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Urinary Tract Infections after Combat-Related Genitourinary Trauma

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Abstract

Background: We examined clinical outcomes among combat casualties with genitourinary injuries after blast trauma.

Methods: Characteristics, clinical care, urologic complications, and infections for subjects enrolled in the Trauma Infectious Disease Outcomes Study (TIDOS) were collected from Department of Defense (DOD) and Department of Veterans Affairs (VA) sources. Logistic regression identified predictors for urinary tract infections (UTIs) after genitourinary trauma.

Results: Among 530 TIDOS enrollees who entered VA care, 89 (17%) sustained genitourinary trauma. The majority of subjects (93%) were injured via a blast and 27% had a dismantled complex blast injury (DCBI). Sexual dysfunction was reported with 36% of subjects, whereas 14% had urinary retention/incontinence and 8% had urethral stricture. Urologic complications were comparable between patients with and without DCBIs. Nineteen (21%) subjects had one or more UTI with a total of 40 unique UTI events (25% during initial hospitalization and 75% during subsequent DOD or VA care). The UTI incidence rate was 0.89 per patient-year during initial hospitalization, 0.05 per patient-year during DOD follow-up, and 0.07 per patient-year during VA healthcare. Subjects with UTIs had a higher proportion of bladder injury (53% vs. 13%; $p < 0.001$), posterior urethral injury (26% vs. 1%; $p = 0.001$), pelvic fracture (47% vs. 4%; $p < 0.001$), soft-tissue infection of the pelvis/hip (37% vs. 4%; $p = 0.001$), urinary catheterization (47% vs. 11%; $p < 0.001$), urinary retention or incontinence (42% vs. 6%; $p < 0.001$), and stricture (26% vs. 3%; $p = 0.004$) compared with patients with genitourinary trauma and no UTI. Independent UTI risk factors were occurrence of a soft-tissue infection at the pelvis/hip, trauma to the urinary tract, and transtibial amputation.

Conclusions: Among combat casualties with genitourinary trauma, UTIs are a common complication, particularly with severe blast injury and urologic sequelae. Episodes of UTIs typically occur early after the initial injury while in DOD care, however, recurrent infections may continue into long-term VA care.

Keywords: blast injury; combat-related infections; combat trauma; genitourinary trauma; urinary tract infections

GENITOURINARY TRAUMA historically accounts for 0.7% to 8% of all combat-related injuries [1]. Largely comprising renal trauma from explosive projectiles in past conflicts, many genitourinary wounds were not survivable. Advances in body armor, hemorrhage control, aeromedical

evacuation, and trauma resuscitation have improved clinical outcomes dramatically after combat-related genitourinary trauma [2–4].

Approximately 5% of U.S. combat casualties injured in support of operations in Iraq and Afghanistan sustained

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genitourinary trauma [5–8], often caused by an improvised explosive device (IED). Specifically, genitourinary injuries increased substantially in 2010 after transition of military personnel into Afghanistan where a novel injury pattern termed dismantled complex blast injury (DCBI) was described among service members sustaining IED-related blast trauma while conducting foot patrol. To be classified as a DCBI requires an amputation of one lower extremity (at or above the knee), an amputation or severe injury to the opposite lower extremity, and pelvic, abdominal, or urogenital injury [9].

At Landstuhl Regional Medical Center (Germany), which is the primary destination for medical evacuation prior to returning to the continental United States, genitourinary trauma admissions ranged from 10% to as high as 19% between October and December 2010 [9]. Unlike previous wars, genitourinary injuries sustained in Iraq and Afghanistan largely involved the external genitalia and lower urinary tract, with many occurring in combination with other signature blast-related injuries, including lower extremity traumatic amputations, pelvic fractures, severe perineal injuries, colorectal injuries, and traumatic brain injuries [5,10,11]. In particular, there was a 90% correlation between lower extremity traumatic amputations and genital injuries among casualties injured by IEDs in Afghanistan [9].

Although epidemiology related to genitourinary trauma have been examined through the Department of Defense (DOD) Trauma Outcomes and Urogenital Health Project [5,10], and literature has described acute management and short-term clinical outcomes associated with these complex injuries [4,7,12,13], late and recurrent infectious complications have not been well-characterized. Altered urinary tract anatomy, voiding dysfunction, and fecal incontinence after severe genitourinary trauma create circumstances that are conducive to development of UTIs in this unique patient population. We characterized the incidence, epidemiology, and risk factors for UTIs after combat-related genitourinary trauma sustained in Iraq and Afghanistan in a longitudinal cohort of U.S. service members participating in the Trauma Infectious Disease Outcomes Study (TIDOS).

