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Impact of Operational Theater on Combat and Noncombat Trauma-Related Infections

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Abstract

The Trauma Infectious Disease Outcomes Study began in June 2009 as combat operations were decreasing in Iraq and increasing in Afghanistan. Our analysis examines the rate of infections of wounded U.S military personnel from operational theaters in Iraq and Afghanistan admitted to Landstuhl Regional Medical Center between June 2009 and December 2013 and transferred to a participating U.S. hospital. Infection risk factors were examined in a multivariate logistic

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regression analysis (expressed as odds ratios [OR]; 95% confidence intervals [CI]). The study population includes 524 wounded military personnel from Iraq and 4766 from Afghanistan. The proportion of patients with at least one infection was 28% and 34% from the Iraq and Afghanistan theaters, respectively. The incidence density rate was 2.0 (per 100 person-days) for Iraq and 2.7 infections for Afghanistan. Independent risk factors included large-volume blood product transfusions (OR: 10.68; CI: 6.73–16.95), high injury severity score (OR: 2.48; CI: 1.81–3.41), and improvised explosive device injury mechanism (OR: 1.84; CI: 1.35–2.49). Operational theater (OR: 1.32; CI: 0.87–1.99) was not a risk factor. The difference in infection rates between operational theaters is primarily due to increased injury severity in Afghanistan from a higher proportion of blast-related trauma during the study period.

Keywords

Combat-related infections; injury severity; trauma-related infections; combat care; military medicine

INTRODUCTION

It is widely recognized that individuals with combat-related injuries are at high risk for infectious complications.[1–4] Combat-related injuries result in circumstances, such as breach of physical host defences, hypoxic tissue damage/necrosis, and implantation of foreign bodies, which greatly increase the risk of infection. The nature of trauma inflicted during combat (e.g., blast injuries) is generally more severe than injuries acquired in civilian settings.[5–7]

Since U.S. military personnel were first deployed to Iraq (Operations Iraqi Freedom [OIF] and New Dawn [OND] and Afghanistan (Operation Enduring Freedom [OEF]), over 52,100 service members have been wounded in action.[8] These military operations saw changes in the patterns and severity of combat-related injuries, primarily due to the expanded utilization of improvised explosive devices (IEDs).[2–4,9–11] Accordingly, combat care evolved through advancements in preventive measures and treatments, along with the implementation of the Joint Theater Trauma System (JTTS) in November 2004.[12,13] In part due to the integrated approach to combat care executed by the JTTS, which emulates successful civilian trauma systems, the overall mortality rate of military personnel decreased during the conflicts in Iraq and Afghanistan (8.8%) when compared to World War II and Vietnam (22.8% and 16.5%, respectively).[12] Nonetheless, the improved survival of wounded military personnel resulted in a rise of infectious complications and consequent effects on morbidity.[2–4,14–17]

In order to better characterize these infections, an observational cohort study of short- and long-term infectious consequences among U.S. service members injured during deployment (Department of Defense [DoD]-Department of Veterans Affairs, Trauma Infectious Disease Outcomes Study [TIDOS]) was initiated in 2009. An examination of data collected from the project reported an overall infection incidence density of 1.8 per 100 person-days among wounded U.S. military personnel medically evacuated to Landstuhl Regional Medical Center (LRMC) in Germany and transitioned to participating military treatment facilities (MTFs) in the U.S. between June and August 2009. In the analysis, infection rates were assessed with

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regards to level of care (LRMC and U.S. MTFs) and admitting units (intensive care versus non-critical ward); however, operational theater where the injury was sustained was not examined.[3] For military personnel with injuries sustained during the recent conflicts, the risk of infection may differ between operational theaters due to diversities in injury mechanism (e.g., gunshot and blast wounds), environment (i.e., arid/urban landscape in Iraq versus the mountainous and agricultural settings in Afghanistan), or infectious exposures. Our objective was to assess infection rates among U.S. military personnel injured during deployment (combat and noncombat) with respect to operational theater (Iraq and Afghanistan).

METHODS

Study Design

The TIDOS project is a multisite, observational cohort study initiated with the goal of describing the incidence, risk factors, and clinical outcomes of infectious complications associated with deployment-related injuries. The study commenced during a period when combat operations were decreasing in Iraq while simultaneously increasing in Afghanistan. Full details regarding the TIDOS project design have been previously published.[3] Eligible subjects include U.S. service members injured during deployment (June 1, 2009 to January 31, 2015) and medically evacuated to LRMC followed by transition to a participating U.S. MTF. This study (IDCRP-024) is approved by the Infectious Disease Institutional Review Board of the Uniformed Services University of the Health Sciences in Bethesda, Maryland.

Data Collection

Trauma information (e.g., injury patterns and severity) were obtained through the DoD Trauma Registry (DoDTR).[12] The TIDOS infectious disease module augmented the DoDTR data by providing detailed information on antimicrobial therapy, microbiology, and infectious outcomes from injury through initial hospitalization at a participating U.S. MTF: National Naval Medical Center and Walter Reed Army Medical Center in the National Capital Region (Walter Reed National Military Medical Center after September 2011), and Brooke Army Medical Center in San Antonio, Texas (San Antonio Military Medical Center after September 2011).

Study Definitions and Endpoints

Traumatic injuries sustained during deployment were categorized using injury codes defined by the Abbreviated Injury Scale (AIS), a consensus-derived anatomically-based injury scoring system.[18] A composite injury severity score (ISS) was calculated for each patient based on the top three maximum AIS anatomical region values across all clinical facilities. Combat-related injuries were identified as traumatic injuries occurring within the operational theater that include the following injury mechanisms: blast, gunshot wound, motor vehicle/helicopter crash, fall/crush, and burns. Noncombat injuries, including sports and training injuries, were sustained while deployed and may include similar mechanisms (i.e., falls/crush, burns, and motor vehicle crashes), but were not directly related to combat operations.

