

The accuracy of burn depth diagnosis: Clinical assessment before and after enzymatic debridement

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ARTICLE INFO

Keywords:

Burn depth
 Diagnosis
 Clinical assessment
 Enzymatic debridement

ABSTRACT

Introduction: The most common technique used to determine burn depth is clinical assessment by experienced burn surgeons, although this has been shown to be reliable in only 60–75% of the cases. Overestimation of burn depth may result in needless surgery, while burn depth underestimation can lead to an increased length of stay in the hospital, risk of contracture and hypertrophic scar formation. The aim of this study was to assess the clinical evaluation of burn depth before and after enzymatic debridement with Nexobrid®.

Methods: The study model was retrospective. 69 patient records were collected at our burn units, from Jan 2018 to Jan 2019. Each target wound was directly assessed by a single expert physician before and after enzymatic debridement. It was investigated whether the expert, by single wound, would have indicated the need for skin grafts before treatment with Nexobrid® and after treatment.

Results: Prior to treatment with Nexobrid®, the expert physician assessed that a graft was necessary for 47/69 patients (68.1%). Following debridement, the same expert deemed that the patients needing a graft were 19/69 (27.5%); analysing K-agreement, a 40.6% discrepancy between the pre and post-treatment opinion with Nexobrid® was observed.

Discussion: The use of Nexobrid® enzymatic debridement can positively affect burn depth clinical assessment, increasing its specificity and sensitivity, without any need for delay. This can lead to a significant change in clinical practice, minimizing the use of surgery, therefore increasing quality and precision of the reconstructive phase.

1. Introduction

According to the depth of the wound and the layers of skin affected, burn injuries are classified as epidermal, superficial partial thickness, deep partial thickness, and full thickness burns [1–3].

Burn surgeons prefer the more useful division of burns into superficial burns that heal on their own and deep burns that need surgical care. Clinical assessment by experienced burn surgeons is currently the most popular method for determining burn depth, but it has only been shown to be reliable in 60–75 percent of cases. Even if typical clinical characteristics (color, capillary refill, skin pliability, sensation, presence of blisters, presence of thrombosed vessels) may aid in clinical decision-making, complex changes in circulation during the acute post-burn

cycle may make the evaluation more difficult [4].

Overestimation of burn depth may result in needless surgery, while underestimation of burn depth may result in an increased duration of stay in the hospital, as well as the possibility of contracture and hypertrophic scar development.

As a consequence, determining the depth of a burn is a critical objective in the treatment of burn patients.

A new Bromelain Based Debridement agent (Nexobrid®) was approved for the European market in December 2012. The findings of previous animal and human burn research indicated that using Nexobrid® decreased the need for surgery and autografting in patients with deep burns, with good long-term results [5–8]. It also provided for earlier eschar removal and, thanks to his selectivity, a reduction in the

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<https://doi.org/10.1016/j.burnso.2021.08.001>

Received 24 July 2021; Accepted 3 August 2021

Available online 12 August 2021

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number and size of burns that required surgical excision.

The aim of this study was to compare the clinical assessment of burn depth before and after enzymatic debridement.

2. Methods

The study model was retrospective. 69 patient records were collected at our burn units, from Jan 2018 to Jan 2019. For each patient a target burn wound was identified for which debridement was performed with Nexobrid®; for each record, the body surface affected by the target wound was noted using a standardized form and if the patient needed grafting as treatment of the target wound after enzymatic debridement (YES / NO).

Each target wound was directly assessed by a single expert physician (GG) before and after enzymatic debridement. It was investigated whether the expert, by single wound, would have indicated the need for skin grafts before treatment with Nexobrid® and after treatment.

The data taken from the records and those related to the expert doctor assessment were reported on specific forms. The completed forms were imported on a database built with Office Excel software and analysed with Office Excel and Stata SE14 software.

Continuous variables were expressed as mean ± standard deviation and range, categorical variables as proportions.

The K agreement test was used to evaluate the concordance between:

- Pre-Nexobrid® indication of the expert on the need for graft (YES / NO) and post-Nexobrid® indication of the need for graft (YES / NO)
- Actual treatment of the patient with graft (YES / NO) and pre-Nexobrid® indication of the expert on the need for graft (YES / NO)
- Actual treatment of the patient with graft (YES / NO) and post-Nexobrid® indication of the expert on the need for graft (YES / NO).

Using the final treatment as gold standard, the sensitivity, specificity, positive and negative predictive values of the expert physician’s opinion (both pre- and post-treatment) were calculated, reporting 95% CI.

