The use of an acidic debridement agent in combination with Negative Pressure Wound Therapy for the development of granulation tissue in skin ulcers

INTRODUCTION

Ulcers of the legs and feet lead to serious morbidity^{1,2} and have an enormous so-The primary objective of the study was to assess the efficacy of the TDA-NPWT cioeconomical impact³⁻⁵. The typical chronic skin lesion is covered with necrosis combination, namely to what extent removal of biofilm and necrosis would lead to and a biofilm and these two characteristics play a role in the chronicity that is typcomplete granulation and how quickly granulation would be complete. The secical for this type of lesion⁶, since they contribute to the hyperinflammatory wound ondary objective was to assess safety. environment¹³. Therefore, removal of the detrimental effects of infection, biofilm, and necrosis is crucial¹²⁻¹⁴ and, consequently, debridement is necessary^{15,16}. Once a lesion has been debrided, granulation tissue can start developing. Most ulcers The lesions of ten female and two male patients, with an average age of 77,9 years heal by secondary intention^{17,18}, and thus, granulation tissue is essential. (range: 55-91) were included. Five lesions were venous leg ulcers, two were arteri-Topical desiccation agent (TDA^I) is a methane-sulfonic-acid containing compound al, and one was of mixed venous/arterial origin. For three lesions the etiology was that works through an exothermic reaction that destroys most molecular bonds. not recorded, and one lesion was post-trauma. The average size was 308 cm² The reaction is initiated by the acid coming in contact with water. The stratum (range: 60-1750) and the lesions had been in existence on average for 13 months corneum contains very little water and is, therefore protected while necrosis, (range: 4-48). slough and biofilm hold a great deal of water and, thus, are strongly affected. TDA Two patients took medications, known to interfere with wound healing is designed as an alternative to surgical debridement and removes biofilm and ne-(Azathioprine (N=1), prednisone (N=1)). crosis effectively and rapidly, but without the need of a great deal of specific ex-All patients suffered from hypertension. In addition, four were diabetic and three pertise, nor a specialized setting, which both are necessary for surgical debridepatients suffered from hypercholesteremia. Other concomitant conditions and disment¹⁹⁻²¹.

The desiccation effect is virtually immediate; biological materials denature and coagulate together and tend to rapidly separate from the underlying tissues. Negative pressure wound therapy (NPWT), through different mechanisms, contributes positively to the formation of granulation tissue²². In our study, the application of TDA, followed by the subsequent use of NPWT, was assessed with regard to the impact on the development of granulation tissue.

METHODS, TREATMENT

A prospective, IRB-approved, non-comparative case series was conducted to assess the time to complete granulation of ulcers of the lower limb. The main inclusion criterion for this study was the presence of an ulcer that had not responded to ambulatory treatment for a period of at least four weeks and that was clinically infected. The infection was confirmed with wound cultures. The patient also had to be a candidate for surgical debridement. Typical exclusion criteria included, but were not limited to, ischemia of the leg, the presence of osteomyelitis, and signs of systemic infection (i.e. septic shock).

The treatment protocol included cleaning of the wound and periwound, the use of an anesthetic, and subsequent application of TDA over the lesion. After 60 seconds the agent was removed by rinsing with saline. NPWT^{II} with standard foam was applied in the same session (set at -125 mm Hg, five minutes "on", two minutes "off") for a total of seven days.



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The lesions were subsequently dressed with vaseline gauze until granulation formation, the primary outcome of this study, was complete.

eases that each were present in one patient included severe Vit. D deficiency, severe obesity, lymphedema of the lower limbs, COPD, scleroderma, and depression.

