

Evaluation of posttraumatic stress disorder diagnosis and therapy on diurnal blood pressure patterns from 24-hour ambulatory blood pressure monitoring

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Abstract

Introduction: The veteran population has a high incidence of posttraumatic stress disorder (PTSD), which is associated with increased risk of hypertension and cardiovascular death. Ambulatory blood pressure monitoring (ABPM) can identify abnormal diurnal blood pressure (BP) patterns, which are associated with increased risk of cardiovascular events. The intent of this evaluation was to examine prior ABPM studies to determine whether veterans with PTSD are more likely to have abnormal nocturnal dipping patterns compared with the general veteran population.

Methods: Retrospective chart review was performed on all archived ABPM studies and classified by nocturnal dipping status and BP control rates. Pertinent patient demographics of age, sex, concomitant PTSD, and use of selected PTSD therapies were identified at the time of ABPM study. Association between dipping status, BP control rates, and patient demographics were analyzed using appropriate statistical tests.

Results: A total of 470 ABPM studies were determined to be valid and included. There were no differences in the distribution of nocturnal dipping patterns in veterans with or without PTSD. Likewise, rates of nocturnal, awake, and 24-hour hypertension were similar between groups. In patients with PTSD who were treated with evening PTSD therapy, there was a higher rate of normal dipping status compared with those without treatment (66.7% vs 29.7%, $P = .03$).

Discussion: Veterans with PTSD had similar distributions of dipping patterns and rates of overall, awake, and nocturnal hypertension compared with the general veteran population. The association of nocturnal PTSD therapy prescription in patients with PTSD and higher rates of normal dipping status may warrant further investigation.

Keywords: posttraumatic stress disorder, ambulatory blood pressure monitoring, blood pressure, veterans, nocturnal dip, hypertension

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Introduction

Hypertension is the leading cause of cardiovascular disease, and the prevalence increases with age.¹ The veteran population has a high incidence of posttraumatic stress disorder (PTSD), which has been associated with an increased risk of hypertension and cardiovascular death.²⁻⁵ It has been postulated that these findings may be due to increased stress, catecholamine release, and sleep disturbances related to PTSD symptoms.^{6,7} A potential

manifestation of these effects is the lack of a nocturnal “dip” in blood pressure (BP). Information regarding a patient’s “dipping” status is derived from the results of 24-hour ambulatory BP monitoring (ABPM).⁸ The use of ABPM and the prognostic impact on cardiovascular events have been documented previously. A full review of the outcomes associated with nocturnal “dip”—drop in BP during nocturnal versus diurnal state—is beyond the scope of this article. In brief, recent meta-analyses^{9,10} demonstrated that nocturnal systolic BP independently predicts cardiovascular events compared with daytime or clinic BP readings, and failure to have an appropriate 10% to 20% drop in nocturnal BP is associated with increased cardiovascular events. Furthermore, in cases where a nocturnal blood pressure increase occurred, an association with increased mortality was observed.¹⁰ Current clinical practice at the West Palm Beach Veterans’ Affairs Medical Center, in accordance with published guidelines, is to investigate for secondary or precipitating factors for abnormal dipping patterns in an effort to improve cardiovascular risk management.⁸

Studies in patients with PTSD have used ABPM as a tool for cardiovascular monitoring and to examine the correlation with PTSD symptoms.¹¹⁻²³ Many of these studies^{12,19-23} have been conducted in the veteran population, although study populations are generally small. Results from these trials have shown increases in heart rate, systolic BP, and diastolic BP in PTSD patients compared with non-PTSD patients. However, only 3 studies¹¹⁻¹³ have examined nocturnal dipping status as a cardiovascular marker. These studies found significant increases in the presence of nondipping in patients with disrupted sleep patterns resulting from traumatic or stressor symptoms. The populations evaluated were women and young African American adults, but none was solely a veteran population. Studies¹⁹⁻²³ have suggested the utility of ABPM for identification of cardiovascular risk but have been limited by sample size. Evaluation of historical ABPMs at West Palm Beach Veterans’ Affairs Medical Center will provide an opportunity to examine BP status and nocturnal dipping patterns in a veteran population to characterize trends in veterans with and without PTSD.