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As described in Tribble et al.,[3] infections were identified utilizing a combination of clinical findings and laboratory test results via review of medical records and were classified based upon the National Healthcare Safety Network (NHSN) standardized definitions for healthcare-associated infections.[19] Furthermore, an infection was included if, in the absence of meeting *a priori* defined criteria, there was a clinical diagnosis associated with the initiation of directed antimicrobial therapy that was continued for more than five days. Infections were excluded from the analysis if medical records provided an alternative diagnosis combined with the termination of antimicrobial treatment. Multidrug-resistant (MDR) isolates were identified in accordance with definitions published by the NHSN.[20] Isolates were classified as colonizing if they were collected via infection control-based surveillance. Isolates were considered infecting if they were collected as part of a clinical infection work-up and met infection clinical syndrome criteria.

Statistical Analysis

Tests of association for categorical variables were conducted using Chi-square and Fisher's exact tests, while medians were compared by the Kruskal-Wallis test. Logistic regression models were used to assess the relationship between potential risk factors and outcomes (presence or absence of infection). The risk factor analysis was restricted to data collected from patients who transferred to participating U.S. MTFs. For each of the variables, the best-fitting parsimonious model was sought. A correlation analysis was also conducted to evaluate the relationship between potential risk factors. Models were compared on the basis of the Akaike Information Criterion and Hosmer and Lemeshow Goodness of Fit. Analysis was conducted with SAS® version 9.3 (SAS, Cary, NC). Data are expressed as odds ratios with 95% confidence intervals. Statistical significance was defined as $p<0.05$.

RESULTS

Study Population and Injury Patterns

A total of 5290 wounded military personnel were admitted to LRMC between June 2009 and December 2013 (Figure 1), of which 4766 sustained injuries in Afghanistan (82% combat-related) and 524 in Iraq (54% combat-related). As previously mentioned, the start of the study period coincided with declining combat operations in Iraq (OIF ended on August 31, 2010 and peacekeeping support with OND began on September 1, 2010), while operations increased in Afghanistan. Specifically, 327 and 197 were wounded in support of OIF (62% combat-related) and OND (42% combat-related), respectively (Figure 2). For both theaters, the population was predominantly young enlisted men (>90%) serving in the U.S. Army (83% and 67%, respectively) or U.S. Marines (4% and 25%, respectively; Table 1). Furthermore, 52% and 72% of combat casualties sustained a blast injury in the Iraq and Afghanistan theaters, respectively, of which 67% and 78%, respectively, were the result of an IED. In addition, 14% of military personnel in Iraq and 33% in Afghanistan were injured while on foot patrol. The predominant injury mechanisms among personnel with noncombat trauma were falls (31% and 32% for Iraq and Afghanistan theaters, respectively) and sports-related injuries (21% and 15%, respectively).

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Combat-related injuries among personnel serving in the Afghanistan theater were more severe than noncombat trauma (Table 1), as indicated by the significantly higher ISS (median of 12 versus 4; p<0.0001) and greater proportion of admittance to the intensive care unit (ICU; 30% versus 5%; p<0.0001). The pattern of injury was also significantly different with a higher proportion of open injuries (skin/soft-tissue and fractures) sustained by combat casualties (84%; p<0.0001) compared to noncombat (27%). Furthermore, the proportion of wounded service members receiving massive transfusions of packed red blood cells plus whole blood (RBC; >10 units) within the first 24 hours was significantly higher among those with combat-related trauma compared to noncombat (15% versus 0.4%; p<0.0001). Lastly, significantly more patients with combat-related injuries were also prescribed prophylactic antibiotics for prevention of infections within 48 hours following injury (73% versus 23%; p<0.0001).

A similar pattern was observed among military personnel injured in the Iraq theater (Table 1). Specifically, military personnel with combat-related trauma had significantly higher ISS (median of 10 versus 4; p<0.0001), occurrence of open injuries (76% versus 26%; p<0.0001), proportion of patients admitted to the ICU (25% versus 8%; p=0.015), any amount of RBCs transfused within 24 hours (24% versus 0.8%; p<0.0001), and receipt of prophylactic antibiotics within 48 hours (56% versus 18%; p<0.0001).

Infection Characteristics

From the population of 2513 patients transferred to participating U.S. MTFs (Table 2), 852 patients (34%) developed at least one infection (94% from Afghanistan and 6% from Iraq). Of the 54 patients from Iraq with at least one infection, 40 sustained injuries in OIF (78% combat-related) and 14 in OND (71% combat-related). A total of 2003 and 103 unique infections were diagnosed from military personnel wounded in Afghanistan and Iraq, respectively, of which 99% and 80% were combat-related, respectively (Table 2). Comparison of the incidence density rate ratio found that there was a significantly higher proportion of combat-related infections compared to noncombat in the Afghanistan theater (p<0.0001), but not in the Iraq theater of operation (p=1.0).

Skin and soft-tissue infections (SSTIs) and pneumonia were common for patients injured in both theaters regardless of whether they had combat-related or noncombat trauma (Table 2). Specifically, 47% of unique infections were SSTIs among both combat and noncombat trauma patients from Afghanistan, whereas pneumonia contributed 14% of infections among combat casualties and 23% among noncombat trauma patients. Regarding patients from Iraq, 22% and 24% of unique infections in combat and noncombat trauma patients were SSTIs, respectively, while it was 21% and 29% for pneumonia, respectively. Among those with an infection, most were diagnosed after transfer to a participating U.S. MTF (70% and 67% of patients from Afghanistan and Iraq theaters, respectively). In addition, the overall rate of infections was higher among patients initially admitted to the LRMC ICU compared to the noncritical ward for both theaters of operation (p<0.0001). The rates were also statistically significant when combat casualties for both theaters and noncombat trauma from the Iraq theater were considered (p<0.001); however, the ratio was not significant among personnel with noncombat trauma from the Afghanistan theater (p=0.083).

