Psychiatric Diagnoses and Neurobehavioral Symptom Severity among OEF/OIF VA Patients with Deployment-Related Traumatic Brain Injury: A Gender Comparison

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Abstract

Background: Traumatic brain injury (TBI) has substantial negative implications for the post-deployment adjustment of veterans who served in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF); however, most research on veterans has focused on males. This study investigated gender differences in psychiatric diagnoses and neurobehavioral symptom severity among OEF/OIF veterans with deployment-related TBI.

Methods: This population-based study examined psychiatric diagnoses and self-reported neurobehavioral symptom severity from administrative records for 12,605 United States OEF/OIF veterans evaluated as having deployment-related TBI. Men (n = 11,951) and women (n = 654) who were evaluated to have deployment-related TBI during a standardized comprehensive TBI evaluation in Department of Veterans Affairs facilities were compared on the presence of psychiatric diagnoses and neurobehavioral symptom severity among OEF/OIF veterans with deployment-related TBI.

Findings: Posttraumatic stress disorder (PTSD) was the most common psychiatric condition for both genders, although women were less likely than men to have a PTSD diagnosis. In contrast, relative to men, women were 2 times more likely to have a depression diagnosis, 1.3 times more likely to have a non-PTSD anxiety disorder, and 1.5 times more likely to have PTSD with comorbid depression. Multivariate analyses indicated that blast exposure during deployment may account for some of these differences. Additionally, women reported significantly more severe symptoms across a range of neurobehavioral domains.

Conclusion: Although PTSD was the most common condition for both men and women, it is also critical for providers to identify and treat other conditions, especially depression and neurobehavioral symptoms, among women veterans with deployment-related TBI.

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Freedom (OIF) have led researchers, policy makers, and the media to pay considerable attention to the identification and treatment of TBI and its comorbidities. The prevalence of TBI is between 12% and 20% for OEF/OIF veterans, with most cases being mild in severity (Hendricks et al., 2011; Hoge et al., 2008; Schneiderman, Braver, & Kang, 2008; Tanielian & Jaycox, 2008). Although women are serving in the military at higher rates than ever before and have expanded their occupational roles during deployments (Murdoch et al., 2006; Street, Vogt, & Duttra, 2009), the impact of deployment-related TBI on women’s health is largely unknown. However, 12.7% of the Department of Veterans Affairs (VA) OEF/OIF women patients screen positive for TBI or report a prior TBI diagnosis (Hendricks et al., 2011).

Among veterans, psychiatric and neurobehavioral disturbances often co-occur with TBI, which can complicate recovery and add to the challenge of coordination of care (Sayer et al., 2009). For example, a recent investigation of VA patients with TBI documented in their medical charts found that nearly two thirds (63.9%) also had a diagnosis of post-traumatic stress disorder (PTSD), and large pluralities had diagnoses of depression (46.3%), non-PTSD anxiety disorders (35.6%), and substance use disorders (26.2%) documented at least once in a VA mental health, primary care, or rehabilitation clinic since separation from the military (Carlson et al., 2010). Despite the potential impact of these conditions, there exists no published investigation of gender differences in the psychiatric and neurobehavioral comorbidities of TBI among OEF/OIF veterans.

Such research is needed in veterans because a growing literature suggests that women tend to fare worse than men in terms of psychiatric and neurobehavioral symptoms after TBI (Colvin et al., 2009; Fann et al., 2004; Jensen & Nielsen, 1990; McCarthy et al., 2006). For instance, among a health maintenance organization sample with no history of psychiatric illness, Fann et al. (2004) found that women were at greater risk, relative to men, for developing psychiatric problems subsequent to TBI. It is unclear, however, whether these findings would generalize to OEF/OIF VA patients given the large age range of the sample (15–95 years). A meta-analysis of eight studies concluded that TBI neurobehavioral outcomes were worse in women than in men for 85% of 20 measured outcomes, including memory, headaches, dizziness, fatigue, irritability, anxiety, and depression (Farace & Alves, 2000). Moreover, the sports concussion literature suggests there may be gender differences in postconcussive symptom reporting among athletes (Dick, 2009). For example, in a sample of soccer players with a history of concussion, women reported a significantly higher number of discrete neurobehavioral symptoms than their male counterparts (Colvin et al., 2009).