Methods

All archived ABPM recordings from January 14, 2008, through September 21, 2016, performed at West Palm Beach Veterans’ Affairs Medical Center were retrospectively reviewed in addition to pertinent data from each individual medical record. Ambulatory BP monitoring studies were conducted using AND software version 2.20 (A&D Company Ltd, Tokyo, Japan) until February 2014 and subsequently transitioned to AccuWin Pro

TABLE 1: Dipping statuses and definition⁸

Dipping Classification	Ratio: Nocturnal SBP/Awake SBP
Normal dip—“dipper”	0.8-0.9
Mild dip—“nondipper”	1.0-0.9
Extreme dip	<0.8
Reverse dip	>1.0

SBP = systolic blood pressure.

version 3.4 software (Suntech Medical, Morrisville, NC) and Suntech Oscar2 Model 222 ABPM devices (Suntech Medical) thereafter. Ambulatory BP monitoring results were classified by dipping status and uncontrolled BP rates. Dipping status was calculated as the average nocturnal systolic BP divided by the average awake systolic BP and defined by current consensus definitions as normal dip (>0.8 and <0.9 or 10%-20% nocturnal BP fall), reduced or mild dip (<1.0 and >0.9 or 1%-10% nocturnal BP fall), reverse dip (>1.0 or rise in nocturnal BP), and extreme dip (<0.8 or greater than 20% nocturnal BP fall; Table 1).⁸ Rates of uncontrolled BP were defined by consensus definition for ABPM in respective time periods (overall >130/80 mm Hg; awake >135/85 mm Hg; asleep >120/70). Ambulatory BP monitoring results were considered invalid and excluded if it was determined there were more than 30% of unacceptable readings during evaluation, a minimum number of readings was not obtained in the nocturnal period, the veteran did not sleep, or the results were determined invalid by provider. Specific details regarding exclusion are available in the Figure.

Pertinent patient demographics (age and sex), concomitant PTSD diagnosis, and nocturnal PTSD treatment were collected as documented at the time of ABPM measurement by chart review of the Veterans’ Affairs Computerized Patient Record System. The Computerized Patient Record System is an electronic medical record that allows review of a patient’s medical problems, progress notes, laboratory and diagnostic results, and records of outpatient and inpatient medications. Nocturnal pharmacologic treatments identified for data collection, as most commonly used at the West Palm Beach Veterans’ Affairs Medical Center, were nighttime administrations of prazosin, clonidine, and quetiapine. The primary end point of this evaluation was the rates of various dipping status between patients with or without a PTSD diagnosis. Secondary end points evaluated were the rates of uncontrolled BP in regard to PTSD diagnosis and also the effect of nocturnal PTSD pharmacotherapy on these aforementioned ABPM parameters.

Descriptive statistics were used to characterize patient demographics. Statistical significance among the popula-