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Between the two operational theaters regardless of combat status, the duration from injury to development of any type of infection was comparable (median: 6 days). When specific infection syndromes were considered, osteomyelitis had the longest duration from injury to diagnosis (median of 26 and 28 days for Afghanistan and Iraq, respectively), whereas pneumonia, bloodstream infections, and sepsis developed a median of 5 to 7 days after injury (data not shown). Among patients with diagnosed infections, the proportion who had only one infection while hospitalized was also similar between the Afghanistan and Iraq theaters (45% versus 43%, respectively); however, 21% of patients from Afghanistan were diagnosed with at least four infections compared to 9% of patients from Iraq (Table 2). When the data were restricted to noncombat trauma, 83% of personnel from the Afghanistan theater had only one infection compared to 46% from the Iraq theater. Overall, the incidence density rate (number of infections/100 person-days) was higher for military personnel serving in Afghanistan compared to patients with Iraq-related traumatic injuries (2.7 and 2.0, respectively).

Clinical Microbiology and Post-Trauma Antibiotic Prophylaxis

At admission to LRMC, 353 (7%) of wounded personnel were colonized with MDR gram-negative bacteria, as determined from surveillance groin swabs collected at hospital admission. Among the Afghanistan theater, 8% and 0.9% of personnel with combat-related and noncombat injuries were colonized at LRMC admission, respectively. For the Iraq theater, 6% of military personnel with combat-related injuries were colonized with MDR gram-negative bacteria compared to 0.8% of patients with noncombat injuries at LRMC admission. Among the 2513 patients that transferred to a participating U.S. MTF, 258 (10.2%) were colonized with MDR gram-negative bacteria at admission (10.7% and 4.6% of personnel injured in Afghanistan and Iraq, respectively). From patients injured in the Afghanistan theater, 2354 colonizing isolates were collected (27% MDR) across all levels of care, whereas 188 isolates were collected from Iraq (18% MDR). Overall, *Escherichia coli* and *Klebsiella pneumoniae* were the most common colonizing organisms for both the Afghanistan (43% of *E. coli* and 28% of *K. pneumoniae* were MDR, respectively) and Iraq theaters (30% and 12% MDR, respectively). In addition, *Acinetobacter calcoaceticus baumannii* (ACB) complex isolates were also frequently MDR from both Afghanistan (46%) and Iraq (22%).

While not performed at LRMC, surveillance for methicillin-resistant *Staphylococcus aureus* (MRSA) using nares swabs was conducted at the U.S. MTFs and the rate of colonization was 4.3% overall (95% confidence interval: 3.5–5.1%) with no significant difference between theaters and combat versus noncombat. Specifically, 5.1% of patients from the Iraq theater who transferred to a participating U.S. MTF had MRSA colonization, while it was 4.2% from the Afghanistan theater. In addition, 4.1% and 6.2% of personnel with combat and non-combat injuries were colonized with MRSA.

A total of 1542 unique infections (73.2% of 2106) had a corresponding infection work-up that yielded bacterial growth, of which 80.4% and 49.1% grew gram-negative and gram-positive organisms, respectively. Gram-negative organisms (susceptible and MDR) isolated from infection workups were predominantly collected from combat casualties (25% and

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20% in Afghanistan and Iraq, respectively), compared to 5% and 6% of personnel with noncombat trauma, respectively. Overall, 68% of the patients with infections had gram-negative bacteria isolated in infection work-ups. Among personnel with combat-related injuries sustained in Afghanistan, the gram-negative organisms most commonly identified during infection workups were *Pseudomonas aeruginosa*, followed by *E. coli* and ACB complex, of which 10%, 73%, and 78% were MDR, respectively (Table 3). Combat casualties from Iraq had a similar microbiological profile with 14% of *P. aeruginosa*, 57% of *A. baumannii*, and 60% of *E. coli* determined to be MDR. *S. aureus* contributed 11.8% to the gram-positive organisms isolated from infection work-ups, of which 44% were MRSA.

Overall, 1923 (77%) patients transferred to a participating U.S. MTF received prophylactic antibiotics, of which 1806 (94%) and 117 (6%) sustained injuries in Afghanistan and Iraq, respectively. Among the 852 patients who developed an infection, 761 (89%) received prophylactic antibiotics within 48 hours post-injury. In addition, 90% of patients who sustained injuries in Afghanistan and developed infections received prophylactic antibiotics, while it was 72% for Iraq. Patients who received prophylactic antibiotics more commonly had ISS >15 (65%) and sustained injuries via a blast mechanism (72%). Furthermore, 87% of patients with culture growth of MDR organisms (surveillance or infection work-up) received prophylactic antibiotics (data not shown).

In a Chi-square analysis, the association of prophylactic antibiotics and occurrence of any infection was significant (odds ratio [OR]: 3.6; 95th confidence interval [CI]: 2.8–4.6; $p<0.0001$). The data remained significant when the Afghanistan and Iraq theaters were considered separately ($p<0.0001$ and $p=0.03$, respectively). Furthermore, there was also a significant association between prophylactic antibiotic use and isolation of MDR organisms via colonization surveillance or infection work-up among patients (OR: 2.6; CI: 2.0–3.4; $p<0.0001$).

Risk Factor Analysis

From the patients that transferred to U.S. MTFs, operational theater, circumstances of injury (i.e., combat-related and mechanism), composite ISS, RBC transfusion requirements within 24 hours of injury, open injury, branch of service, MDR gram-negative colonization at LRMC admission, post-trauma antibiotic prophylaxis, and admission to the ICU were examined in a logistic regression analysis (Table 4). The composite ISS and RBC requirements were evaluated as ranked variables. Injuries sustained via an IED blast mechanism and during combat, ISS >15, RBC requirements ≥1 unit, MDR gram-negative colonization, occurrence of open wounds, service in the U.S. Marines, use of prophylactic antibiotics, and admission to the ICU were significantly associated with development of infections in the univariate model ($p<0.0001$). In addition, injuries that occurred in the Iraq theater were significantly less likely to be associated with the development of infection compared to the Afghanistan theater ($p<0.0001$).