Given the growing number of women veterans seeking care within the VA (Yano et al., 2010), as well as evidence of gender differences in psychiatric and neurobehavioral comorbidities of TBI in non-veteran samples, it is important to determine whether gender differences exist among OEF/OIF VA patients with deployment-related TBI. This study examined gender differences in the presence of psychiatric diagnoses and neurobehavioral symptom severity among the population of OEF/OIF VA patients judged to have deployment-related TBI. Consistent with the research described, we hypothesized that women veterans would be more likely than their male counterparts to experience more psychiatric diagnoses as well as more severe neurobehavioral symptoms.

### Methods

#### Data Sources

This study used VA administrative data, extracted from the Patient Care Services patient-level TBI screening database, to identify the subgroup of OEF/OIF veterans who were judged to have deployment-related TBI during a Comprehensive TBI Evaluation conducted within the VA between April 1, 2007, and August 7, 2009 (for a detailed description of the OEF/OIF screened population, see Hendricks et al. [2011]). The protocol was approved by the VA Boston Healthcare System Institutional Review Board. We obtained records for this study population from VA’s National Patient Care Database, which includes VA utilization data and some demographic information. Psychiatric diagnostic information was derived from these VA data. Veterans’ military service information (i.e., component, rank, and years of service) was provided by the Department of Defense’s Defense Management Data Center database. The Defense Management Data Center identifiers were converted to scrambled social security numbers and merged with VA administrative data. General demographics for the current study population are provided in Table 1.

#### Measures

**TBI screening and evaluation instruments**

The VA is mandated to administer a national TBI screen as part of its electronic medical records system for clinical reminders to all veterans who report OEF/OIF deployment. The screen consists of four sequential sets of questions concerning: 1) Exposure to events that may increase risk of TBI (i.e., blast or explosion, vehicular or aircraft accident, fragment or bullet wound above the shoulders, fall); 2) Symptoms that occurred immediately after the injury (i.e., disorientation, alterations in consciousness, memory problems); 3) New or exacerbated symptoms after the injury (i.e., memory problems, dizziness, difficulties with balance, sensitivity to light, irritability, headaches, sleep problems); and 4) Symptoms that have persisted through the past week. Veterans who respond positively to one or more problems in each of the four sections are considered to screen positive for TBI and are eligible for a referral for a Comprehensive TBI Evaluation.

The Comprehensive TBI Evaluation is conducted by a VA clinician who uses a defined protocol to assist in making a clinical judgment about whether a TBI occurred and in developing a treatment plan (Department of Veterans Affairs and Department of Defense, 2009). During this evaluation, the clinician conducts a targeted physical examination and psychiatric history. The clinician also asks a series of standardized questions about deployment-related experiences regarding blast exposure and non-blast-related head injuries (i.e., bullet, vehicular accident, fall, or “other” blunt trauma), as well as pre-and post-deployment TBIs. Blast exposure is assessed based on patients’ self-report of the number of blast exposures experienced during deployment. Response options include one, two, three, four, and five or more blasts. Neurobehavioral symptoms are assessed using the 22-item Neurobehavioral Symptom Inventory (Cicerone & Kalmar, 1995). This self-report measure asks patients to rate the severity of common postconcussive symptoms (e.g., vision, sleep, headaches, fatigue) over the past 30 days on a 5-point scale, ranging from 0 (none) to 4 (very severe). The Comprehensive TBI Evaluation also includes an
item about the prevalence of general pain over the past 30 days. An exploratory factor analysis on the 23 items (22 Neurobehavioral Symptom Inventory items, plus pain) yielded four distinct factors: Affective (e.g., irritability, anxiety/tension, fatigue), somatosensory (e.g., pain, headaches, nausea), cognitive (e.g., poor concentration, forgetfulness, difficulties making decisions), and vestibular (e.g., loss of balance, dizziness, poor coordination). The fit of the exploratory factor analysis–based models to the data was verified using confirmatory factor analysis and is described elsewhere (Meterko et al., 2011).

