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Original Article

# Clinical outcomes associated with orthostatic hypotension among oncology patients in the inpatient rehabilitation setting

Michael Ranando[1], Amy Ng[2], Ekta Gupta Sharma[2], Yi Huang[3], Melany Martin[4], Stacey Rivers[4], Ying Guo[2]

[1]University of Texas Medical Branch, School of Medicine, Galveston, United States
[2]Department of Palliative, Rehabilitation and Integrative Medicine, University of Texas MD Anderson Cancer Center, Houston, United States
[3]Dexcom Incorporated, Clinical Studies, San Diego, United States
[4]Department of Rehabilitation Services, University of Texas, MD Anderson Cancer Center, Houston, United States

## Abstract

**Objectives:** This study aims to identify the prevalence of orthostatic hypotension (OH) in inpatient rehabilitation (IPR) in a comprehensive center and to assess the associated risk factors, treatment applied and its association with length of stay (LOS) and overall survival (OS).

**Patients and methods:** Between February 2023 and September 2024, a total of 199 consecutive oncology patients who were admitted to IPR unit and had orthostatic vital signs were retrospectively analyzed. The patients were divided into two groups according to the OH status as the OH group (n = 107) and non-OH group (n = 92). Data including demographics, disease characteristics, OH risk factors, management, Functional Independence Measure (FIM) transfer and ambulation scores, hospital and IPR LOS and OS were recorded. The OH status was assessed during the initial and final physical therapy evaluations.

**Results:** Of the patients, 117 were male and 82 were female with a median age of 68 (range, 57 to 75) years. Treatment of OH were as follows: compression stocking (47/92, 51%), abdominal binder (36/92, 39%), hydration (22/92, 24%), midodrine (11/92, 12%), discontinuation of antihypertensive medication (15/92, 16%) and fludrocortisone (4/92, 4%). Hospital and IPR LOS were similar between those who had OH and those who did not ($p$ = 0.13 and $p$ = 0.056, respectively).

**Conclusion:** Our study results showed that OH was common among oncology patients admitted to IPR. Although OH was not significantly associated with FIM transfer scores, IPR LOS, or mortality, its high prevalence indicates the importance of early identification and appropriate management in the rehabilitation setting. The strongest association observed was between OH and the use of alpha-2 adrenergic agonists, highlighting the importance of careful medication review and blood pressure monitoring in this population. Close monitoring of orthostatic vital signs, volume status, and medications upon admission may facilitate the early identification and management of patients at increased risk for OH.

***Keywords:*** Inpatient rehabilitation, length of stay, neoplasms, orthostatic hypotension, risk factors, survival.

Orthostatic hypotension (OH) refers to a failure of the cardiovascular and autonomic nervous systems to compensate for postural changes in hemodynamics.[1,2] Under circumstances of inadequate cardiac reserve, volume depletion, or autonomic nervous system failure, patients with

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**Correspondence:** Michael Ranando, DPT. University of Texas Medical Branch, School of Medicine, Galveston, United States.

**E-mail:** mdranand@utmb.edu

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OH mount inadequate hemodynamic responses to changes in position that reduce venous return, resulting in impaired homeostatic adaptation and manifestations may include presyncopal symptoms, syncope, lightheadedness, dizziness, fatigue and falls due to postural changes.[3]

Orthostatic hypotension is highly prevalent among elderly patients, with up to 20% of patients above the age of 65 meeting diagnostic criteria in a recent meta-analysis.[2,4] Despite a variety of therapeutic strategies, including both non-pharmacological (e.g., lower extremity compression, abdominal binder, oral or intravenous hydration) and pharmacological (e.g., midodrine, droxidopa), OH contributes significantly to morbidity and mortality in this population. Falls of any etiology in the elderly (age > 65) are associated with an estimated $50 billion in annual United States healthcare costs.[5,6]

Patients with cancer represent a population at increased risk of both developing OH and experiencing its adverse outcomes.[1] In addition to increased risk of injuries associated with falls, activity limitations associated with OH contribute to impaired rehabilitation capacity and lower functional status in patients with cancer.[1] Reduced function renders patients less able to tolerate cancer treatment. Prevalence estimates for OH among patients with cancer range from 16.7 to 57.5%, with patients with advanced disease and those receiving radiotherapy of the head and neck at greatest risk.[7,8] However, the data regarding the impact of OH on patients with cancer is limited. The prevalence of OH in cancer inpatient rehabilitation (IPR) setting has not been examined in the literature. In this study, we aimed to identify the prevalence of OH in IPR in a comprehensive center and to assess the associated risk factors, treatment applied and its association with length of stay (LOS) and overall survival (OS).