In the multivariate model (Table 4), the risk for infection was highest among patients who received >20 units of RBCs within 24 hours of injury ($p<0.0001$). Injuries from IEDs ($p<0.0001$), post-trauma antibiotic prophylaxis ($p=0.033$), ISS >15 ($p<0.002$), and ICU admission ($p<0.0001$) were also significantly associated with the development of infections.

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Operational theater was not an independent risk factor for an infection following traumatic injury (p=0.193). Furthermore, when the analysis was repeated after separating Afghanistan into two time periods (June 2009–May 2012 and May 2012–December 2013), there was no significant association with operational theater (data not shown).

DISCUSSION

This analysis assessed characteristics and rates of infectious complications among 5290 U.S. service members with deployment-related injuries in association with two combat operational theaters (Iraq and Afghanistan). Overall, a higher rate of infection was observed with the Afghanistan theater compared to Iraq during a contemporaneous period (2.7 versus 2.0 infections per 100 person-days). After controlling for injury severity and other factors, there was no statistical association between operational theater and the risk of developing an infection. It is also notable that personnel with noncombat injuries also had high rates of infection (1.0 and 2.0 per 100 person-days for Afghanistan and Iraq, respectively). Our data corroborate prior analyses which reported associations of infectious consequences among wounded military personnel with the severity and mechanism of injury.[14,15,21–23]

Measures of injury severity (i.e., ICU admission, ISS, and hemorrhage as indicated by RBC transfusion requirements within 24 hours) primarily explain the statistical difference in infection rate independent of operational theater as data in our analysis suggest that injuries sustained in Afghanistan were generally more severe and likely due to the high proportion of blast injuries and dismounted status during the same time period. In addition, large-volume transfusions of blood products have been previously shown to be an independent risk factor for infection following deployment-related trauma, possibly due to inducing a transient state of immunosuppression.[22,23] Furthermore, the association of prophylactic antibiotics within 48 hours is also consistent with use within a higher at-risk population.[5] Patients who received prophylactic antibiotics were observed to have higher injury severity as indicated by increased proportion with ISS >15, ICU admissions, and predominance of blast injuries. Nonetheless, a more detailed exploration of antimicrobial regimens and related infection outcomes is warranted. The role of antecedent bacterial colonization and subsequent infection is unknown[24] and the variable was not statistically significant in the risk factor analysis (p=0.08), our results suggest that colonization with MDR gram-negative organisms may be a risk factor and should be investigated further. The colonization data are consistent with our prior analysis that found similar annual rates of MDR gram-negative bacilli colonization over a three-year period (2009–2012).[25] It is also noteworthy that the rate of MDR gram-negative colonization at admission to the U.S. MTFs was higher than the rate of MRSA colonization (10.2% versus 4.3%).

Although a great deal of focus has been placed on injuries sustained during combat, a high rate of infection was found among personnel with noncombat injuries. Many noncombat injuries in an operational zone involve mechanisms such as motor vehicle collisions, falls, and burns, which often result in open wounds. In a prior retrospective analysis of 4566 military personnel with noncombat injuries not sustained in a war zone found that 8.2% had at least one related infection. Pneumonia was predominant (4%) with a lower proportion of cellulitis/wound infections (2.4%) and sepsis (0.9%).[7] When considering all noncombat

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trauma patients from both theaters of operation, 15% had at least one infection, with pneumonia and SSTIs contributing the greatest proportion to unique infections.

While the majority of previous analyses have not examined data on a per theater basis, infection rates from the recent conflicts have been published. Data from 16,742 deployment-injured patients were collected from a trauma registry and determined an infection rate of 5.5% (annual range: 0.6–10.9%).[14] Moreover, an early evaluation from the TIDOS project reported 5% of LRMC admissions and approximately 27% of patients transferred to the U.S. developed infections.[3] In our analysis, the proportion of infections among the total number of patients admitted to LRMC was consistent with the prior analyses (5%); however, the overall infection rate among wounded personnel who transferred to one of the participating U.S. MTFs was higher (34%). Analysis of data from the United Kingdom has also found a high rate of infection related to extremity injuries (24%), which corresponds to our finding of the predominance of SSTIs and minor contribution of osteomyelitis.[26]

In general, the rate of infections among wounded personnel from the Iraq theater was lower than Afghanistan (2.0 and 2.7 infections per 100 person-days, respectively). One reason for the differing infection rates may be the reduction of combat-related injuries as military operations ceased in Iraq during the study period (OIF concluded in August 2010 and was followed by OND peacekeeping efforts); however, it is important to note that despite the shift to peacekeeping efforts, a risk of combat-related injuries still occurs. Specifically, 42% of the injuries sustained in Iraq during OND were combat-related. Another possible explanation is that as combat operations transitioned, patterns of injury changed due to differences in military tactics (on both sides) affecting casualties. During 2010, as combat operations were concluding in Iraq and increasing in Afghanistan, the number of traumatic amputations substantially increased. Between 2010 and 2011, the amputation rate rose from 3.5 to 14 per 100 combat support facility trauma admissions, and was primarily the result of dismounted patrols encountering IEDs in Afghanistan.[9,27] The consequent dismounted complex blast injuries were characterized by lower extremity amputations (unilateral or bilateral), upper extremity amputations, pelvic and urogenital injuries, and spinal injuries.[27] United Kingdom military personnel were also greatly impacted by this injury pattern with 2.8% of combat casualties sustaining bilateral lower limb amputations over a six-year period.[11] Due to the severity of these injuries, patients generally required large-volume blood transfusions (>10 units), debridements, and further surgical procedures in response to complications, such as infections.[11,27,28] One example was the unexpected surge in invasive fungal wound infections among military personnel who sustained blast injuries in Afghanistan. Specifically, nearly 7% of the combat casualties admitted to LRMC between June 2009 and August 2011 were diagnosed with an invasive fungal wound infection.[29–31] A similar emergence of invasive fungal wound infections was also reported among United Kingdom military personnel with blast injuries sustained in Afghanistan.[32]

While information is available on injury patterns and infection rates,[2,3,14,15,28,33–35] further data defining the progression of infections and resultant short- and long-term outcomes are necessary. The findings in this military setting provide support for the identification of infection risk factors related to trauma sustained during deployment; however, the feasibility of using these factors in predictive modeling with clinical care application still needs to be

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assessed. Nonetheless, this information emphasizes the need for forward medical support in the deployed setting and a high index of suspicion for infectious complications following traumatic injuries, regardless of whether they are sustained during combat or noncombat. A limitation of this analysis that should be considered is that infection data were collected exclusively from patients who transferred to a TIDOS-participating U.S. MTFs (approximately 48% of subjects admitted to LRMC). In general, these patients experienced more severe injuries compared to those who transferred to U.S. MTFs other than the ones included in this analysis. Thus, the applicability of data reported herein to all U.S. injured service members is uncertain.