Patients and Methods

Study population

The TIDOS project is an observational study designed to evaluate short- and long-term infectious complications of deployment-related trauma [14]. Patients were eligible for inclusion if they sustained a deployment-related injury (June 2009 through December 2014) requiring medical evacuation to Landstuhl Regional Medical Center followed by transfer to a participating military hospital in the National Capital Region (National Naval Medical Center or Walter Reed Army Medical Center; consolidated into Walter Reed National Military Medical Center in September 2011) or San Antonio, Texas (Brooke Army Medical Center). Eligible subjects were given the opportunity to enroll during their initial hospitalization in a longitudinal cohort, which collects infection-related information after hospital discharge. Enrolled participants who left active-duty military service and transitioned to Department of Veterans Affairs (VA) healthcare were contacted to obtain a second informed consent to allow for data abstraction of relevant VA healthcare records (TIDOS-VA cohort). This analysis is restricted to TIDOS-VA cohort subjects who sus-

tained combat-related genitourinary trauma. This study was conducted under a protocol approved by the Institutional Review Boards of the Uniformed Services University of the Health Sciences (IRB #351767) and the VA St. Louis Health Care System (IRB #1155413).

Study design and data collection

Data pertaining to patient demographics, injury characteristics, trauma history, and early trauma care were collected through the DOD Trauma Registry [2]. Information on clinical care and infections during the initial hospitalization were obtained via the supplemental TIDOS infectious disease module [14]. After the initial hospitalization, infection-related data were collected from service members through telephonic interviews and review of DOD electronic medical records at pre-defined intervals [14,15]. Data on infections and medical and surgical treatment occurring within VA healthcare were collected through abstraction of VA electronic medical records using the Compensation and Pension Records Interchange (CAPRI) [16]. Additional parameters specific to genitourinary trauma complications in VA care were also abstracted, including documentation of urinary catheterization or other urologic procedures (e.g., cystoscopy), non-infectious urologic complications (e.g., elevated creatinine, urinary retention/incontinence, urethral stricture, and sexual dysfunction), and urology clinic utilization.

As previously described [14,15], infections during the initial hospitalization were identified through use of clinical findings and laboratory test results and were classified in accordance with standardized definitions of the U.S. Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN) [17]. In cases in which the a priori definitions were not met, infections were included if there was a clinical diagnosis of an infection associated with directed antimicrobial treatment (≥ 5 days). Infections were excluded if an alternate non-infectious diagnosis was documented in the medical record and antimicrobial therapy was discontinued. Infections (skin and soft-tissue infections and UTIs) using NHSN-based infection syndromes documented in DOD electronic medical records or VA healthcare during follow-up were only collected if they were determined to be complications of the initial traumatic injury [15]. If an infection occurred at an identical anatomic site, it was considered to be a new infection if previous treatment had been completed and there was an absence of signs and symptoms of the infection after discontinuation of treatment.

Statistical analysis

Incidence of UTIs was assessed among patients with genitourinary trauma and expressed per unit time, measured from time of initial injury through last VA data collection. Clinical characteristics of patients with and without UTI, as well as with and without DCBI, were compared using χ^2 testing for categorical parameters and non-parametric testing for continuous parameters. A logistic regression model was used to identify associations between potential risk factors and risk of developing a UTI. Parameters associated with UTI risk in the unadjusted univariable model were evaluated with stepwise selection for inclusion in the adjusted multivariable model. Statistical significance was defined as $p < 0.05$. All analyses were conducted using SAS[®] version 9.3 (SAS, Cary, NC).