## PATIENTS AND METHODS

This single-center, retrospective study was conducted at a comprehensive cancer center, Department of Physical Medicine and Rehabilitation between February 2023 and September 2024. Of a total of 490 consecutive oncology patients, 199 who were admitted to IPR unit and had orthostatic vital signs were included. Those who did not have orthostatic vital signs were excluded from the study. Patients diagnosed with OH were medically managed by Physical and Rehabilitation Medicine (PRM) physicians utilizing compression stockings, abdominal binders, hydration, midodrine, fludrocortisone, and discontinuation of antihypertensive medications. A written informed consent was obtained from each patient. The study protocol was approved by the University of Texas MD Anderson Cancer Center Institutional Review Board (IRB) (Date: June 23, 2023, IRB no: 2023-0414).

The patients were divided into two groups according to the OH status as the OH group (n = 107) and non-OH group (n = 92). The EPIC electronic medical records were reviewed, and the following data were collected: patient demographics (i.e., age, race, sex), admission and discharge Functional Independence Measure (FIM) score for transfer and ambulation, disease characteristics, risk factors, clinical documentation and management of OH, hospital and IPR LOS, as well as OS. Clinical documentation of OH for admission was performed during initial PT evaluations, and documentation of OH for discharge was performed during the patient's final PT session. The FIM instrument uses an ordinal scale to rate the level of assistance required in the performance of activities of daily living and mobility tasks, with a score of 1 for total assistance and 7 for complete independence.[9] The terms "orthostatic" and "orthostasis" were searched, with confirmation by documentation of OH defined by the consensus criteria of a decrease in systolic blood pressure ≥ 20 mmHg and/or diastolic blood pressure ≥ 10 mmHg within 3 min in the upright position. Subsequent management of OH was searched and summarized.[1]

### Statistical analysis

Statistical analysis was performed using the R version 4.6.1 software (R Foundation for Statistical Computing, Vienna, Austria). Continuous data were presented in mean ± standard deviation (SD) or median (min-max), while categorical data were presented in number and

frequency, where applicable. The proportion of OH along with a 95% confidence interval (CI) was estimated. Demographic and clinical variables of interest by OH (Yes/No) using t-test, rank-sum test, chi-square test of Fisher exact test depending on the underlying distribution of the data. Two-sided Wilcoxon rank-sums test were used to compare the LOS between the group. Overall survival was estimated using the methods of Kaplan-Meier test and compared by OH using a log-rank test. The Cox proportional hazards regression was conducted to estimate the hazard ratio and 95% CI for OH. Overall survival was calculated from date of IPR admission to earliest date of death or last follow up. A $p$ value of $< 0.05$ was considered statistically significant.

## RESULTS

Of a total of 199 patients included in the study, 117 were male and 82 were female with a median age of 68 (range, 57 to 75) years. Baseline demographic and clinical characteristics of the patients are shown in Table 1.

The majority of patients (84%) were White, and a minority (41%) were women. There was an even distribution across the various categories of cancer diagnoses with central nervous system (CNS) tumors (21%), leukemia (12.5%), and lymphoma (13%), demonstrating the highest prevalence. A majority (64%) were found to have advanced disease, which we defined as a Stage III or Stage IV diagnosis. The most common comorbidities were