The univariate analysis was used to evaluate the association between the final treatment of the patient with graft (YES / NO) and the body surface affected by the target wound; the Odds Ratio was calculated, with an indication of the 95% CI and the calculation of the z score.

For all the tests used, a value of $p < 0.05$ was considered significant.

3. Results

The study sample consisted of 69 burn patients. The average body surface area affected by the wound target was $5.8 \pm 2.4\%$ (range: 3.0–11.0). 31.9% of the sample ($n = 22/69$) underwent skin grafting as final treatment.

Prior to treatment with Nexobrid®, the expert physician assessed that a graft was necessary for 47/69 patients (68.1%). Following debridement, the same expert deemed that the patients needing a graft were 19/69 (27.5%); analysing K-agreement, a 40.6% discrepancy between the pre and post-treatment opinion with Nexobrid® was observed ($\kappa = 0.3$; $p = 0.000$).

K-agreement demonstrated a concordance of 55.1% between the assessment of the expert physician on the need to graft, pre-treatment with Nexobrid®, and the number of subjects that actually underwent grafting ($\kappa = 0.2$; $p = 0.013$).

Comparing patients who actually underwent grafting with the assessment of the expert physician on the need of grafting, before the debridement with Nexobrid® (YES / NO) (Table 1), the sensitivity of the medical assessment was 86.4% (95% CI = 65.1% – 97.1%), the specificity 40.4% (95% CI = 26.4% – 55.7%) and the negative predictive value 86.4% (95% CI = 65.1% – 97.1%).

K-agreement showed a concordance of 95.7% between the

Table 1

Comparison of patients undergoing grafting (YES / NO) with the expert physician assessment on the need for grafting, before debridement with Nexobrid® (YES / NO).

Physician assessment on grafting need, pre debridement with Nexobrid®	Final outcome: graft (YES)	Final outcome: no graft (NO)
YES	TP = 19	FP = 28
NO	FN = 3	TN = 19

assessment of the expert physician on the need to graft, after treatment with Nexobrid®, and the number of subjects that actually underwent grafting ($\kappa = 0.9$; $p = 0.000$).

Comparing patients who actually underwent grafting with the assessment of the expert physician on the need to graft, post debridement with Nexobrid® (YES / NO) (Table 2), the sensitivity of the medical assessment was 86.4% (95% CI = 65.1% – 97.1%), the specificity 100.0% (one sided IC 97.5% = 92.5% – 100.0%), the positive predictive value 100.0% (one sided IC 97.5% = 82.4% – 100.0%) and the negative predictive value 94.0% (95% CI = 83.5% – 98.7%).

Univariate analysis did not show statistically significant associations between having treated the patient with skin grafting and the body surface affected by the target wound (OR = 1.1; 95% CI = 0.9–1.4; $z = 0.9$; $p = 0.346$).

Example cases are shown in Figs. 1 and 2.

4. Discussion

Since burn depth is a critical determinant of burn patient care, an accurate assessment of burn depth is critical for choosing appropriate treatment [9].

Thermal imaging, vital dyes, ultrasound, biopsy with histological examination, and laser doppler imaging (LDI) have all been suggested for burn depth assessment in addition to clinical evaluation [10,11]. Most consider histological examination of burn depth to be the gold standard among them [12]. Although the latter remains excellent for laboratory study, it has little practical application in the clinical setting [10,11] because it is invasive, leaves additional scars, and is hampered by pathology experts’ lack of experience in the complexities of burn injury, which adds to the subjective nature of this assessment.

LDI has emerged as a modern, accurate, and cost-effective diagnostic tool with high sensitivity and specificity in recent years [13–16]. Recent studies, however, have shown that the sensitivity of LDI in burn assessment was slightly lower than its specificity, with a reduction in LDI sensitivity compared to previous studies [17].

The main issue with clinical burn depth evaluation is that a false positive result will lead to unnecessary surgery. Early excision and skin grafting are the current standard of care for treating deep burns in modern burn therapy because they minimize the risk of infection, healing time, hospital stay, expense, and the production of hypertrophic scar [10]. Excisional surgical debridement is successful and fast, but it is also painful and non-selective, and it often results in the removal of viable tissue. Due to the difficulty of determining an accurate burn depth, especially in the early days after the injury, surgical care is often postponed before an appropriate clinical diagnosis is made, confirming the need for surgery [18].

In this article, we demonstrated how the use of Nexobrid® enzymatic

Table 2

Comparison of patients undergoing graft (YES / NO) with the expert physician assessment on the need for grafting, after debridement with Nexobrid® (YES / NO).