TABLE 1. CHARACTERISTICS OF SUBJECTS WITH GENITOURINARY TRAUMA WITH AND WITHOUT UTIS

| Characteristics, no. (%) | Total (n=89) | Subjects with UTIs (n=19) | Subjects without UTIs (n=70) | p |
|--|--------------|---------------------------|------------------------------|--------|
| Male | 88 (98.9) | 18 (94.7) | 70 (100) | 0.214 |
| Age, median years (IQR) | 24 (21, 27) | 23 (22, 29) | 24 (21, 26) | 0.526 |
| Afghanistan theater | 87 (97.8) | 18 (94.7) | 69 (98.6) | 0.383 |
| Blast injury mechanism | 83 (93.3) | 17 (89.5) | 66 (94.3) | 0.604 |
| Injury while dismounted ^a | 51 (83.6) | 8 (61.5) | 43 (89.6) | 0.015 |
| DCBI ^{b,c} | 23 (27.4) | 2 (11.8) | 21 (31.3) | 0.135 |
| Burn injury | 12 (13.5) | 1 (5.3) | 11 (15.7) | 0.449 |
| Open wound | 87 (97.8) | 19 (100) | 68 (97.1) | ~1.00 |
| Open injury to pelvis/hip | 31 (34.8) | 11 (57.9) | 20 (28.6) | 0.017 |
| Genitourinary trauma location | | | | |
| Anterior urethra | 5 (5.6) | 3 (15.8) | 2 (2.9) | 0.063 |
| Posterior urethra | 6 (6.7) | 5 (26.3) | 1 (1.4) | 0.001 |
| Bladder | 19 (21.3) | 10 (52.6) | 9 (12.9) | <0.001 |
| Ureter | 3 (3.4) | 0 | 3 (4.3) | ~1.00 |
| Kidney | 5 (5.6) | 1 (5.3) | 4 (5.7) | ~1.00 |
| Testicular, unilateral | 31 (34.8) | 5 (26.3) | 26 (37.1) | 0.380 |
| Testicular, bilateral | 19 (21.3) | 5 (26.3) | 14 (20.0) | 0.551 |
| Other ^d | 46 (51.7) | 8 (42.1) | 38 (54.3) | 0.346 |
| Associated injury | | | | |
| Amputation | | | | |
| Transfemoral, unilateral | 20 (22.5) | 6 (31.6) | 14 (20.0) | 0.286 |
| Transfemoral, bilateral | 17 (19.1) | 1 (5.3) | 16 (22.9) | 0.107 |
| Transtibial | 24 (27.0) | 9 (47.4) | 15 (21.4) | 0.024 |
| Fracture | | | | |
| Pelvic | 12 (13.5) | 9 (47.4) | 3 (4.3) | <0.001 |
| Femur, unilateral | 4 (4.5) | 1 (5.3) | 3 (4.3) | ~1.00 |
| Femur, bilateral | 0 | 0 | 0 | |
| Tibia/fibula, unilateral | 17 (19.1) | 2 (10.5) | 15 (21.4) | 0.347 |
| Tibia/fibula, bilateral | 4 (4.5) | 2 (10.5) | 2 (2.9) | 0.199 |
| Humerus, unilateral | 9 (10.1) | 1 (5.3) | 8 (11.4) | 0.678 |
| Humerus, bilateral | 1 (1.1) | 0 | 1 (1.4) | ~1.00 |
| Radius/ulna, unilateral | 18 (20.2) | 3 (15.8) | 15 (21.4) | 0.753 |
| Radius/ulna, bilateral | 2 (2.2) | 1 (5.3) | 1 (1.4) | 0.383 |
| Spinal cord injury/paralysis | 14 (15.7) | 5 (26.3) | 9 (12.9) | 0.153 |
| Intra-abdominal | 48 (53.9) | 15 (78.9) | 33 (47.1) | 0.014 |
| ISS, median (IQR) | 33 (21, 38) | 38 (33, 43) | 30 (21, 36) | 0.009 |
| 1-9 (minor) | 7 (7.9) | 0 | 7 (10.0) | 0.563 |
| 10-15 (moderate) | 3 (3.4) | 0 | 3 (4.3) | |
| 16-25 (severe) | 15 (16.9) | 3 (15.8) | 12 (17.1) | |
| ≥26 (critical) | 64 (71.9) | 16 (84.2) | 48 (68.6) | |
| Blood units 24h post-injury, median (IQR) | 16 (6, 26) | 26 (11, 40) | 16 (6, 23) | 0.113 |
| None | 2 (2.2) | 0 | 2 (2.9) | 0.233 |
| 1-9 | 22 (24.7) | 4 (21.1) | 18 (25.7) | |
| 10-20 | 23 (25.8) | 3 (15.8) | 20 (28.6) | |
| ≥21 | 28 (31.5) | 10 (52.6) | 18 (25.7) | |
| Missing | 14 (15.7) | 2 (10.5) | 12 (17.1) | |
| ICU admission | | | | 0.410 |
| None | 19 (21.3) | 2 (10.5) | 17 (24.3) | |
| LRMC only | 15 (16.9) | 4 (21.1) | 11 (15.7) | |
| U.S. hospital ± LRMC | 55 (61.8) | 13 (68.4) | 42 (60.0) | |
| Any urinary catheterization during VA care | 17 (19.1) | 9 (47.4) | 8 (11.4) | <0.001 |
| Catheter type | | | | |
| Foley | 11 (12.4) | 5 (26.3) | 6 (8.6) | 0.037 |
| Intermittent | 5 (5.6) | 4 (21.1) | 1 (1.4) | 0.007 |
| Suprapubic | 5 (5.6) | 4 (21.1) | 1 (1.4) | 0.007 |
| Urostomy | 1 (1.1) | 1 (5.3) | 0 | 0.214 |
| Soft-tissue infection at pelvis/hip | 10 (11.2) | 7 (36.8) | 3 (4.3) | 0.001 |

