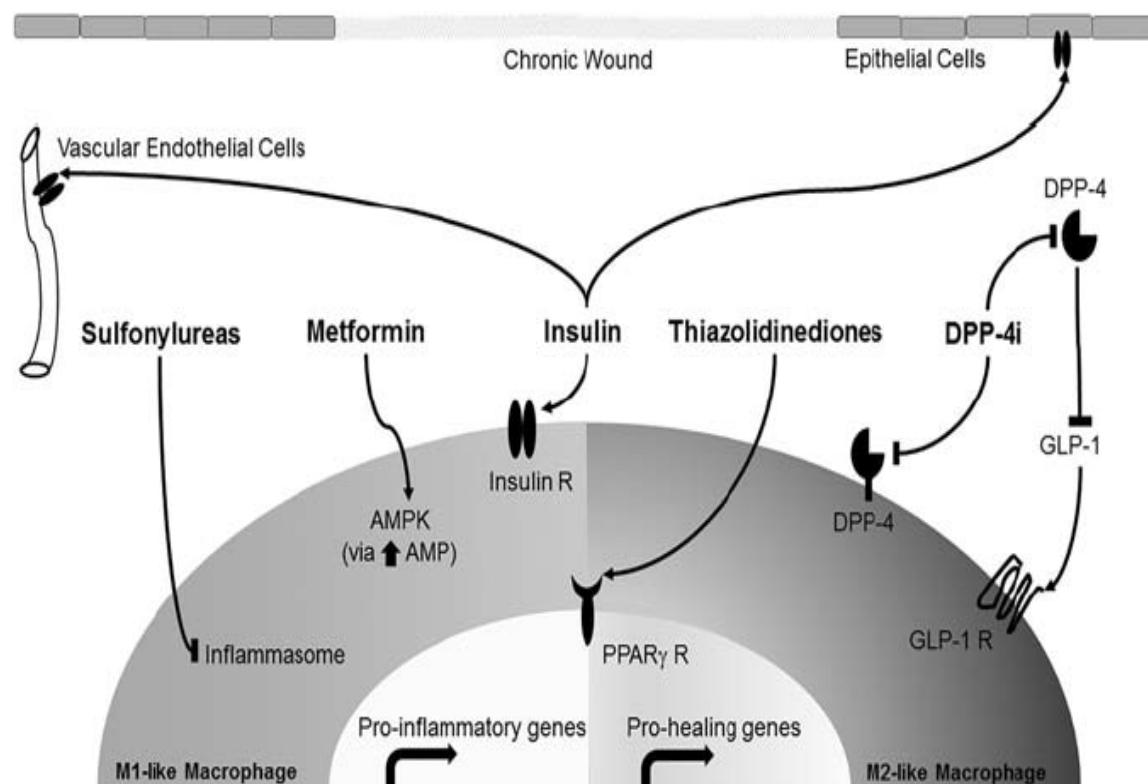


Fig. 1. Diabetes medications associated mechanisms of action involved in wound healing. The figure shows signaling pathway that may be targeted by diabetic medications on epithelial cells (keratinocytes), vascular endothelial cells, “classically activated” M1-like macrophages, and “alternative activated” M2-like macrophages present in chronic wounds. Classically activated M1-like macrophages produce pro-inflammatory gene products that maintain wounds on a persistent inflammatory state. Alternative activated M2-like macrophages produce more pro-healing gene products that allow wound to resolve the inflammatory state and proceed to healing. All receptors (Insulin R, PPAR γ R and GLP-1 R) and cell targets are present in both types of macrophages.

NUOVI ELEMENTI

- **Le nuove tecnologie aprono un nuovo percorso** e potrebbero essere utili o suggerite in specifici casi in relazioni alle disponibilità cliniche e dei pazienti e basate sul costo-beneficio
- Possibilità di medicazioni/devices di supporto **nell'approccio integrato** alle lesioni croniche e post-chirurgiche
- **Prime evidenze** cliniche nel trattamento delle ulcere neuro-ischemiche
- **Maggior conoscenza dei bias** negli studi clinici e degli elementi ostacolanti la guarigione dell'ulcera

Marzo 2017



Luglio 2017



Dicembre 2017



Gennaio 2018



Febbraio 2018



INERZIA TERAPEUTICA

- Nella discussione è CHIARAMENTE emerso che spesso nelle linee guida non viene mai riportata una valutazione temporale della lesione
- Questo a volte potrebbe indurre l'operatore ad una situazione di inerzia terapeutica che impedisce di raggiungere l'obiettivo in un tempo più breve.
- Bisognerebbe quindi costruire un percorso con un algoritmo che determina in maniera puntuale il tempo (giorni) in cui il trattamento topico dovrà essere rivisto alla luce dei risultati negativi o neutri sulla lesione

CRITICITA' ATTUALI E PUNTI NON DEFINITI

✓ WOUND CARE

C'è un **chiaro bisogno di evidenza** per supportare l'uso di un particolare intervento nella gestione delle DFUs e per giustificare l'uso di una particolare terapia

✓ MISURE DI OUTCOMES PER GLI STUDI DI INTERVENTO

C'è la necessità di aumentare la **qualità della metodologia degli studi e dei trials clinici**. La carenza di evidenze è spesso legata alla **scelta delle misure di esito** negli studi di intervento (es. Fase dell'ulcera, regressione, guarigione, qualità di vita, costo beneficio) e **popolazione** (ulcere neuropatiche, ischemiche, superficiali o profonde, comorbidità, real life)

✓ LETTO DELL'ULCERA, MICROAMBIENTE, TERAPIA RIGENERATIVA

Nell'applicazione dello Standard of Care, **il letto dell'ulcera** dovrebbe essere valutato specialmente nelle ulcere croniche (attività proteasica, stato infiammatorio, etc) e le medicazioni/devices più idonei a creare un pathway di guarigione dovrebbero essere identificate; **il ruolo potenziale del monocita** dovrebbe essere approfondito per un nuovo approccio alle ulcere croniche con l'utilizzo della "terapia rigenerativa"

Grazie per l'attenzione