Physician assessment on grafting need, post debridement with Nexobrid®	Final outcome: graft (YES)	Final outcome: no graft (NO)
YES	TP = 19	FP = 0
NO	FN = 3	TN = 47

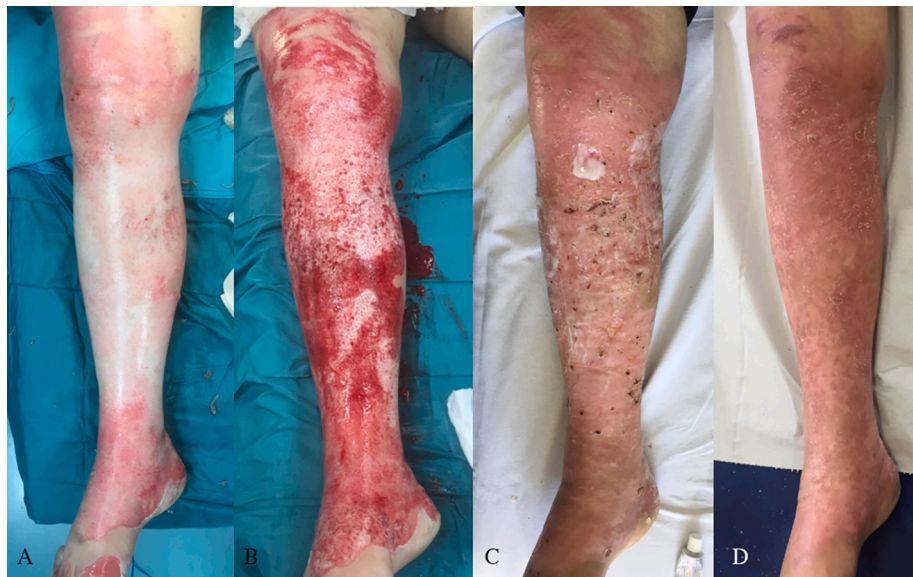


Fig. 1. Example case 1. A) Before enzymatic debridement. Indication of the expert on the need for graft: YES. B) After enzymatic debridement. Indication of the expert on the need for graft: NO. C) Spontaneous healing at 27 days. D) 1 month follow up. No abnormal scarring was noted.



Fig. 2. Example case 2. A) Before enzymatic debridement. Indication of the expert on the need for graft: YES. B) After enzymatic debridement. Indication of the expert on the need for graft: NO. C) 1 month follow up. Spontaneous healing has occurred. No abnormal scarring was noted.

debridement can positively affect burn depth clinical assessment, increasing its specificity and sensitivity, without any need for delay. In particular we found a sensitivity of 86.4%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 94% when comparing patients who actually underwent grafting with the assessment of the expert physician after enzymatic debridement. These values are significantly higher than those we found comparing those

same patients with the assessment of the expert physician before enzymatic debridement (sensitivity 86.4%, specificity 40.4%, positive predictive value 40.4%, negative predictive value 86.4%).

These findings have a direct effect on clinical practice because early and accurate burn depth diagnosis reduces the need for surgery, improving the efficiency and precision of the reconstructive process.

In fact, when compared to the standard of care, the use of enzymatic

debridement with Nexobrid® has shown a substantial reduction in time to complete debridement, the need for surgery, autografting, and the area of burn excised in several studies [18,19]. Our findings point to a potential explanation for “why” Nexobrid® outperforms conventional surgical debridement: more precise burn depth diagnosis will mean fewer surgeries and autografts, lower morbidity, and better long-term outcomes. Furthermore, despite the fact that using Nexobrid® adds to the product’s expense, studies have shown that using it reduces overall burn care costs [20].

In terms of the study’s limitations, we had a small sample size and all cases were evaluated by the same expert physician; although this ensured that the evaluation was consistent across all cases, more research with multiple evaluating experts and inter-rater agreement scores may be beneficial. Further research relating clinical assessment after enzymatic debridement to histological examinations or LDI evaluations may be useful.

In conclusion, the use of enzymatic debridement with Nexobrid® provides the burn surgeon with a powerful tool to increase the sensitivity and specificity of burn depth clinical assessment when compared to clinical assessment before enzymatic debridement, without the additional burden and costs of other supporting technologies (eg. LDI). This effectively distinguishes between burn wounds that will need surgery and those that will heal spontaneously, thus providing better quality of care overall.

5. Patient consent statement

All patients included in this article have given their written consent for the publication of identifiable details, which can include photograph (s) and/or videos and/or case history and/or details within the text to be published.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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