^aMounted status is missing for 28 subjects (6 with UTI and 22 without UTI). Percentages and p value exclude missing.

^bDCBI is defined by sustaining a blast injury while dismounted, having a traumatic lower extremity injury (at or above knee), serious injury (or amputation) to the opposite lower extremity injury, and pelvic, abdominal, or urogenital injury.

^cTwenty-three subjects with missing mounted status did not meet at least one of the other DCBI criteria and were therefore classified and non-DCBI. Five subjects who met criteria for DCBI except for dismounted injury where mounted status was missing were excluded (2 subjects with UTI and 3 subjects without UTI). Percentages and p value exclude missing.

^dIncludes penile and scrotal injuries.

DCBI=dismounted complex blast injury; ICU=intensive care unit; IQR=interquartile range; ISS=Injury Severity Score; LRMC=Landstuhl Regional Medical Center; VA=Veterans Affairs.

Results

Study population

Among 530 TIDOS-VA enrollees, 89 (17.0%) sustained combat-related genitourinary trauma, largely resulting from a blast mechanism (93%) while serving in support of operations in Afghanistan (98%; Table 1). After excluding five patients with missing information regarding whether the injury occurred while mounted or dismounted, 23 (27% of 84) patients met criteria for a DCBI. Approximately 56% of subjects had a testicular injury, whereas 21% a bladder injury, 12% a urethral injury, 6% a kidney injury, and 3% a ureteral injury. Frequent concurrent non-genitourinary injuries included intra-abdominal injuries (54%), transfemoral traumatic amputations (42%), transtibial traumatic amputations (27%), spinal cord injuries (16%), and pelvic fractures (14%).

Urinary tract infections and other urologic complications

Nineteen (21.3%) TIDOS-VA enrollees with genitourinary trauma had documented evidence of one or more UTI, with a total of 40 unique UTIs identified across DOD and VA care (median: 1; interquartile range [IQR]: 1–2.5). Among the 19 patients, 9 (47%) had their first UTI during their inpatient hospitalization, whereas the first UTI was identified during DOD and VA follow-up for 4 (21%) and 6 (32%) patients, respectively. Of the 40 UTIs, 10 (25%) occurred during the initial hospitalization, 11 (27.5%) during follow-up within the DOD healthcare system, and 19 (47.5%) after transitioning to VA healthcare.

Between patients with and without UTIs, there was no substantial difference in duration of inpatient hospitalization (median of 44 days, [IQR: 19–88] vs. 38 days [IQR: 22–54]; $p=0.233$). Furthermore, there was no substantial difference in length of follow-up after hospital discharge for the DOD (median of 1,017 days [IQR: 632–1,180] vs. 1,146 days [IQR: 635–1,357]; $p=0.509$) or VA healthcare (median of 1,097 days [IQR: 873–1,477] vs. 1,178 days [IQR: 935–1,282]; $p=0.509$), although DOD and VA follow-up times frequently overlapped. All UTIs occurring after initial contact with the VA healthcare system were attributed to VA follow-up time, irrespective of whether the patient was also receiving DOD follow-up. The median time-to-first UTI was 49 days (IQR: 35.8–168.8 days). The incidence rate for UTIs was 0.89 per patient-year during initial hospitalization, 0.05 per patient-year during follow-up within DOD healthcare, and 0.07 per patient-year during time in VA healthcare.