**Psychiatric diagnoses**

Patient-level data from the Comprehensive TBI Evaluation were merged to *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM; National Center for Mental Health Statistics and the Centers for Medicare &
Medicaid Services, 2008) diagnostic codes from VA administrative data. As in previous studies of psychiatric diagnoses in OEF/OIF VA patients (e.g., Carlson et al., 2010; Kimerling et al., 2010), we used ICD-9 codes to identify men and women who were diagnosed in VA with PTSD, depression, non-PTSD anxiety disorders, adjustment disorders, stress reactions, alcohol-related disorders, drug-related (non-alcohol) disorders, number of psychiatric diagnoses, and PTSD with comorbid depression (see Table 1 footnotes for a list of all ICD-9 codes used to classify psychiatric diagnoses). Consistent with a previous examination of psychiatric comorbidities among OEF/OIF veterans with TBI (Carlson et al., 2010), we confined our inclusion of psychiatric conditions to those that are most commonly observed among OEF/OIF veterans (Seal, Berthenthal, Miner, Sen, & Marmar, 2007). Less common diagnoses, such as psychotic disorders, were not examined in the current study. We included ICD-9 codes that were assigned in primary care, mental health, women’s health, rehabilitation, or a combination of these outpatient clinics, as well as those assigned from an acute or extended care inpatient stay during fiscal years 2007 through 2009. A psychiatric diagnosis was considered present when it was listed for a total of two or more separate outpatient and/or inpatient visits during fiscal years 2007 through 2009.

Procedure

The TBI-screened population of OEF/OIF veterans for our observational period consisted of 327,633 veterans. Figure 1 illustrates the screening and subsequent evaluation of female and male patients in this population. A total of 40,448 women and 287,185 men were screened for TBI, with rates of positive screens at 10.5% and 21.3%, respectively. Compared with all screened patients, those with positive TBI screens were about half as likely to be women (6.3% vs. 12.4%; p < .01); were 2 years younger, on average (31.6 vs. 33.7 years; p < .01), with significantly fewer years of military service (18% with 8 or more years compared with 27%; p < .01; data not shown).

Approximately half of the women (n = 1,912) and men (n = 31,873) who screened positive for TBI subsequently completed a Comprehensive TBI Evaluation. Of the veterans who completed the evaluation, nearly equivalent proportions of women (34%) and men (37%) were judged to have deployment-related TBI. Veterans who reported that they had a TBI before or after deployment to Iraq or Afghanistan (n = 6,840) were excluded from the current analyses. There were no other exclusions based on psychiatric or medical diagnoses. Thus, the total study sample of 12,605 veterans was composed of 654 women and 11,951 men judged to have deployment-related TBI. Compared with all screened OEF/OIF VA patients, the sample of veterans judged to have deployment-related TBI had fewer than half the proportion of women (5% vs. 12%), officers (4% vs. 8%), and Navy/Air Force personnel (9% vs. 23%; Hendricks et al., 2011).

Data Analysis

First, descriptive statistics were generated to determine the percentage of the sample, stratified by gender, with psychiatric diagnoses and severe neurobehavioral symptoms. Scores on the neurobehavioral symptom scales (22 Neurobehavioral Symptom Inventory items plus pain item) were dichotomized into ‘none/mild/moderate’ (mean scale score < 3) or ‘severe/very severe’ (mean scale score ≥ 3) groups to examine clinically relevant severity of neurobehavioral symptoms. Second, we conducted binary logistic regression analyses with the presence of psychiatric diagnoses and severe/very severe neurobehavioral symptoms as dependent variables and gender as the predictor variable to examine the univariate relationships for women compared with men on those outcome variables. Third, we adjusted for the potentially important confounder of blast exposure (i.e., experienced one or more blasts while deployed as reported during the Comprehensive TBI Evaluation), because blast exposure may uniquely contribute to the odds of psychiatric and neurobehavioral outcomes (Sayer et al., 2008). Additionally, these analyses were adjusted for etiology (blast, bullet, fall, vehicle, other blunt trauma) and all demographic variables. For all regression analyses, odds ratios and 95% confidence intervals were calculated. Alpha levels were adjusted to correct for multiple tests (p < .005 was the significance criterion for psychiatric diagnoses and p < .012 was the significance criterion for neurobehavioral symptom severity).