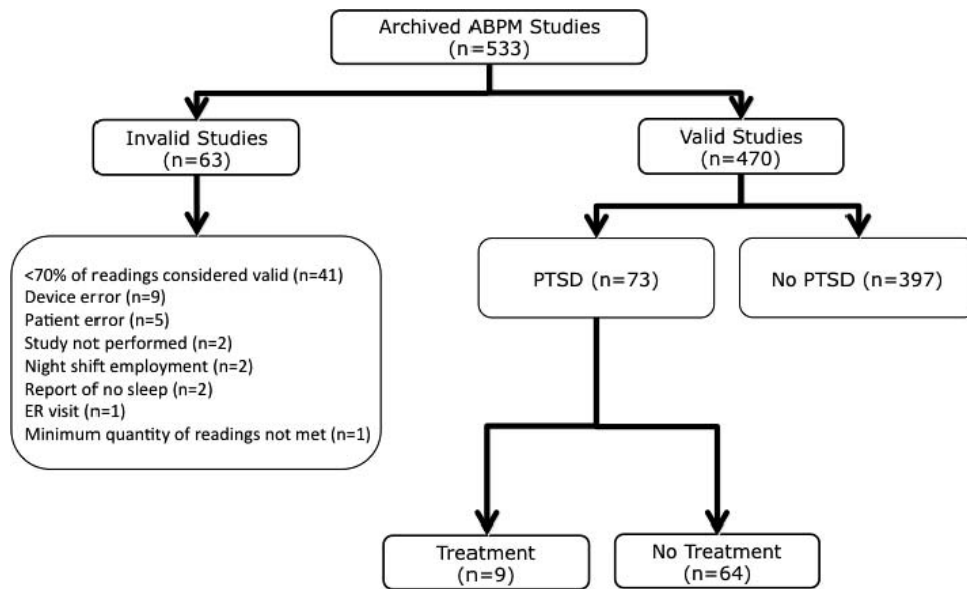


FIGURE: Evaluation of ambulatory blood pressure monitoring (ABPM) studies for inclusion and exclusion (ER = emergency room; PTSD = posttraumatic stress disorder)

tion was determined for continuous data by Student *t* test. The χ^2 test for independence was used to determine statistical significance between dipping status, BP control rates, and selected patient demographics. All analyses were performed using Microsoft Excel 2000 (Redmond, WA).

The West Palm Beach Veterans' Affairs Medical Center's Scientific Advisory Committee approved the protocol for

TABLE 2: Baseline patient demographics and study outcomes

	PTSD (%), n = 73	No PTSD (%), n = 397	<i>P</i> Value ^a
Age, y, mean ± SD	66.3 ± 11.1	70.1 ± 10.7	.005
Male	97.3	93.5	.21
Dipping status			.39
Normal	34.2 (25)	36.0 (143)	.77
Mild	41.1 (30)	34.0 (135)	.24
Extreme	13.7 (10)	11.8 (47)	.65
Reverse	11.0 (8)	18.1 (72)	.13
Ambulatory blood pressure monitoring results			
Awake BP >135/85	47.9 (35)	52.6 (209)	.46
Nocturnal BP >120/70	53.4 (39)	61.2 (243)	.21
Overall BP >130/80	52.1 (38)	59.4 (236)	.24
PTSD nocturnal treatment	12.3 (9)
Prazosin	11.0 (8)
Quetiapine	1.4 (1)
Clonidine	0 (0)

BP = blood pressure; PTSD = posttraumatic stress disorder.
^aStatistical significance is based on χ^2 tests or Student *t* test, as appropriate.

this evaluation as part of the facility's ongoing performance improvement efforts, as defined by Veterans' Health Administration Handbook 1058.05.²⁴

Results

A total of 533 ABPM studies were completed and available to review for inclusion (Figure). Of those, 88 (16.5%) had been performed for veterans with concomitant PTSD. After initial review, 63 studies were excluded from the analysis: 15 studies for veterans with PTSD and 48 for veterans without PTSD. The reasons for exclusion are available in the Figure. Veterans with PTSD had numerically higher rates of invalid studies compared with veterans without PTSD: 17.0% versus 10.8%, respectively (*P* = .096).

Veterans with a diagnosis of PTSD who underwent ABPM were relatively similar to those without PTSD except they tended to be younger (66.3 ± 11.1 vs 70.1 ± 10.7 years, *P* = .005). There were no differences in the distribution of the rates of dipping statuses in veterans with PTSD compared with those without PTSD. Individually, the frequencies of normal dippers (34.2% vs 36.0%), mild dippers (41.1% vs 34.0%), extreme dippers (13.7% vs 11.8%), and reverse dippers (11.0% vs 18.1%) were similar in veterans with PTSD compared with veterans without PTSD, respectively (*P* > .05 for all comparisons; Table 2).