Combat casualty care is continuously advancing as new technology and data become available; however, infectious complications remain a serious cause of morbidity. The implementation of epidemiologic and surveillance projects, such as TIDOS and the Multidrug-Resistant Organism Repository and Surveillance Network (MRSN),[36] are integral in informing the military health system on these key issues. With the emergence of new challenges, such as MDR bacterial organisms, healthcare-associated transmission across evacuation and MTFs, and invasive fungal wound infections, further examination of infection predictive factors, microbiological findings, real-time surveillance and support for control of outbreaks of MDR bacterial organisms through the MRSN, and specific infectious disease syndromes among deployed service members is warranted to improve crucial elements of combat casualty care including trauma systems, infection control policies, early detection, and antimicrobial selection.

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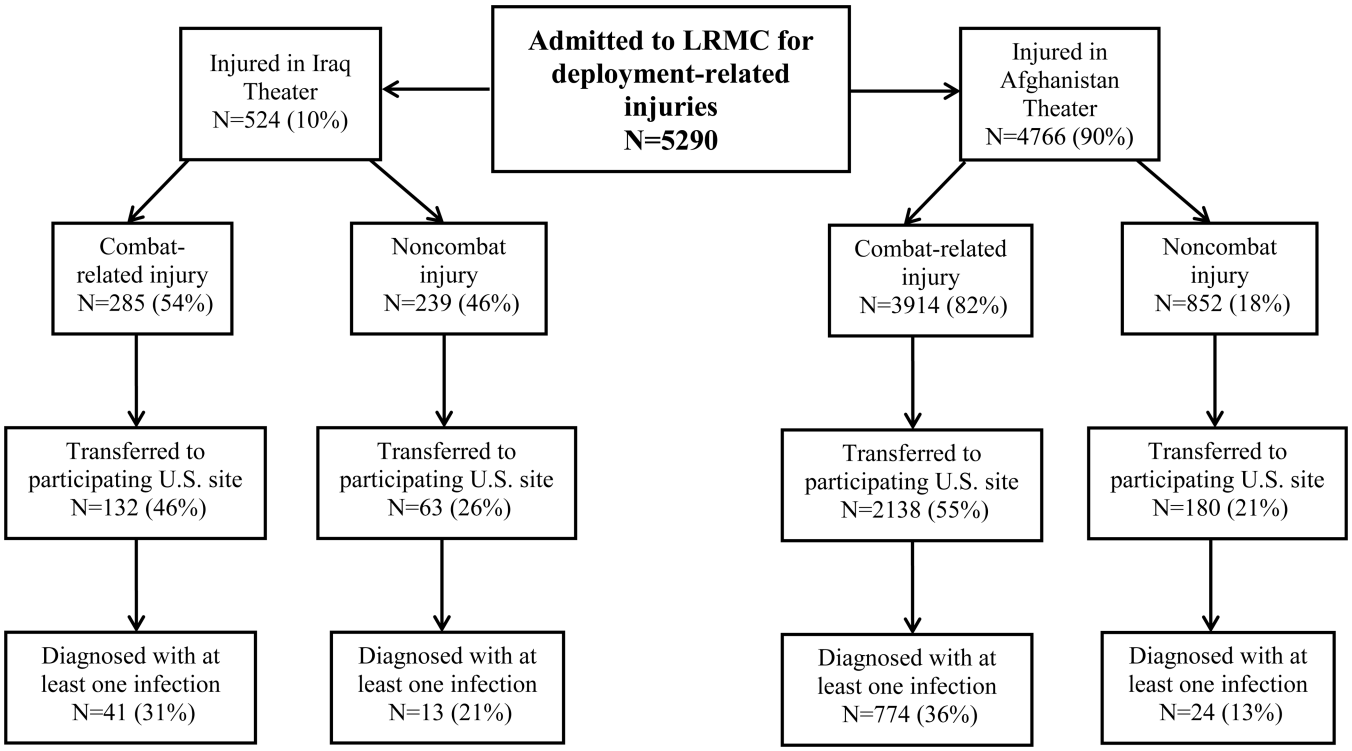

Figure 1.

Flow chart for disposition of patients admitted to Landstuhl Regional Medical Center (LRMC) between June 2009 and December 2013 with deployment-related injuries.