Injury severity was higher among subjects with a UTI (median Injury Severity Score [ISS]: 38 vs. 30), however, there was no difference in intensive care unit admissions or DCBI status between the groups (Table 1). Subjects with a UTI had a higher proportion of open injuries involving the pelvis/hip (58% vs. 29%) and genitourinary trauma localized to the posterior urethra (26% vs. 1%) and bladder (53% vs. 13%). There was no difference in the proportion of spinal cord injuries between the subjects with and without UTIs (26% vs. 13%). With the high frequency of blast injuries, polytrauma was common in both groups; however, the injury pattern varied. Pelvic fractures (47% vs. 4%), transtibial amputations (47% vs. 21%), and intra-abdominal injuries (79% vs. 47%) were more frequent in subjects with UTIs. A

TABLE 2. UROLOGIC OUTCOMES AND COMPLICATIONS OF SUBJECTS WITH GENITOURINARY TRAUMA DURING VETERANS AFFAIRS HEALTHCARE

| Characteristics, no. (%) | Total (n=89) | Subjects with UTIs (n=19) | Subjects without UTIs (n=70) | p |
|---|--------------|---------------------------|------------------------------|--------|
| Hospitalization | | | | |
| For UTI | 2 (2.2) | 2 (10.5) | 0 | 0.044 |
| For other urologic complication | 4 (4.5) | 3 (15.8) | 1 (1.4) | 0.029 |
| Urologic procedure | 7 (7.9) | 5 (26.3) | 2 (2.9) | 0.004 |
| Cystoscopy (+) stent | 2 (2.2) | 2 (10.5) | 0 | 0.044 |
| Cystoscopy (–) stent | 2 (2.2) | 2 (10.5) | 0 | 0.044 |
| Nephrostomy | 0 | 0 | 0 | |
| Genital surgery | 1 (1.1) | 0 | 1 (1.4) | ~1.00 |
| Urinary tract surgery | 2 (2.2) | 1 (5.3) | 1 (1.4) | 0.383 |
| Other | 1 (1.1) | 1 (5.3) | 0 | 0.214 |
| Non-infectious urologic complication | 39 (43.8) | 12 (63.2) | 27 (38.6) | 0.055 |
| Elevated creatinine/azotemia ^a | 0 | 0 | 0 | |
| Urinary retention/incontinence | 12 (13.5) | 8 (42.1) | 4 (5.7) | <0.001 |
| Urethral stricture | 7 (7.9) | 5 (26.3) | 2 (2.9) | 0.004 |
| Sexual dysfunction | 32 (36.0) | 8 (42.1) | 24 (34.3) | 0.529 |
| Number of urologic visits | | | | 0.005 |
| None | 26 (29.2) | 3 (15.8) | 23 (32.9) | |
| 1–5 | 48 (53.9) | 8 (42.1) | 40 (57.1) | |
| 6–10 | 7 (7.9) | 2 (10.5) | 5 (7.1) | |
| 11–15 | 6 (6.7) | 4 (21.1) | 2 (2.9) | |
| 16–20 | 0 | 0 | 0 | |
| 21–25 | 1 (1.1) | 1 (5.3) | 0 | |
| 26–30 | 0 | 0 | 0 | |
| ≥31 | 1 (1.1) | 1 (5.3) | 0 | |

^aCreatinine >1.5 two times at least 6 mo apart.
UTI=urinary tract infection.

higher proportion of soft-tissue infections involving the pelvis/hip during the initial hospitalization was also observed with subjects who had a UTI (37% vs. 4%).

After entry into VA care, two subjects were hospitalized for a UTI and four were admitted for other urological complications (Table 2). Subjects who developed UTIs had a higher proportion of chronic continuous or intermittent urinary catheterization (47% vs. 11%), urinary retention/incontinence (42% vs. 6%), and urethral stricture (26% vs. 3%). The proportion of sexual dysfunction was similar between the subjects with and without a UTI (42% and 34%).

Pseudomonas aeruginosa (32.5%), *Escherichia coli* (17.5%), and *Klebsiella pneumoniae* (10%) were the most common micro-organisms isolated in urine culture from the 40 UTIs. Among the 10 UTIs occurring during initial hospitalization, eight (80%) were caused by *Pseudomonas aeruginosa*, involving seven unique patients. In contrast, of the 30 UTIs occurring during subsequent DOD or VA care, only

five (16.7%) were attributable to *Pseudomonas aeruginosa*, involving three unique patients.

Dismounted complex blast injury and urologic complications

Urologic complications were also assessed within the subset of subjects assessed for DCBI (Table 3). Except for a higher proportion of bilateral testicular injury among subjects with DCBI (35% vs. 10%; p=0.006), patterns of genitourinary trauma were comparable to those without DCBI. None of the patients with DCBI were hospitalized for either an UTI or other urologic complication. Occurrence of urinary retention/incontinence, urethral stricture, and sexual dysfunctions were also comparable between subjects with and without DCBI.