Results

As noted, analyses were focused on the 12,605 OEF/OIF veterans who were evaluated as having deployment-related TBI during the observation period. Patient demographic characteristics, percentages with psychiatric diagnoses and severe/very severe neurobehavioral symptoms are presented separately for women (n = 654) and men (n = 11,951) in Table 1. The mean scores for the neurobehavioral symptoms domains are as follows: Affective (women, M = 2.53, SD = 0.96; men, M = 2.43, SD = 0.96), somatosensory (women, M = 1.80, SD = 0.79; men, M = 1.55, SD = 0.76), cognitive (women, M = 2.29, SD = 1.05; men: M = 2.16, SD = 1.04), and vestibular (women, M = 1.54, SD = 0.91; men, M = 1.28, SD = 0.86).
Univariate relationships for women compared with men on psychiatric diagnoses and severe/very severe neurobehavioral symptoms revealed gender differences in both types of outcomes (see Table 2 for unadjusted relationship values). For psychiatric diagnoses, women were 0.70 times less likely than men to have a PTSD diagnosis. Women were also significantly less likely than men to have substance abuse diagnoses as well as only one psychiatric diagnosis. In contrast, relative to men, women were nearly 2 times more likely to have a depression diagnosis, 1.3 times more likely to have a non-PTSD anxiety disorder, and over 1.5 times more likely to have PTSD with comorbid depression. In terms of neurobehavioral symptoms, women were significantly more likely than men to report severe somatosensory, cognitive, and vestibular symptoms, with odds ratios ranging from 1.3 to 1.9.

Some of the gender difference findings were no longer significant after accounting for participants’ exposure to blasts while on deployment (see Table 2 for blast-adjusted relationship values). Specifically, women were no longer less likely than men to have a PTSD diagnosis, drug-related diagnoses, or have only one psychiatric diagnosis after controlling for blast exposure. Additionally, women were no more likely than men to have a diagnosis of a non-PTSD anxiety disorder after controlling for blast exposure. In contrast, women were more likely to report severe/very severe symptoms on all four neurobehavioral symptom domains.

Discussion

To our knowledge, this is the first study analyzing gender differences in psychiatric conditions and neurobehavioral

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Psychiatric Diagnoses and Severe/Very Severe Neurobehavioral Symptoms for Women Relative to Men</th>
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<tbody>
<tr>
<td></td>
<td>Unadjusted Model</td>
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<tr>
<td></td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Psychiatric diagnoses (n = 12,507)</td>
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<tr>
<td>PTSD</td>
<td>0.70 0.60–0.82</td>
</tr>
<tr>
<td>Depression</td>
<td>1.95 1.67–2.29</td>
</tr>
<tr>
<td>Non-PTSD anxiety disorders</td>
<td>1.31 1.08–1.60</td>
</tr>
<tr>
<td>Adjustment disorders/stress reactions</td>
<td>1.22 0.95–1.57</td>
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<tr>
<td>Alcohol-related disorders</td>
<td>0.52 0.42–0.65</td>
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<tr>
<td>Drug-related disorders</td>
<td>0.59 0.41–0.84</td>
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<tr>
<td>1 diagnosis only</td>
<td>0.75 0.62–0.90</td>
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<tr>
<td>2 or more diagnoses</td>
<td>1.20 1.02–1.40</td>
</tr>
<tr>
<td>PTSD and depression</td>
<td>1.53 1.30–1.80</td>
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<tr>
<td>Severe neurobehavioral symptoms (n = 12,605)</td>
<td></td>
</tr>
<tr>
<td>Affective</td>
<td>1.21 1.03–1.42</td>
</tr>
<tr>
<td>Somatosensory</td>
<td>2.09 1.57–2.78</td>
</tr>
<tr>
<td>Cognitive</td>
<td>1.26 1.06–1.49</td>
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<tr>
<td>Vestibular</td>
<td>1.86 1.40–2.48</td>
</tr>
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Abbreviations: CI, confidence interval; OR, odds ratio.