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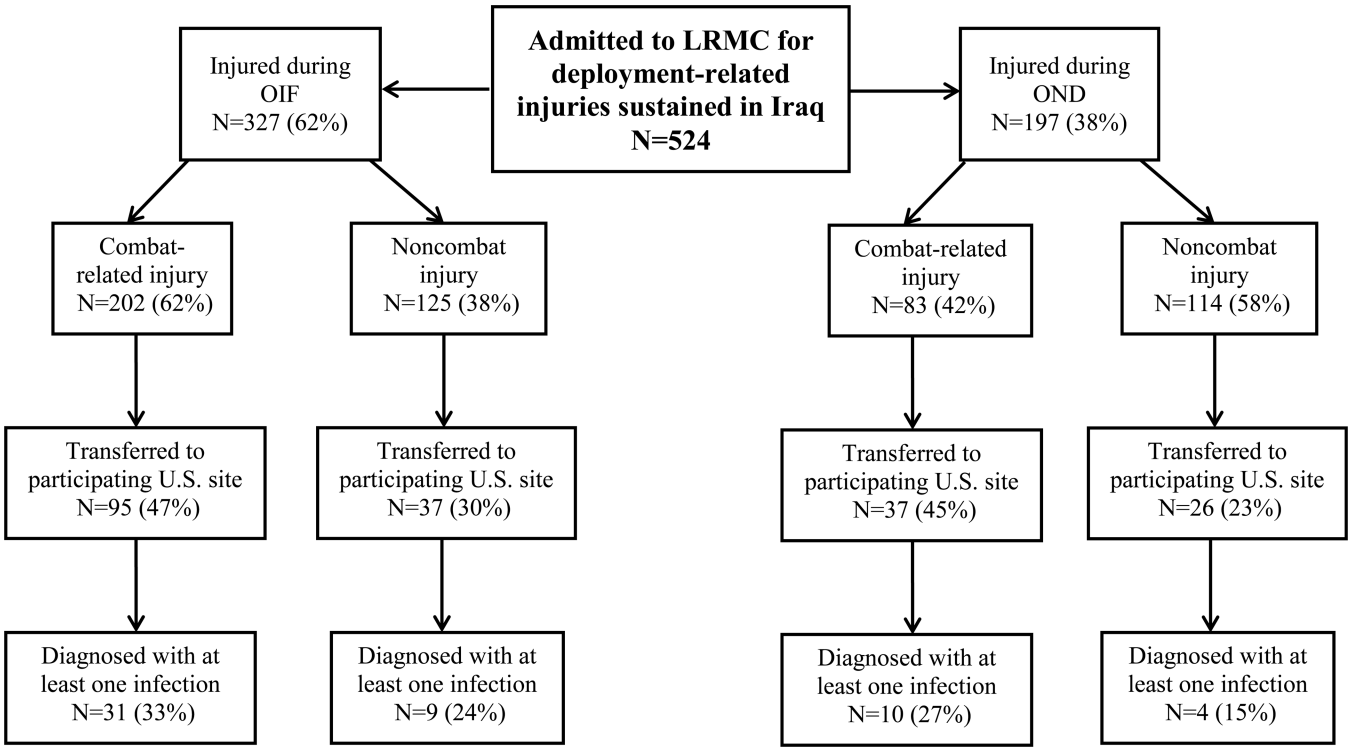

Figure 2.

Flow chart for disposition of patients admitted to Landstuhl Regional Medical Center with deployment-related injuries sustained in the Iraq theater. Combat operations in Iraq (Operation Iraqi Freedom [OIF]) ended on August 31, 2010 and were followed by peacekeeping efforts (Operation New Dawn [OND]) which began on September 1, 2010 and ended on December 31, 2011.

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Table 1

Patient Demographics and Injury Characteristics, No. (%) by Theater of Operation (June 2009 – December 2013)

Characteristic[1]	Total (N = 5290)	Afghanistan (N = 4766)			Iraq (N = 524)		
		Noncombat Injury (N=852)	*Combat-related Injury (N=3914)*	*p-value*[2]	*Noncombat Injury (N=239)*	*Combat-related Injury (N=285)*	*p-value*[3]
Male	5160 (97.5)	813 (95.4)	3853 (98.4)	<0.0001	223 (93.3)	271 (95.0)	0.382
Age, median (IQR)	24.9 (22.1, 29.6)	26.4 (22.6, 34.4)	24.4 (22.0, 28.3)	<0.0001	28.1 (22.8, 35.8)	25.7 (22.6, 30.8)	0.012
Branch of Service				<0.001			0.031
Army	3608 (68.2)	552 (64.7)	2619 (66.9)		187 (78.2)	250 (87.7)	
Marine	1206 (22.7)	151 (17.7)	1034 (26.4)		14 (5.8)	7 (2.4)	
Military Grade/Rank				0.003			0.462
Enlisted	4790 (90.5)	747 (87.6)	3573 (91.2)		213 (89.1)	257 (90.1)	
Officer / Warrant	379 (7.2)	80 (9.4)	256 (6.5)		22 (9.2)	21 (7.4)	
Mechanism of Injury				<0.0001			<0.0001
Blast	2912 (55.0)	0	2764 (70.6)	<0.0001	0	148 (51.9)	<0.0001
IED	2262 (42.8)	0	2163 (55.3)		0	99 (34.7)	
Non-IED	650 (12.3)	0	601 (15.4)		0	49 (17.2)	
Gunshot wound only	965 (18.2)	0	918 (23.5)		0	47 (16.5)	
Motor vehicle collision only	195 (3.7)	10 (1.2)	110 (2.8)		6 (2.5)	69 (24.2)	
Helicopter crash	35 (0.7)	0	30 (0.8)		0	5 (1.8)	
Blunt object	118 (2.2)	79 (9.3)	3 (<0.1)		33 (13.8)	3 (1.1)	
Fall	384 (7.3)	273 (32.0)	31 (0.8)		74 (31.0)	6 (2.1)	
Sports	180 (3.4)	130 (15.3)	0		50 (20.9)	0	
Other[4]	499 (9.4)	358 (42.0)	58 (1.5)		76 (31.8)	7 (2.5)	
Dismounted at time of injury	1708 (32.3)	283 (33.2)	1299 (33.2)	<0.0001	85 (35.6)	41 (14.4)	<0.0001
Injury Severity Score, median (IQR)	10 (5, 22)	4 (4, 8)	12 (6, 27)	<0.0001	4 (4, 8)	10 (5, 21)	<0.0001
RBC Transfusions: 1st 24 Hours				<0.0001			<0.0001
0/missing units[5]	3927 (74.2)	838 (98.3)	2634 (67.2)		237 (99.1)	218 (76.4)	
1–9 units	761 (14.3)	11 (1.2)	698 (17.8)		2 (0.8)	50 (17.5)	
10 – 20 units	336 (6.3)	2 (0.2)	322 (8.2)		0	12 (4.2)	