Urinary tract infection risk factors

In the univariable model, higher ISS, 21 or more units of blood transfused within 24 hours of injury, open injury to the

TABLE 3. UROLOGIC OUTCOMES AND COMPLICATIONS OF SUBJECTS WITH DCBI^{a,b}

| Characteristics, no. (%) | Total (n=84) | Subjects with DCBI (n=23) | Subjects without DCBI (n=61) | p |
|--|--------------|---------------------------|------------------------------|-------|
| Genitourinary trauma location | | | | |
| Anterior urethra | 5 (6.0) | 0 | 5 (8.2) | 0.316 |
| Posterior urethra | 5 (6.0) | 1 (4.4) | 4 (6.6) | ~1.00 |
| Bladder | 16 (19.1) | 1 (4.4) | 15 (24.6) | 0.058 |
| Ureter | 3 (3.6) | 0 | 3 (4.9) | 0.558 |
| Kidney | 5 (6.0) | 1 (4.4) | 4 (6.6) | ~1.00 |
| Testicular, unilateral | 31 (36.9) | 9 (39.1) | 22 (36.1) | 0.795 |
| Testicular, bilateral | 14 (16.7) | 8 (34.8) | 6 (9.8) | 0.006 |
| Other ^c | 44 (52.4) | 10 (43.5) | 34 (55.7) | 0.316 |
| Hospitalization during VA healthcare | | | | |
| For UTI | 2 (2.4) | 0 | 2 (3.3) | ~1.00 |
| For other urologic complication | 4 (4.8) | 0 | 4 (6.6) | 0.571 |
| Urologic procedure during VA healthcare | | | | |
| Cystoscopy (+) stent | 2 (2.4) | 0 | 2 (3.3) | ~1.00 |
| Cystoscopy (-) stent | 1 (1.2) | 0 | 1 (1.6) | ~1.00 |
| Nephrostomy | 0 | 0 | 0 | / |
| Genital surgery | 1 (1.2) | 0 | 1 (1.6) | ~1.00 |
| Urinary tract surgery | 2 (2.4) | 0 | 2 (3.3) | ~1.00 |
| Other | 1 (1.2) | 0 | 1 (1.6) | ~1.00 |
| Non-infectious urologic complication | | | | |
| Elevated creatine/azotemia ^d | 0 | 0 | 0 | / |
| Urinary retention/incontinence | 10 (11.9) | 1 (4.4) | 9 (14.8) | 0.272 |
| Urethral stricture | 5 (6.0) | 0 | 5 (8.2) | 0.316 |
| Sexual dysfunction | 29 (34.5) | 4 (17.4) | 25 (41.0) | 0.070 |
| Number of urologic visits | | | | |
| None | 24 (28.6) | 5 (21.7) | 19 (31.2) | 0.510 |
| 1-5 | 47 (56.0) | 17 (73.9) | 30 (49.2) | |
| 6-10 | 7 (8.3) | 1 (4.4) | 6 (9.8) | |
| 11-15 | 4 (4.8) | 0 | 4 (6.6) | |
| 16-20 | 0 | 0 | 0 | |
| 21-25 | 1 (1.2) | 0 | 1 (1.6) | |
| 26-30 | 0 | 0 | 0 | |
| ≥31 | 1 (1.2) | 0 | 1 (1.6) | |

^aDCBI is defined by sustaining a blast injury while dismounted, having a traumatic lower extremity injury (at or above knee), serious injury (or amputation) to the opposite lower extremity injury, and pelvic, abdominal, or urogenital injury.

^bTwenty-three subjects with missing mounted status did not meet at least one of the other DCBI criteria and were therefore classified and non-DCBI. Five subjects who met criteria for DCBI except for dismounted injury where mounted status was missing were excluded. Percentages and p value exclude missing.

^cIncludes penile and scrotal injuries.

^dCreatinine >1.5 two times at least 6 mo apart.

DCBI=dismounted complex blast injury; UTI=urinary tract infections; VA=Veterans Affairs.

pelvis/hip, pelvic soft-tissue infection during initial hospitalization, urinary or urinary plus testicular injury, pelvic fracture, transtibial amputation, intra-abdominal injury, urinary catheterization, urinary retention/incontinence, and urethral stricture were significantly associated with risk of UTI development (Table 4). Upon multivariable analysis, soft-tissue infection at pelvis/hip, trauma involving the urinary tract, and sustaining a transtibial amputation were statistically significant independent risk factors for UTI (Table 4).