Note. Reference group is males.

All of the analyses that adjust for blast have also been adjusted for etiology (blast, bullet, fall, vehicle, other blunt trauma), marital status, education, employment, rank, service, age, and years of service. The four neurobehavioral symptom domains were obtained from a factor analysis of the Neurobehavioral Symptom Inventory-22 (described under Methods). Neurobehavioral symptom severity scores were dichotomized into ‘none/mild/moderate’ (mean scale score < 3) or ‘severe/very severe’ (mean scale score ≥ 3) groups.

* p < .005 (corrected for multiple comparisons).

† Any isolated diagnosis from the above categories.

‡ Two or more diagnoses included any two of the above categories.

§ p < .012 (corrected for multiple comparisons).

Regarding other gender differences in psychiatric diagnoses, consistent with the general population of OEF/OIF VA patients (Maguen et al., 2010), univariate analyses demonstrated women were more likely than men to have a non-PTSD anxiety disorder (20.3% vs. 16.3%) and less likely than men to have alcohol (16.2% vs. 27.0%) and drug-related disorders (4.9% vs. 8.2%). However, the magnitude of these gender differences are more pronounced in the current sample relative to the general population of OEF/OIF VA patients (Maguen et al., 2010). It is noteworthy that the gender effect for non-PTSD anxiety disorders and drug-related disorders was not maintained once controlling for blast exposure. Despite these important gender differences, women and men did not differ significantly in terms of adjustment disorders or stress reactions. Additionally, contrary to our hypotheses, women were no more likely than men to have multiple psychiatric diagnoses, with approximately half of veterans of either gender (53.2% of women, 48.7% of men) being diagnosed with two or more psychiatric conditions.

The univariate associations between gender and PTSD (59.6% of the women compared with 67.8% of the men) was not maintained after controlling for blast exposure. This finding suggests that men’s greater likelihood of blast exposure (Table 1), possibly from greater combat exposure (Hoge, Clark, & Castro, 2007), may account for their higher likelihood of having a PTSD diagnosis. This adjusted finding is consistent with previous research demonstrating a lack of gender differences in terms of PTSD among veterans, controlling for specific deployment-related stressors (Kimerling, Ouimette, & Weitlauf, 2007). Additionally,
approximately 38% of women had diagnoses of PTSD with comorbid depression compared with 28% of the men. Thus, PTSD with comorbid depression is a prominent women’s health issue among VA patients judged to have deployment-related TBI.

Findings did support our hypothesis that women would report more severe neurobehavioral symptoms. Specifically, women were significantly more likely to report ‘severe’ or ‘very severe’ symptoms on three of the four neurobehavioral symptom domains in the univariate analyses (the exception being affective symptoms) and all four of the symptom domains in the multivariate analyses adjusting for blast exposure. These findings match results from studies examining gender differences in neurobehavioral symptoms among athletes with TBI (Colvin et al., 2009; Dick, 2009). Although the mechanisms associated with these worse outcomes remain unknown, these findings suggest that in addition to the identification and treatment of psychiatric conditions, it is critical that clinicians attend to the affective, somatosensory, cognitive, and vestibular symptoms experienced by women veterans with deployment-related TBI. Recognition of these symptoms in women veterans enables clinicians to better tailor treatment approaches for women’s specific health care needs. For example, a woman who reports severe cognitive symptoms may benefit from cognitive remediation (French, Iverson, & Bryant, 2011). Likewise, increased detection of neurobehavioral symptoms among women veterans may lead to improvements in coordination of care for women in mental health, as well as physical and occupational rehabilitation settings. Consistent with the literature pertaining to VA care for women (Yano, Washington, Goldzweig, Caffrey, & Turner, 2003), the current findings also suggest the importance of interdisciplinary treatment of women VA patients with mild TBI.