Most of our population who underwent ABPM had hypertension that was not controlled during at least 1 measured period (overall, awake, or asleep). The rates of uncontrolled hypertension were similar between veterans

TABLE 3: Subgroup analysis for nocturnal posttraumatic stress disorder treatment

	Treatment (%) n = 9	No Treatment (%) n = 64	P Value ^a
Age, y, mean ± SD	57.9 ± 12.4	67.4 ± 10.5	.018
Male	100	96.9	.59
Dipping status			.14
Normal	66.7 (6)	29.7 (19)	.029
Mild	11.1 (1)	45.3 (29)	.051
Extreme	11.1 (1)	14.1 (9)	.81
Reverse	11.1 (1)	10.9 (7)	.99
Ambulatory blood pressure monitoring results			
Awake BP >135/85	88.9 (8)	42.2 (27)	.008
Nocturnal BP >120/70	77.8 (7)	50.0 (32)	.12
Overall BP >130/80	88.9 (8)	46.9 (30)	.018

BP = blood pressure.

^aStatistical significance is based on χ^2 tests or Student *t* test, as appropriate.

with PTSD and without PTSD in the awake period (47.9% vs 52.6%, respectively), asleep period (53.4% vs 61.2%, respectively), and overall period (52.1% vs 59.4%, respectively).

Among veterans with a diagnosis of PTSD, only 9 (12.3%) were prescribed nocturnal PTSD pharmacologic treatment. A total of 8 veterans were prescribed prazosin, and 1 veteran was taking evening quetiapine. No veterans were prescribed clonidine exclusively to be administered in the evening. Further analysis of the PTSD population did not reveal a significant difference in the rate of dipping statuses between those receiving or not receiving nocturnal PTSD pharmacotherapy (Table 3). However, patients with PTSD taking versus not taking nocturnal PTSD therapy had a higher likelihood of having a normal dipping status ($P=.029$; Table 3). Also, nocturnal PTSD treatment appeared to influence rates of uncontrolled nocturnal BP in patients with PTSD, because those on treatment had a higher incidence of uncontrolled awake ($P=.008$) and overall ($P=.018$) BPs but no nocturnal values (Table 3).

Discussion

The utility of ABPM to evaluate cardiovascular effects has previously been established, although further analysis is needed in larger populations, especially in the veteran population, where the prevalence of PTSD is high. To our knowledge, our study is the largest evaluation of ABPMs in a veteran population with PTSD. The prevalence of PTSD in the veteran population is estimated to be

between 15% and 30%, and this was also true with our observations in our ABPM cohort.² The analysis of our cohort revealed no differences in dipping statuses between veterans with PTSD and those without. However, upon further analysis of veterans with PTSD receiving nocturnal pharmacotherapy, treatment was associated with a higher rate of normal dipping pattern, although this was a very small population. Also, although patients on nocturnal treatment had significantly higher rates of uncontrolled BP in the awake and overall periods, this was not seen in the nocturnal period following the administration of nocturnal treatment. This finding may be evidence of a prescribing bias, in that a veteran with more severe PTSD symptoms would have elevated BP during the awake period (potentially attributed to daytime PTSD symptoms), yet with nocturnal treatment results in a double fashion of pharmacologic BP lowering (α adrenergic inhibition) and reduction in symptoms.

Mellman et al¹³ conducted the first study to evaluate BP dipping and PTSD, in which a significant relationship was found between dipping status and both current and lifetime PTSD severity in young African American adults. In this population, they found a nondipping rate, defined as dip less than 10%, of 43%, with a majority (specific values not given) in the “mild,” or 0% to 10%, range. In a follow-up study in a larger cohort of young adult African Americans with urban stressors and a lower incidence of PTSD, Mellman et al¹¹ found a lower percentage (38%) of participants with dipping ratio less than 10%, but they maintained a significant correlation with dipping status and urban stressors. Although we were unable to correlate dipping status with degree of PTSD symptom severity through a validated PTSD assessment tool or to ask about PTSD symptoms occurring during the ABPM study period because of our study’s retrospective nature, patients are questioned during the appointment for device removal for abnormal events during the session. However, questioning is relatively informal and there were very few documented occurrences of PTSD symptoms, if reported. Yet, in terms of frequency of dipping ratios, we report findings similar to those of prior studies in the rates of “mild” dipping status, which was the predominant classification of our PTSD cohort.