Discussion

Approximately 17% of combat-injured veterans participating in the longitudinal TIDOS-VA cohort sustained combat-related genitourinary trauma, with the majority resulting from a blast mechanism while serving in support of operations in Afghanistan (27% with a DCBI). One in five of these veterans developed one or more UTI during the study period, of which half occurred after enrollees had left military service and transitioned from DOD to VA healthcare. Trauma involving the urinary tract, sustaining a transtibial amputation, and pelvic soft-tissue infections complicating the initial genitourinary injury were identified as independent predictors for UTI in this complex polytrauma population.

Within our study cohort, U.S. service members who developed a UTI after genitourinary trauma had a higher proportion of voiding dysfunction, as evidenced by urinary retention and/

or incontinence. Voiding dysfunction can promote urinary stasis, creating ideal growth conditions for uropathogens, and is a well-recognized risk factor for UTI [18–20]. Spinal cord injury accompanying genitourinary trauma in this population was relatively uncommon (15.7%) and the proportion did not differ between those who did or did not develop UTI. This would suggest that functional issues involving the pelvic floor, bladder, or urethral sphincter, as well as anatomic obstruction (e.g., urethral stricture) likely play a greater part in voiding dysfunction than neurogenic bladder in this population. The occurrence of urinary trauma was identified as an independent predictor of developing an UTI in our study, which supports this conjecture. Interestingly, patterns of genitourinary trauma among subjects with and without DCBI did not differ substantially and DCBI, previously associated with invasive fungal infections [9,21], was not found to be a unique risk factor for UTI.

It is not surprising that along with voiding dysfunction, those who developed a UTI had a greater occurrence of chronic or intermittent urinary catheterization or urologic instrumentation. These procedures allow peri-urethral enteric flora, as well as bacterial flora on the skin to access the bladder and kidneys directly. Prolonged urinary catheterization can lead to UTIs involving uropathogens that have colonized either the extraluminal or intraluminal surfaces of the catheter or the urine collection bag [20,22]. *Pseudomonas aeruginosa* is a common cause of hospital-acquired UTI with compromised

TABLE 4. ANALYSIS OF CANDIDATE RISK FACTORS FOR UTIs AFTER GENITOURINARY TRAUMA

| Characteristics | Univariable OR (95% CI) | Univariable p value | Multivariable OR (95% CI) | Multivariable p value |
|---|----------------------------|------------------------|------------------------------|--------------------------|
| Blood transfusion within 24 h (units) | | 0.042 | | |
| 1–20 | Reference | | – | |
| ≥21 | 3.18 (1.04– 9.68) | | – | |
| ISS, continuous | 1.04 (1.01– 1.08) | 0.028 | – | |
| DCBI ^a | 0.29 (0.061– 1.39) | 0.123 | – | |
| ICU admission during initial trauma hospitalization | 2.73 (0.57– 13.02) | 0.209 | – | |
| Open injury to pelvis/hip | 3.44 (1.21– 9.80) | 0.021 | – | |
| Soft-tissue infection at pelvis/hip | 13.03 (2.95– 57.55) | 0.001 | 28.11 (3.45–228.67) | 0.002 |
| Genitourinary trauma location | | 0.002 | | 0.018 |
| Urinary ^b | 26.28 (2.79–247.91) | | 27.97 (2.04–383.19) | |
| Testicular ^c | 2.87 (0.30– 27.43) | | 1.52 (0.12– 18.58) | |
| Both | 17.25 (1.79–166.03) | | 3.57 (0.25– 51.61) | |
| Associated injury | | | | |
| Pelvic fracture | 20.10 (4.64– 87.06) | <0.001 | – | |
| Transfemoral amputation, unilateral | 1.85 (0.60– 5.72) | 0.288 | – | |
| Transfemoral amputation, bilateral | 0.19 (0.02– 1.52) | 0.116 | – | |
| Transtibial amputation | 3.30 (1.14– 9.59) | 0.028 | 6.96 (1.22– 39.73) | 0.029 |
| Spinal cord injury/paralysis | 2.42 (0.70– 8.35) | 0.161 | – | |
| Intra-abdominal | 4.20 (1.27– 13.94) | 0.019 | – | |
| Urinary catheterization during VA care | 6.98 (2.18– 22.32) | 0.001 | – | |
| Urinary retention/incontinence during VA care | 12.00 (3.08– 46.73) | <0.001 | – | |
| Urethral stricture during VA care | 12.14 (2.14– 69.03) | 0.005 | – | |

^aDCBI is defined by sustaining a blast injury while dismounted, having a traumatic lower extremity injury (at or above knee), serious injury (or amputation) to the opposite lower extremity injury, and pelvic, abdominal, or urogenital injury.