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Characteristic[1]	Total (N = 5290)	Afghanistan (N = 4766)			Iraq (N = 524)		
		Noncombat Injury (N=852)	*Combat-related Injury (N=3914)*	*p-value*[2]	*Noncombat Injury (N=239)*	*Combat-related Injury (N=285)*	*p-value*[3]
>20 units	266 (5.0)	1 (0.1)	260 (6.6)		0	5 (1.7)	
Occurrence of open injury	3793 (71.7)	233 (27.3)	3281 (83.8)	<0.0001	61 (25.5)	218 (76.4)	<0.0001
ICU Admission[6]				<0.0001			0.015
LRMC only	361 (6.8)	15 (1.8)	313 (8.0)		9 (3.8)	24 (8.4)	
U.S. MTFs ± LRMC	965 (18.2)	29 (3.4)	879 (22.5)		11 (4.6)	46 (16.1)	
Non-ICU	1180 (22.3)	135 (15.8)	940 (24.0)		43 (18.0)	62 (21.8)	
Prophylactic antimicrobial use within 48 hours of injury	3248 (61.3)	196 (23.0)	2849 (72.7)	<0.0001	44 (18.4)	159 (55.7)	<0.0001

ICU – intensive care unit; IED – improvised explosive device; IQR – Interquartile Range; LRMC – Landstuhl Regional Medical Center; MTFs – military treatment facilities; RBC – packed red blood cells plus whole blood

[1] Data are missing for some of the variables (branch of service missing 47; military rank missing 75; mechanism of injury missing 2; ICU admittance missing 2784). The high amount of ICU admission missing is due to the transfer of approximately half of the patients to non-participating sites.

[2] P-value compares the noncombat and combat-related injury data for Afghanistan. Missing values are not included in calculation.

[3] P-value compares the noncombat and combat-related injury data for Iraq. Missing values are not included in calculation.

[4] Other includes burns, machinery/equipment accidents, noncombat explosions, and crush injuries.

[5] Missing RBC transfusion data are not randomly distributed. Patients with missing RBC data are characterized by lower injury severity scores and shock indices. In addition, the majority of patients with missing RBC data did not sustain a traumatic amputation and were not admitted to the LRMC ICU.

[6] Admission to the ICU is recorded within the first week of care at each facility.

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Table 2

Characteristics of Inpatient Infections among Wounded Military Personnel after Transfer to a United States Military Treatment Facility (2009 – 2013)[1]

	Afghanistan Theater			Iraq Theater		
	Noncombat Injury (N=180)	***Combat-related Injury (N=2138)***	***Total (N=2318)***	***Noncombat Injury (N=63)***	***Combat-related Injury (N=132)***	***Total (N=195)***
Total Days of Patient Observations, No.	3138	71,410	74,548	1043	4131	5174
Unique Infections, No.	30	1973	2003	21	82	103
Infections per 100 person-days, No. (95% CI)	1.0 (0.6–1.4)	2.8 (2.6–2.9)	2.7 (2.6–2.8)	2.0 (1.2–3.1)	2.0 (1.6–2.5)	2.0 (1.6–2.4)
Patients admitted initially to LRMC ICU[2]	1.4 (0.8–2.3)	3.7 (3.5–3.9)	3.6 (3.5–3.8)	4.1 (2.4–6.7)	2.6 (2.1–3.3)	2.8 (2.3–3.5)
Patients admitted initially to LRMC Ward[2]	0.7 (0.4–1.2)	0.7 (0.6–0.8)	0.7 (0.6–0.8)	0.8 (0.2–1.8)	0.8 (0.4–1.4)	0.8 (0.4–1.2)
Incidence density rate ratio (95% CI): Combat versus Noncombat[3]	NA	NA	2.9 (2.0–4.3)	NA	NA	0.99 (0.6–1.7)
Incidence density rate ratio (95% CI): LRMC ICU versus Ward[4]	2.0 (0.9–4.6)	5.1 (4.3–6.0)	5.0 (4.3–5.9)	5.4 (1.9–18.9)	3.5 (1.8–7.3)	3.7 (2.2–6.8)
Patients with ≥1 infection, No. (%)	24 (13)	774 (36)	798 (34)	13 (21)	41 (31)	54 (28)
Infections per patient, No. (%)[5]						
1 event	20 (83.3)	339 (43.8)	359 (45.0)	6 (46.2)	17 (41.5)	23 (42.6)
2 events	3 (12.5)	174 (22.5)	177 (22.2)	6 (46.2)	14 (34.1)	20 (37.0)
3 events	0	97 (12.5)	97 (12.2)	1 (7.7)	5 (12.2)	6 (11.1)
≥ 4 events	1 (4.2)	164 (21.2)	165 (20.7)	0	5 (12.2)	5 (9.3)
Level of care location for infection, No. (%)[5]						
LRMC only	5 (20.8)	84 (10.9)	89 (11.2)	3 (23.1)	6 (14.6)	9 (16.7)
U.S. MTF only	19 (79.2)	536 (69.3)	555 (69.5)	7 (53.8)	29 (70.7)	36 (66.7)
Both LRMC and U.S. MTF	0	154 (19.9)	154 (19.3)	3 (23.1)	6 (14.6)	9 (16.7)
Type of Infection, No. (%)[6]						
Skin and soft-tissue infections (SSTI)	14 (46.7)	918 (46.5)	932 (46.5)	5 (23.8)	18 (22.0)	23 (22.3)
Pneumonia	7 (23.3)	273 (13.8)	280 (14.0)	6 (28.6)	17 (20.7)	23 (22.3)
Bloodstream infection	3 (10.0)	276 (14.0)	279 (13.9)	4 (19.1)	13 (15.9)	17 (16.5)
Sepsis (excluding SIRS)	0	86 (4.4)	86 (4.3)	1 (4.8)	2 (2.4)	3 (2.9)
Osteomyelitis	2 (6.7)	121 (6.1)	123 (6.1)	0	17 (10.7)	17 (16.5)

CI – Confidence Interval; ICU – intensive care unit; LRMC – Landstuhl Regional Medical Center; MTF – military treatment facility; NA – Not applicable; SIRS – systemic inflammatory response system

[1]Data are restricted to patients who transferred to a participating U.S. MTF following treatment at Landstuhl Regional Medical Center.