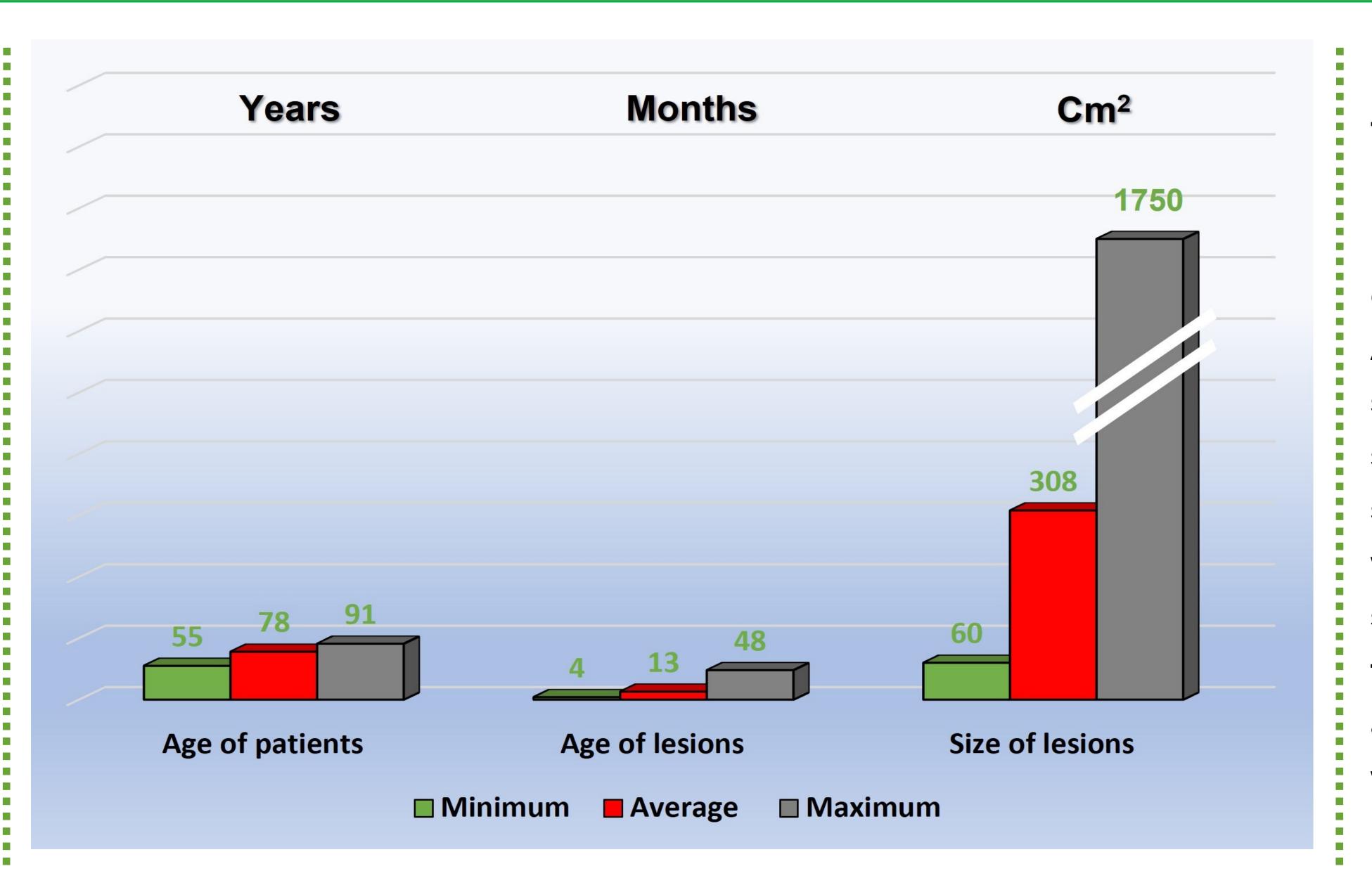
All patients reached complete granulation in, on average, 13,2 days (range: 7-21). When granulation was complete, the lesions were treated with an autologous split skin graft (N=2), a meshed epidermal substitute (equine pericardium^{III}) (N=3) or vaseline gauze (N=7: changed weekly, until reepithelialization was complete).

