Procalcitonin Levels in Serum Predict Heterotopic Ossification in Combat Related Extremity Wounds

Donald N. Hope¹, Elizabeth Polfer¹, Shawn Safford¹, Eric Elster¹, Felipe Lisboa², Trevor Brown², Jonathan Forsberg¹,², Benjamin K. Potter¹.
¹Walter Reed National Military Medical Center, Bethesda, MD, USA, ²Naval Medical Research Center, Silver Spring, MD, USA.

Disclosures:

Introduction: Heterotopic ossification and wound dehiscence represent significant complications of wound healing. Traditionally, quantitative microbiology, culture assays, and gram stains have guided the management of complicated wound to help guide management. These methods however are impractical in providing timely and accurate information. Ideally, surrogate markers such as inflammatory cytokines could be used to predict complications of wound healing. One candidate marker includes procalcitonin for which elevated serum procalcitonin (ProCT) levels correlate severity of infection, sepsis, and outcome. ProCT is found both in the serum and exudate of the wounds. We propose that either serum or exudate ProCT will objectively predict heterotopic ossification and wound healing in the combat related extremity wounds.

Methods: The prospective analysis included 200 combat wounded soldiers who sustained extremity only wounds. Of the 200 patients, wound failure data was complete for 176 and heterotopic ossification included 133 patients with complete data. Blood and wound vac effluent were collected for the cytokines. Cytokines included for this analysis included procalcitonin, eotaxin, GM-CSF, interferon-2-alpha, interferon gamma, and tumor necrosis factor alpha. Statistical analysis was performed using Stepwise first order multivariable linear regression to identify the significant variables. The model was then confirmed using both the Partitioned and Goodness of Fit Hosmer and Lemeshow Tests.

Results: In the evaluation of heterotopic ossification, serum procalcitonin level was the only cytokine that was significantly different between groups (110.3 pg/ml versus 207.8 pg/ml, p<0.01). All other cytokines in the serum and exudate were not significantly different. For the logistic regression modeling, the point estimate was 2.9, with a corresponding odds ratio estimate of 18.2 (95% CI, 1.565,211.7). The final model including only serum ProCT demonstrated an excellent fit based on the Hosmer and Lemeshow Goodness-of-Fit test (p=0.57). For wound failure, we did not identify any significant cytokine predictors in either the serum or exudate.

In evaluating the relationship between HO and wound failure, a Mantel Haenzel chi-square analysis was performed for these variables and demonstrated the significant relationship between these two variables. The presence of heterotopic ossification was associated with an odds risk ratio of 5.34 (95% CI, 1.14,25.0). Additionally, those wounds with heterotopic ossification had were significantly larger wounds (349.6 cm² v. 181.5 cm², p<0.001).

Discussion: Procalcitonin levels in the serum can predict the development of heterotopic ossification in extremity wounds. This has implications for the using procalcitonin as a screening marker for the development of HO. In contrast, no other cytokine marker was found to be predictive in determining HO. Similarly, no cytokine was identified in the exudate that was predictive of either wound failure or HO. Supporting previous studies, we have also demonstrated the increased risk of wound failure in the presence of HO. A limitation of this study is the first order analysis of the various cytokine factors and in fact, a network higher order analysis may be essential to accurately screen for possible wound complications. This network analysis is the focus of our future efforts in identifying higher order associations between cytokines in the prediction of wound failure.

Significance: Heterotopic ossification and wound dehiscence are significant complications seen in combat related extremity wounds. ProCT is a potential marker to identify at risk wounds prior to closure.

Acknowledgments:

References:

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