Our findings also echo the findings of Ulmer et al¹² in women with PTSD, in which a small proportion (15%) were military veterans. The frequency of nondippers versus dippers did not differ among those with a PTSD diagnosis (68% vs 53%, $P=.23$); however, a greater number of traumatic events were associated with nondipping status. It is possible that no difference was found, despite prior evidence suggesting PTSD is associated with abnormalities in dipping status, due to confounding by indication. Veterans are referred to the ABPM clinic for suspicions of abnormal BP findings and may not

adequately represent a true control group to compare PTSD diagnosis.

With the reported prevalence of PTSD in our study near the lower threshold of the expected range, it is possible that PTSD was underestimated in our ABPM population for a number of reasons and reduced the likelihood of observing a difference if one were present. First, because chart reviews rely on correct and adequate documentation, it is possible that veterans with undocumented PTSD were included in the non-PTSD group. Second, we found that 5 patients, who did not have a PTSD diagnosis at the time of ABPM, did in fact receive a diagnosis of PTSD at a later time. It is unlikely that the reclassification of these individuals into the PTSD cohort would have influenced results, but it highlights a potential confounding issue.

Limitations of our study include its retrospective design, resulting in the possibility of residual or unmeasured confounding. As stated above, chart reviews rely on correct and adequate documentation, which potentially could have allowed undocumented PTSD to be included in the PTSD group. Also, other factors associated with variable dipping statuses (eg, obstructive sleep apnea, elderly, resistant hypertension in which antihypertensives are solely administered in the morning, etc) were not evaluated, which could have had an impact on the evaluations of dipping profiles and had an impact on interpretation of results with regard to impact of possible PTSD on dipping status.²⁵ Strengths of the Veterans' Affairs Computerized Patient Record System include the ability to link and review medical and pharmacy records from other VA hospitals nationally. Drawbacks to this system are the inability to capture admissions to outside hospitals and medications prescribed by these hospitals. However, medication reconciliation is performed at each ABPM consult visit by a clinical pharmacy specialist, with non-Veterans' Affairs medications entered into the medical record manually, potentially controlling as able for thorough medication documentation.

First-line treatment for PTSD is reserved for selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs).²⁶ However, we did not collect data on SSRI or SNRI use, for several reasons. As first-line treatments for PTSD, SSRIs and SNRIs are prescribed to a large majority of veterans with PTSD, and these classes of medications are also indicated for a variety of disease states, both mental health–related and non–mental health-related, and use would be prevalent in the non-PTSD group as well. With a focus on examining effects on dipping status, and given the pharmacologic understanding that SSRIs and SNRIs are of continuous action once steady-state is achieved, a reduction of symptoms would affect all periods of BP measurement and have little effect on the dipping ratio. However, our

findings do suggest that treatment may have an effect on ABPM parameters, despite the fact that there was no correlation in prior study.¹⁰ Further study of SSRI/SNRI use, or administration of benzodiazepines (although not recommended in PTSD) and their potential influence on nocturnal dipping status may be of merit.

Although the effect of PTSD on dipping status remains unclear, it appears that nocturnal pharmacotherapy may increase the likelihood of normal dipping status. Reverse dipping status is associated with an increased risk of cardiovascular events, but evidence is not available to confirm whether adjusting therapy to target a normal dipping status improves cardiovascular outcomes. Future research is needed to determine whether it is necessary to try and normalize dipping ratios.

In a single-center review, veterans with PTSD had similar distributions of nocturnal dipping patterns compared to the general veteran population, and there appears to be no difference in the rates of elevated overall, awake, and nocturnal BPs in patients with PTSD and the general population referred for ABPM. The association of nocturnal PTSD therapy prescription in patients with PTSD and higher rates of normal dipping status may warrant further investigation.

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