^bIncludes anterior urethra, posterior urethra, bladder, ureter, and kidney

^cIncludes unilateral and bilateral.

UTI=urinary tract infection; OR=odds ratio; CI=confidence interval; ISS=Injury Severity Score; DCBI=dismounted complex blast injury; ICU=intensive care unit; VA=Veterans Affairs.

host defenses, urinary catheterization, and urologic instrumentation. *Pseudomonas aeruginosa*, which has unique resistance patterns, was the predominant micro-organism associated with UTI during initial hospitalization after genitourinary trauma. Alone or in combination, voiding dysfunction and urinary tract instrumentation are well-recognized UTI risk factors.

A pelvic soft-tissue infection complicating genitourinary trauma during the initial hospitalization was also identified as a significant predictor for UTI. Among 83 United Kingdom service members with perineal trauma from blast injuries sustained during combat operations in Afghanistan, specimens from 52 (63%) demonstrated bacterial or fungal growth (approximately half collected from blast wounds at arrival in Birmingham) [23]. Pelvic soft-tissue infection could arise from enteric flora in the setting of colorectal injury. In the civilian population, penetrating bladder trauma, primarily caused by gunshot wounds, has been associated with concomitant colorectal injury in as high as 66% of cases [24–27].

In our predominantly blast-injured cohort, more than half sustained a concomitant intra-abdominal injury, with a substantially higher proportion observed among those who developed a UTI than those who did not (79% vs. 47%). It is likely that pelvic soft-tissue infection is a marker for overall injury severity, along with genitourinary trauma severity, rather than a direct cause of UTI, because 75% of UTIs in our study occurred after the initial hospitalization and many well into VA care. Patients with early pelvic soft-tissue infections likely sustained heavily contaminated wounds and complicated genitourinary and/or colorectal blast-related injuries, requiring extensive medical and surgical care not only to address significant trauma, but for debridement of infected tissue. Similarly, the association of sustaining a transtibial amputation with UTI risk is also likely a surrogate for injury severity resulting from the high preponderance of blast trauma within our population.

This study has limitations that should be considered. First, the population herein represents a subset of U.S. service members with severe combat-related trauma requiring medical evacuation and does not include patients with minor genitourinary trauma treated within the theater of operations. Severely injured patients are more likely to experience complications, including infections. Despite the potential for selection bias in the TIDOS-VA cohort, a prior analysis found no difference in the proportion of dismounted blast-related trauma between patients who did and did not enroll in TIDOS at participating sites [15].

Second, our data sources drew exclusively upon DOD and VA healthcare system electronic medical records. It is possible that TIDOS-VA enrollees could have received additional healthcare at civilian U.S. healthcare facilities, including ambulatory clinics, emergency departments, and urgent care centers for UTI episodes, which may not have been captured in DOD or VA records. Therefore, it is possible that UTI rates were higher than reported in our analysis. In terms of urologic outcomes and complications, data were abstracted only from VA medical records, which could have led to underestimation of the total number of urinary procedures (including urinary catheterization) and non-infectious sequelae affecting this population over the entire continuum of DOD-VA care.

Last, historical risk factors for UTI predating combat-related genitourinary trauma were not explicitly captured, in-

cluding a pre-existing urinary tract abnormality, prior urinary tract instrumentation or surgery, or previous UTI. This could have contributed to increased risk for UTI after genitourinary trauma, however, this is unlikely given the young and generally healthy demographic of U.S. service members deployed to combat zones.

Conclusions

Overall, UTI is common among U.S. service members who sustained combat-related genitourinary trauma during the wars in Iraq and Afghanistan, particularly in the setting of severe injury, soft-tissue infection during the initial hospitalization, and chronic urologic sequelae, such as voiding dysfunction. As more TIDOS enrollees enter VA healthcare, future analyses of the TIDOS-VA cohort over longer follow-up periods will provide an increasingly more accurate picture of the burden of UTI and other infectious complications after genitourinary trauma.

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Author Disclosure Statement

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