

## The Surgeon's Catch-22: A Prospective Study on Inflammation, Wound Failure, and Heterotopic Ossification in Combat Wounds

Donald N. Hope, MD; Jonathan A. Forsberg, MD; Benjamin K. Potter, MD;  
Elizabeth M. Polfer, MD; Eric A. Elster, MD, FACS;  
Walter Reed National Military Medical Center, Bethesda, Maryland, USA;  
Naval Medical Research Center, Silver Spring, Maryland, USA

**Background/Purpose:** After a decade of war, we have observed an increase in both combat-related injury survival, as well as a paradoxical increase in injury severity, mainly due to the effects of blasts. These severe injuries leave a devastating impact on each patient's immune system, resulting in massive upregulation of the systemic inflammatory response. In this setting, the timing of wound closure is made based mainly on subjective determinations and the surgeon's anecdotal experience. However, closing a wound either too early or too late can be problematic. By examining the inflammatory mediators, preliminary data suggest that it may be possible to correlate complications such wound failure and heterotopic ossification (HO) with distinct systemic and local inflammatory profiles. We asked whether systemic or local markers of inflammation could be used as an objective means to estimate the likelihood of wound failure and/or HO in patients sustaining combat-related injuries.

**Methods:** 200 combat-wounded active duty servicemembers who sustained high-energy extremity injuries were prospectively enrolled between 2007 and 2013. In addition to injury-specific and demographic data, we quantified 24 cytokines and chemokines in the serum and wound effluent during each debridement. Correlations were investigated between these markers and wound failure or HO.

**Results:** The relationships between inflammatory proteins and wound-specific outcomes varied throughout the debridement process. For patients who formed HO, serum interleukin (IL)-3 ( $P = 0.002$ ), serum IL-12p70 ( $P = 0.0013$ ), effluent IL-3 ( $P = 0.02$ ), and effluent IL-13 ( $P = 0.006$ ) were independently associated with HO formation. Both serum ProCT ( $P = 0.03$ ) and effluent IL-6 ( $P = 0.02$ ) correlated with wound failure.

**Conclusion:** We identified correlates of wound-specific complications such as wound failure and HO by characterizing the patient's systemic and local inflammatory response. Models designed to codify these interactions and estimate the likelihood of complications such as wound failure and HO must accommodate nonlinear relationships that vary over time.

- The FDA has not cleared this drug and/or medical device for the use described in this presentation (i.e., the drug or medical device is being discussed for an "off label" use). For full information, refer to page 600.