In light of the high rates of psychiatric and neurobehavioral comorbidities observed in this study, the current findings can help guide clinicians’ use of specific therapy options for their female patients with TBI and these co-occurring conditions, particularly PTSD and depression. In particular, cognitive–behavioral therapies for PTSD are very effective in ameliorating veterans’ symptoms of both PTSD and depression (Iverson, Lester, & Resick, 2011), and at this time there is no evidence that these treatments need to be significantly altered for patients with mild TBI. On the contrary, there is preliminary evidence that Cognitive Processing Therapy (Resick, Monson, & Chard, 2010), an empirically supported treatment for PTSD that is widely available in the VA, is effective for reducing PTSD and depression symptoms among veterans with TBI with little alteration to the protocol (Chard, Schumm, McIlvain, Bailey & Parkinson, in press). Yet, some clinicians understandably worry that existing cognitive–behavioral therapies, such as Cognitive Processing Therapy, are too reliant on memory and thus may be inappropriate for patients with TBI (Sayer et al., 2009). Clinicians should keep in mind that many evidence-based therapies, such as Cognitive Processing Therapy, can be altered to meet the needs of individual patients with TBI (e.g., longer or shorter sessions, greater repetition of materials, engagement of family members to promote treatment adherence) while still maintaining fidelity to the treatment model.

Several limitations of this study should be noted, because they point to avenues for future research. Although the determination of TBI was established via structured clinical interviews and is thus an asset of the study, the VA Comprehensive TBI Evaluation has not undergone an evaluation of sensitivity and specificity in terms of accuracy of determining TBI. Similarly, the psychiatric diagnoses were derived from ICD-9 codes. Although this method is common in research examining psychiatric conditions among patients of large health care systems (Carlson et al., 2010; Fann et al., 2004; Kimerling et al., 2010), these diagnoses can be subject to false-positive and false-negative cases. Thus, the current findings may not reflect the true rate of psychiatric disorders among this population and findings should be replicated using validated assessments of psychiatric conditions and more rigorous neurobehavioral symptom measures. Another limitation is that this study measured cognitive symptoms via a self-report measure. Additional research is needed to replicate the current findings with cognitive performance measures because subjective cognitive complaints have been found be related to mood, such as depressive symptoms (Marino et al., 2009).

Another study limitation is the cross-sectional nature of the research design. As such, a causal relationship cannot be inferred between deployment-related TBI and the psychiatric conditions and neurobehavioral symptoms. Future longitudinal research should evaluate the nature of these relationships, as well as elucidate mediating and moderating variables that may help to explain gender differences in health outcomes among veterans with deployment-related TBI. In addition to blast exposure, researchers should investigate a broader range of deployment-related stressors that may contribute to gender differences (and lack thereof), including sexual trauma and combat severity. Given that only half of the veterans who screened positive for TBI underwent a Comprehensive TBI Evaluation, it is possible that the current sample is an underestimate of the true rate of OEF/OIF veterans with deployment-related TBI. Research is needed to elucidate patient-, provider-, and facility-level factors that impact the likelihood a patient will go on to receive a Comprehensive TBI Evaluation after a positive TBI screen. For example, patient-level factors, such as mental health diagnoses or cognitive disturbances, may impact a veteran’s willingness or ability to arrange and attend such an appointment. There may also be differences in how clinicians provide feedback about a positive TBI screen and referrals for the evaluation that may influence variation in rates of receiving a Comprehensive TBI Evaluation. Additionally, it is important to remember that the current findings based on VA patients may not generalize to patients in other health care settings. Future inquiries should include samples of veterans who do not utilize VA health care to determine if the pattern of findings presented herein is maintained. Future research is also needed to further identify and treat symptoms (e.g., pain) that are of high clinical relevance in female patients judged to have mild TBI. Finally, it is essential to monitor whether evidence-based treatments for conditions such as PTSD and depression lead to improvements in neurobehavioral symptom severity for women VA patients judged to have deployment-related TBI.

In summary, there are gender differences in the comorbidities of deployment-related TBI among OEF/OIF VA patients. It is important to continue to understand these differences, as well as similarities, to inform practices to provide the highest quality care possible for women veterans.

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