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[2] Total number of patients initially admitted to LRMC ICU was 1195 for Afghanistan (combat: 1152; noncombat: 43) and 88 for Iraq (combat: 69; noncombat: 19). Total number of patients initially admitted to LRMC ward was 1118 for Afghanistan (combat: 982; noncombat 136) and 107 for Iraq (combat: 63; noncombat: 44).

[3] p-value for incidence density rate ratio of combat versus noncombat for Afghanistan and Iraq was <0.0001 and 1.0, respectively

[4] p-value for incidence density rate ratio of LRMC ICU versus ward for Afghanistan was <0.0001 (combat: <0.0001; noncombat: 0.083) and for Iraq was <0.0001 (combat: <0.0001; noncombat: <0.001).

[5] The total number of patients with ≥1 infection was used to calculate percent. P-values comparing the combat and noncombat data from Afghanistan and Iraq were 0.001 and 0.722 for infections per subject, respectively, and 0.010 and 0.448 for location of infection, respectively.

[6] The total number of unique infections was used to calculate percent. Does not include miscellaneous infections, such as sinusitis, central nervous system infections, and urinary tract infections.

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Table 3

Most Common Gram-Negative Bacteria Isolated during Infection Workups among Wounded Military Personnel[1]

Bacterial Organism	Number of Isolates			
	Combat-related Injury	% MDR	Noncombat Injury	% MDR
Afghanistan Theater				
Pseudomonas aeruginosa	204	10	1	0
Escherichia coli	176	73	3	0
Acinetobacter calcoaceticus baumannii	142	78	2	50
Enterobacter cloacae	137	2	4	0
Stenotrophomonas maltophilia	68	51	0	0
Afghanistan Total[2]	**1070**	**33**	**16**	**6**
Iraq Theater				
Pseudomonas aeruginosa	7	14	1	0
Acinetobacter calcoaceticus baumannii	7	57	1	0
Escherichia coli	5	60	0	0
Enterobacter cloacae	5	0	0	0
Haemophilus influenza	3	0	1	0
Iraq Total[2]	**40**	**23**	**4**	**0**

MDR – multidrug-resistant

[1]Data are collected from all infection work-ups (e.g., wound and blood cultures) among wounded personnel who were transferred from Landstuhl Regional Medical Center (LRMC) to a TIDOS-participating US military treatment facility (MTF) at all levels of care (LRMC and/or U.S. military treatment facilities). Patients often have serially positive cultures; however, an organism was counted only once per patient. An organism was counted at MDR if it was MDR at any time isolated during repeated isolation.

[2]Only the top five organisms are reported. Total incorporates all organisms collected during infection workups, so it will be more than the sum of the listed organisms.

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Table 4

Results of Logistic Regression Models to Evaluate Risk Factors for Any Infectious Complications of Deployment-Related Traumatic Injury

Parameter	Univariate Odds Ratio (95% CI)	P-value	Multivariate Odds Ratio (95% CI)	P-value
Operational theater				
Afghanistan	Reference		Reference	
Iraq	0.56 (0.42–0.75)	<0.0001	1.32 (0.87–1.99)	0.193
Combat-related injury	7.13 (5.10–9.99)	<0.0001	0.60 (0.32–1.15)	0.124
Branch of Service[1]				
Army	Reference		–	
Marine	1.66 (1.41–1.95)	<0.0001	–	
Other	0.83 (0.62–1.12)	0.220	–	
Mechanism of Injury				
Gunshot wound	Reference		Reference	
IED blast	3.26 (2.60–4.08)	<0.0001	1.84 (1.35–2.49)	<0.0001
Non-IED blast	0.99 (0.72–1.37)	0.937	0.91 (0.60–1.37)	0.639
Other	0.45 (0.33–0.62)	<0.0001	1.49 (0.84–2.66)	0.174
Injury Severity Score				
≤15	Reference		Reference	
16–25	7.7 (5.9–10.0)	<0.0001	1.72 (1.23–2.42)	0.002
≥ 26	28.5 (23.0–35.4)	<0.0001	2.48 (1.81–3.41)	<0.0001
RBC transfusion requirements				
0/missing units[2]	Reference		Reference	
1–9 units	9.19 (7.45–11.33)	<0.0001	2.50 (1.89–3.30)	<0.0001
10 – 20 units	38.69 (29.57–50.64)	<0.0001	5.66 (3.97–8.08)	<0.0001
> 20 units	83.58 (59.50–117.41)	<0.0001	10.68 (6.73–16.94)	<0.0001
Injury Type				
Closed	Reference		Reference	
Open	6.84 (5.21–9.00)	<0.0001	1.37 (0.93–2.03)	0.114
MDR Gram-negative Colonization at LRMC admission	2.72 (2.15–3.44)	<0.0001	1.39 (0.97–1.99)	0.075
Use of prophylactic antibiotics within 1st 48 hours	6.43 (5.16–8.01)	<0.0001	1.42 (1.03–1.97)	0.033
ICU Admission				
Non-ICU	Reference		Reference	
LRMC only	4.65 (3.49–6.19)	<0.0001	1.98 (1.41–2.76)	<0.0001
U.S. MTFs ± LRMC	13.59 (10.82–17.06)	<0.0001	3.80 (2.85–5.05)	<0.0001

CI – Confidence Interval; ICU – intensive care unit; IED – improvised explosive device; LRMC – Landstuhl Regional Medical Center; MDR – multidrug-resistant; MTFs – military treatment facilities; RBC – packed red blood cells plus whole blood

[1] Due to stepwise selection, the branch of service parameters was not included in the multivariate model.

[2] Missing RBC transfusion data are not randomly distributed. Patients with missing RBC data are characterized by lower injury severity scores and shock indices. In addition, the majority of patients with missing RBC data did not sustain a traumatic amputation and were not admitted to the LRMC ICU.