Early Complications and Outcomes in Combat Injury-Related Invasive Fungal Infections: A Case-Control Analysis

LT Louis Lewandowski, MD^{1,2}; Amy C. Weintrob, MD^{1,3}; David R. Tribble, MD³; CDR Carlos J. Rodriguez, DO^{1,2}; CPT Joseph Petfield, MD⁴; COL Bradley A. Lloyd, DO^{4,5}; COL Clinton K. Murray, MD⁴; MAJ Daniel Stinner, MD⁴; Deepak Aggarwal, MSE, MSPH³; Faraz Shaikh, MS³; LTC Benjamin K. Potter, MD^{1,2}; Infectious Disease Clinical Research Program Trauma Infectious Disease Outcomes Study Group ¹Department of Orthopaedics, Walter Reed National Military Medical Center, America Bethesda, Maryland, USA; ²Department of Surgery, Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA; ³Infectious Disease Clinical Research Program, Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA; ⁴San Antonio Military Medical Center, Fort Sam Houston, Texas, USA; ⁵Landstuhl Regional Medical Center, Landstuhl, Germany

Background/Purpose: Invasive fungal infections (IFIs) have become increasingly prevalent in combat trauma populations. In addition to increased mortality, clinicians have anecdotally noted that IFIs lead to residual limb shortening, additional days and operative procedures prior to initial wound closure, and a high early complication rate. Our objective was to evaluate the validity of these observations and identify risk factors that may impact the time to initial wound closure in a case-control analysis.

Methods: The study population included United States military personnel injured during combat operations (June 2009-August 2011). The IFI cases were identified based upon the presence of recurrent, necrotic extremity wounds with mold growth in culture and/or histopathology demonstrating invasive fungal elements. The non-IFI controls were matched on the basis of injury pattern and severity. Information regarding surgical history, time to initial wound closure, complications, amputation level changes, and loss of femur length were analyzed. Data are expressed as multivariate hazard ratios (HR;95% confidence interval [CI]).

Results: 71 IFI cases (112 fungal-infected extremity wounds) were identified and matched to 160 control patients (315 extremity wounds without fungal infections). Wounds with fungal infections resulted in a significantly (P < 0.001) higher number of operative procedures and longer duration to initial wound closure, along with a greater rate of early complications requiring additional surgery. Additionally, a significantly increased amount of residual limb shortening (P = 0.009) and changes in amputation level (P < 0.001) were observed among the IFI cases compared to controls. The IFI case wounds also demonstrated a higher rate of secondary or concurrent bacterial skin and soft-tissue infections (SSTIs; P < 0.001). A shorter duration to initial wound closure was significantly associated with wounds lacking IFIs (HR: 1.53; CI: 1.17, 2.01) and SSTIs (HR: 2.89; CI: 2.02, 4.11).

Conclusion: Our analysis indicates that IFIs adversely impact wound healing and patient recover, y leading to more frequent proximal amputation revisions and higher early complication rates. Concurrent/secondary bacterial SSTIs also add to the complexity of IFI wounds and may further affect wound healing.

See pages 99 - 147 for financial disclosure information.