

A RAPID POINT OF CARE TEST FOR BACTERIAL PROTEASE IN CHRONIC WOUNDS IS PREDICTIVE OF AMPUTATION RISK

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Introduction

Chronic wounds are open to the environment and are susceptible to contamination by bacteria, potentially leading to infection. Some of the consequences of a chronic wound infection are tissue breakdown, pain, additional impedance of the healing ability of the wound, amputation (e.g. in a diabetic foot ulcer) and systemic infection, which can be life-threatening^{1,2}. Identifying infection in chronic wounds is challenging because current clinical practice employs using clinical signs and symptoms ('NERDS'³) which are not necessarily distinct from other conditions, such as chronic inflammation⁴. Bacteria and their proteases can stimulate a pro-inflammatory host response⁵ and, eventually, clinical signs due to this inflammatory response and tissue damage may be seen (figure 1).⁶

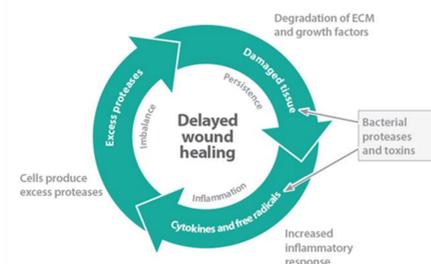


Figure 1. Cycle of chronic wounds showing involvement of bacterial proteases (ECM = extracellular matrix)

Non-traumatic lower limb amputations (LLAs) cause significant morbidity and mortality and are costly to health care systems. The in-patient care cost of a LLA for a diabetic in the UK is estimated to be £9,546 (95%CI: £6,416-£13,463)⁷. In the UK alone, approximately 20 LLAs occur daily⁸, with one year mortality of 13-40% and five year mortality of 39-80%⁹. A patient with a chronic wound is more likely to receive a non-traumatic LLA due partly to increased risk of infection². An indication of pathogenic behaviour of bacteria is the production of enzymatic virulence factors or bacterial proteases¹⁰. The detection of bacterial protease activity (BPA) in a chronic wound is indicative of a period of pathogenesis which is a precursor to observable clinical signs and symptoms of infection. WOUNDCHEK™ Bacterial Status is a rapid, qualitative, point of care test using a wound fluid swab to detect BPA¹¹. In this study, patients asymptomatic for infection were tested for BPA and then monitored for 12 weeks.

Methods

314 chronic wounds (128 venous leg ulcers, 144 diabetic foot ulcers, 31 pressure ulcers, 6 mixed etiology leg ulcers and 5 arterial ulcers) on patients attending 7 US wound clinics, without signs of infection and not currently being treated with topical antimicrobials, were enrolled after informed consent. At Time 0 the wound was swabbed and tested using the WOUNDCHEK™ Bacterial Status device. The test result was blinded to the clinician. The patients were followed for 12 weeks to determine if the wound healed or not and whether an amputation occurred due to the wound.

Results

The analysis combines data from a prospective clinical trial at seven US wound clinics (n=266 wounds) and unaudited data from a preceding pilot cohort (n=48 wounds). 43% (135/314) of the wounds were positive for BPA of which 99 were non-healing at 12 weeks yielding a positive predictive value of 73% (99/135, 95% CI=66.9-78.9%). 124 wounds healed within 12 weeks giving a healing rate of 39% (124/314). Of the 10 patients that received amputations due to their wounds (8 DFU's, 2 VLU's), 8 were positive for BPA.

The relative risk for amputation in patients positive for BPA was 5.3 (p=0.03).

Discussion

Presence of pathogenic bacteria in a wound can cause a period of pathogenesis that leads to local infection, impairs healing and can result in the need for LLA. Clinical examination can wrongly diagnose infection with some chronic wounds failing to exhibit the classic signs of infection and chronic inflammation being misinterpreted as infection⁴. Testing wound fluid for BPA using a rapid point of care test may be useful for detecting the presence of pathogenic bacteria, at a clinically significant stage in the infection continuum, even before the signs of infection are apparent. Integrating a point of care test for BPA as part of routine wound assessment could be a valuable tool in treatment pathways to inform clinicians that the wound is in a period of pathogenesis which could lead to overt infection and be a possible contributor to wound chronicity and increase the risk of amputation⁶.

Case Study

Diabetic foot ulcer, right plantar.

Week 0 :

- No clinical signs of infection
- **Positive for BPA** (result blind to clinician)
- Treatment : Mepilex & Mepitel

Week 4 :

- No clinical signs of infection
- **Positive for BPA** (result blind to clinician)
- Treatment : Aquacel

Week 5 :

- Patient bed ridden with chills and pains. Foot swollen and increased odour
- Third digit is purple and 9x8cm area of redness on dorsal foot
- **Patient referred to surgery for amputation**



Conclusion

The study demonstrates there is a statistically significant increased risk of amputation when bacterial proteases are detected in a wound asymptomatic for infection. Prospective studies are required to confirm that using the WOUNDCHEK™ Bacterial Status test to aid diagnosis and assist in directing appropriate therapy can improve healing outcomes and reduce amputation risk.



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WOUNDCHEK™
LABORATORIES

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