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Comment on: Biology and Biomarkers for Wound Healing

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Chronic wounds are a serious problem that affects a considerable number of subjects and carries a heavy economic cost. Traditionally, the management of chronic wounds was part of nurses' job but during the last five decades there has been considerable research, both basic and clinical, that has resulted in the development of new treatments and requires the collaboration of a large team that includes medical doctors, nurses and other health care providers. The availability of new treatments, mainly growth factors and bioengineered skin, has increased the ability of the treating team to achieve complete wound healing in patients who would otherwise fail to heal their wounds but this is accompanied by a significant increase of the management cost. Furthermore, not all patients respond to such intensive and expensive treatment: in the pivotal clinical trials of these new treatments, a large portion of the participants, sometimes more than half of them, failed to respond and achieve complete wound healing.

Given the great cost of the intensive care for chronic wounds, techniques that can identify patients who are going to fail to respond to regular care can be of paramount importance. The first techniques, which were based on the reduction of ulcer area over a certain period of time in large pivotal clinical trials, were quite successful and are still being used today. Thus, in venous ulcers, large, long-standing ulcers that fail to achieve 40% reduction in size after three weeks of optimal therapy are unlikely to heal¹. In addition, patients with diabetic foot ulcers who fail to heal by 53% over a 4-week period have limited chances to achieve complete wound healing over a 12-week period². Additional techniques that are currently under development include hyperspectral imaging³ and near infrared spectroscopy⁴.

Despite the success of the above techniques, new molecular biomarkers that can accurately identify the stage of the physiological or pathological progress of the chronic wounds have the potential to greatly improve our diagnostic accuracy and promote personalized treatment. In this issue, Dr. Lindley and colleagues, review the current state of wound healing biomarkers. These biomarkers can be obtained by analyzing wound fluid and swabs, tissue specimens and patient serum. An impressive list of biomarkers is presented, which includes the usual suspects that are involved in impaired wound healing, such as metalloproteinases, various growth factors and micro-RNAs. The wound microbiota is another factor that is currently under intense investigation and has the potential to greatly increase our diagnostic

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accuracy. Finally, “omics”- based diagnostics hold the promise to identify numerous new biomarkers and further increase our diagnostic capabilities.

Although these prospects are impressive, it should be emphasized that caution is needed and that the future is not here yet, as much work needs to be done before final conclusions can be drawn. Thus, after potential markers have been identified, their prognostic capability should be tested in large clinical trials, preferably pivotal trials that test the efficacy of new therapeutic interventions. The next step will be to examine whether combining more than one biomarker provides considerably higher accuracy. Finally, they should also be compared to the currently used clinical techniques that are based on ulcer size reduction to evaluate their potential superiority.

Even in case the above steps are successful, additional knowledge will be needed before the biomarkers can be recommended for clinical use. Thus, one very important topic will be their cost. It will be difficult to recommend one or more biomarker that carry a cost that may be prohibitive for daily clinical use. In addition, the ease to measure these factors in busy clinical practices will be a major determining factor as it will signify their acceptance by the practicing clinicians.

Despite the above difficulties, there should be no doubt that the future will eventually arrive at some point and that biomarkers will be one of our main tools to personalize treatment of chronic wounds and greatly approve our therapeutic capabilities. In that sense, Dr. Lindley’s review greatly reflects future capabilities and can be of great service not only to the interested researcher but also to the practicing physician.

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