Testosterone Recovery after Polytrauma and Scrotal Injury in Patients from Operation Enduring Freedom and Operation Iraqi Freedom

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Abbreviations and Acronyms

GU = genitourinary

ISS = Injury Severity Score

NNMC = National Naval Medical Center

OEF = Operation Enduring Freedom

OIF = Operation Iraqi Freedom

T = testosterone

TBI = traumatic brain injury

WRAMC = Walter Reed Army Medical Center

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Purpose: We examined the long-term natural history of testosterone recovery in patients with complex battle injuries.

Materials and Methods: We retrospectively reviewed the charts of patients who participated in Operation Enduring Freedom and Operation Iraqi Freedom, and underwent urological surgical consultation at Walter Reed Army Medical Center, Washington, D.C. or the National Naval Medical Center, Bethesda, Maryland, from 2001 to August 2011. Of the 192 patient charts reviewed 138 (72%) had testosterone values available. The study inclusion criterion of at least 2 testosterone measurements, including 1 made within 40 days of injury, was met by 84 patients (61%) with testosterone data available. Those treated with bilateral orchiectomy were not required to meet this criterion.

Results: Initial patient testosterone after injury in the testosterone recovery group was inversely proportional to the degree of scrotal injury. In patients in whom testosterone recovered to at least 250 ng/dl the recovery occurred a mean of 4.5 months after injury. Patients who required testosterone replacement had lower initial testosterone ($p = 0.0063$) and lower testosterone velocity ($p < 0.0001$).

Conclusions: Monitoring the velocity of testosterone recovery is a viable approach in male patients who receive significant genitourinary trauma. In patients in whom testosterone recovered the recovery occurred within a mean of 5 months after injury. It is reasonable to observe patients with scrotal injuries since testosterone may recover in many of them without intervention.

Key Words: testis, scrotum, wounds and injuries, testosterone, multiple trauma

As of March 2013 more than 50,000 service members had been wounded in action during OIF and OEF.[1] Almost 10% of these injuries include the GU area.[2] Of GU injuries 57% to 83.1% involved the urethra and external genitalia[3–5] with a significant psychological and social impact due to the effect on urinary, hormonal and sexual function.[3] Despite this incidence of external genitalia injuries during combat to our knowledge there has been no study of long-term hormonal and sexual dysfunction after such injuries.

Many animal based studies and human investigations confirm that male T decreases to almost castrate levels due to trauma even without testicular involvement.[6–12] Cernak

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et al prospectively studied male casualties during war in the former Yugoslavia in the 1990s.[12] In this study the severity of gunshot/missile wounds was assessed by the ISS. Baseline T measured at the time of injury was significantly decreased in patients with a significant ISS. T continued to decrease after hospital admission and remained low for 5 days after trauma/surgery. This suggests that tissue trauma leads to a severity dependent decrease in T. However, because study patients were followed for only 5 days, long-term recovery was not evaluated. Additionally, the specific injuries in these patients were not described in detail.

The timing of exogenous T replacement after GU trauma is controversial. The literature supports early T replacement using analogues such as oxandrolone to assist in the recovery of patients who have significant burn injury and tissue loss.[13,14] In that study group patients treated with oxandrolone had less protein loss and muscle wasting, and ultimately a shorter hospital stay. In contrast, other trauma studies suggest that the initial low T level after injury is organ protective. Gee et al reported that in patients admitted to a level 1 trauma center with an ISS of greater than 4 respiratory distress and/or death correlated with higher T.[15] In a mouse trauma model Park et al found that low T was protective against renal ischemic injury and castrated mice had less ischemia/reperfusion injury.[16] Similarly in a rat model of hemorrhagic and burn trauma Anathakrishnan et al observed that increased T potentiated lung and gut injury.[9]

Given these controversies, we retrospectively evaluated long-term T recovery in patients with polytrauma at 2 large military medical centers, WRAMC, Washington, D.C., and NNMC, Bethesda, Maryland. It has been the practice at these centers to determine initial and monthly T levels in combat wounded patients who require urological care.

MATERIALS AND METHODS

Study Sample

Study subjects were identified using the operative log for patients injured in OEF or OIF who had a urological intraoperative surgical consultation between January 2001 and August 2011 at WRAMC or NNMC. We then retrospectively reviewed the charts of all OEF and OIF patients who required urological surgery to identify the mechanism of injury, time from injury, concurrent injuries, severity of scrotal injuries, T values, patient age at injury and receipt of exogenous T. Patients generally arrived within 1 week of injury and were sent to the operating room within 1 day of arrival at WRAMC or NNMC. In the operating room it was our practice to examine and/or explore any patient with a documented scrotal or penile injury while in theater even if it had been repaired before transfer.

Of the 192 patient charts reviewed 138 (71.9%) showed T data. A total of 84 men met the study inclusion criteria of at least 2 T values on record with the baseline value obtained within 40 days of injury. Patients with bilateral orchiectomy were also included in analysis.

T was measured during first morning blood draws. Patients with a T of 250 ng/dl or greater were defined as hormonally recovered according to our study protocol since this was the lower limit of normal on our T assays. Patients who received exogenous T were started on T cypionate 200 mg intramuscularly every 2 weeks and then adjusted based on mid dosing T levels. The degree of scrotal injury was divided into 4 categories, including 1) no scrotal injury, 2) scrotal injury without testicular tissue loss, 3) scrotal injury with testicular tissue loss, which included any testicular tissue débridement up to just less than bilateral orchiectomy, and 4) bilateral orchiectomy.

Statistical Analysis

The frequency is reported for categorical patient features (scrotal injury type and exogenous T use). Measures of central tendency and dispersion are reported for continuous patient features (age, baseline T, T velocity and time to recovery). Patient features were compared across injury type strata and T replacement categories (yes/no), and then jointly for each factor with the Student t-test or ANOVA used for approximately normal distributed features (eg age) and the Wilcoxon rank sum or Kruskal-Wallis test used for nonnormal distributed features (eg baseline T, T velocity and time to T recovery). Unadjusted Kaplan-Meier time to event analysis was done to examine time to T recovery by T velocity quartiles. The log rank p value is reported. T velocity was calculated as the slope of the linear regression using all T measurements (minimum of 2 values) with time. Analysis was done with SAS®, version 9.3.

RESULTS

Of the 84 patients eligible for analysis 7 (8.3%) and 77 (91.7%) participated in OIF and OEF, respectively. Average patient age was 24.2 years.

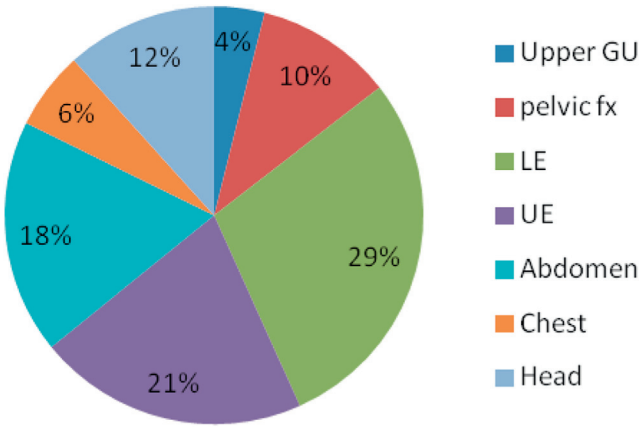

Figure 1. Additional injuries. *fx*, fracture. *LE*, lower extremity. *UE*, upper extremity.