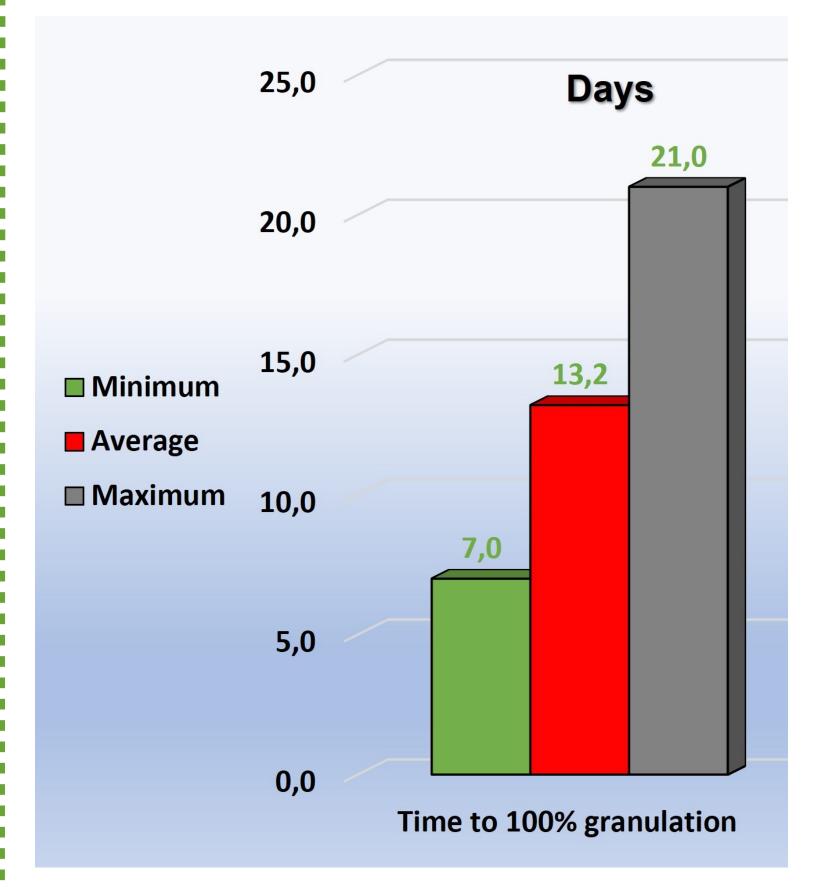
DISCUSSION

The lesions assessed in this study were relatively large compared to typical ulcers that are enrolled in clinical trials: often, a limitation to the size is one of the inclusion criteria^{23 24}. Medications or comorbidities that have a negative influence on wound healing, typical exclusion criteria in most trials, were allowed in this case series. In addition, per the protocol, all lesions were clinically infected to be allowed to enroll. It is, therefore, fair to say that they were hard to heal, although a run-in period was not used to confirm this clinically. In spite of these detrimental factors, granulation completely filled the lesions within, on average, 13.2 days with a combination therapy of TDA and NPWT, without any adverse events. As mentioned, for complete wound closure to proceed, the presence of granulation is essential.

Complete debridement in a single session and the fact this intervention does not need to be performed in the OR by highly specialized physicians was seen as a practical advantage, as was the limited number of dressing changes necessary. The administration of antibiotics was not allowed in the study and was, indeed, shown not to be necessary. All these aspects of TDA-NPWT interventions may contribute to cost savings. Indeed, in a recent study with venous leg ulcers as a model it was shown that the use of TDA is highly cost-effective²⁵.

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Negative pressure wound therapy^{II}, applied immediately after rinsing off TDA



Figure a: venous leg ulcer, prior to TDA-application Figure b: typical aspect, immediately post TDA-application Figure c: full granulation, 7 days post-TDA application.

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LIMITATIONS

This is a single centre, small, prospective, non-comparative case series with a number of patients with different diagnoses, anatomical locations, and different comorbidities. Also, the patients' sex was unequally divided. Thus, the results obtained cannot necessarily be extrapolated to other settings.

At the same time, biofilm and necrosis are virtually omnipresent in the type of lesions included in this study, and there is no specific reason why their removal should not be one of the major objectives in wound healing: after all, healing per secondary intention, the way these lesions typically heal, cannot start without a wound bed filled with granulation tissue²⁶⁻²⁸. Indeed, the primary purpose of assessing the TDA-NPWT combination, the removal of necrotic material or biofilm from leg ulcers, was proven successful, as reflected by the fact that, after only one application of TDA and only one week of NWPT with subsequent wound treatment with vaseline gauze, all lesions reached complete granulation within, on average, 13.2 days. Because the presence of granulation is essential for healing by secondary intention or, in certain types of eligible lesions, the success of some types of grafting, it can be stated that fast granulation contributes to an overall faster healing process.

CONCLUSION

While this study has several limitations, the combination of TDA and NWPT was proven successful in removing biofilm and necrosis from a series of relatively large lesions with different etiologies, in elderly patients with serious comorbidities and **t** medications that negatively affect wound healing. After the application of TDA and NPWT granulation tissue rapidly filled the lesions. Clinical implications include the fact that, within the proper indications for TDA (with or without NPWT), effective and rapid debridement (as an alternative to surgical methods) can be achieved in simple ways and outside a hospital (OR) setting.

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