**Table 1. Patient characteristics (n = 199)**

| Variable | n | % | Median | Min-Max |
|---|---|---|---|---|
| Age (year) | | | 68 | 57-75 |
| Sex | | | | |
| Female | 82 | 41 | | |
| Race or ethnic group | | | | |
| Asian | 7 | 3.6 | | |
| Black or African American | 9 | 4.7 | | |
| White | 172 | 84 | | |
| Other | 9 | 6.6 | | |
| Cancer type | | | | |
| Leukemia | 24 | 12.5 | | |
| Lymphoma | 25 | 13 | | |
| Multiple myeloma | 7 | 3.5 | | |
| Breast cancer | 5 | 2.5 | | |
| Lung | 14 | 7 | | |
| Head and neck | 16 | 8 | | |
| Melanoma | 9 | 4.5 | | |
| GI | 17 | 8.5 | | |
| GU | 17 | 8.5 | | |
| Gyn | 3 | 1.5 | | |
| Sarcoma | 17 | 8.5 | | |
| Central nervous system tumor | 42 | 21 | | |
| Other | 3 | 1.5 | | |
| Advanced disease | 128 | 64 | | |
| PMH | | | | |
| Parkinson's disease | 2 | 1 | | |
| Hypertension | 118 | 59 | | |
| Diabetes mellitus | 43 | 22 | | |
| Peripheral neuropathy | 81 | 41 | | |
| Syncope | 11 | 5.5 | | |
| Fall | 17 | 8.5 | | |
| Comorbidities during hospitalization | | | | |
| Malnutrition | 49 | 25 | | |
| Adrenal insufficiency | 9 | 4.5 | | |
| Atrial fibrillation or other arrhythmia | 57 | 29 | | |
| Median hospital stay (days) | | | 26 | 21-38 |
| Median IPR stay (days) | | | 11 | 8-14.5 |

GI, gastrointestinal; GU, genitourinary; Gyn, gynecological; PMH, past medical history; IPR, inpatient rehabilitation.

hypertension (59%), atrial fibrillation (29%), and malnutrition (25%) (Table 2).

The OH group had a higher median age, although there was not a statistically significant difference in the demographic characteristics between the two groups ($p > 0.05$). We compared the risk factors and comorbidities between the groups, and the only significant difference was a higher prevalence of alpha-2 adrenergic agonist medication use in the OH group ($p < 0.0001$). Anti-hypertensive medications such as beta-blockers and calcium channel blockers, as well as diuretics had a similar between-group prevalence. Comorbidities such as malnutrition,

**Table 2. Comparison of patients with and without OH**

| | Non-OH group (n = 107) | | | | | OH group (n = 92) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | Mean ± SD | Median | Min-Max | n | % | Mean ± SD | Median | Min-Max | *p* |
| Age (year) | | | 62.4 ± 15.4 | | | | | 66.6 ± 14.6 | | | 0.054 |
| Sex<br>Female | 46 | 43 | | | | 36 | 39 | | | | 0.54 |
| Race<br>Asian<br>Black<br>Other<br>White | <br>5<br>5<br>7<br>89 | <br>4.7<br>4.7<br>6.6<br>84 | | | | <br>2<br>4<br>2<br>83 | <br>2.2<br>4.4<br>2.2<br>91 | | | | 0.37 |
| Advanced cancer | 66 | 62 | | | | 62 | 67 | | | | 0.40 |
| BMI | | | 28 ± 23.32 | | | | | 28 ± 24.31 | | | 0.87 |
| Parkinson's disease | 0 | 0 | | | | 2 | 2.2 | | | | 0.21 |
| Hypertension | 61 | 57 | | | | 57 | 62 | | | | 0.48 |
| Diabetes mellitus | 21 | 20 | | | | 22 | 24 | | | | 0.49 |
| Peripheral neuropathy | 49 | 46 | | | | 32 | 35 | | | | 0.11 |
| Syncope | 8 | 7.5 | | | | 3 | 3.3 | | | | 0.19 |
| Fall | 7 | 6.5 | | | | 10 | 11 | | | | 0.28 |
| Malnutrition | 21 | 20 | | | | 28 | 30 | | | | 0.078 |
| Adrenal insufficiency | 4 | 3.7 | | | | 5 | 5.4 | | | | 0.74 |
| Atrial fibrillation or other arrhythmia | 31 | 29 | | | | 26 | 28 | | | | 0.091 |
| Dopamine agonist | 0 | 0 | | | | 3 | 3.3 | | | | 0.1 |
| Anti-depressant/antipsychotic | 50 | 47 | | | | 37 | 41 | | | | 0.39 |
| SSRI/SNRI | 26 | 24 | | | | 24 | 26 | | | | 0.77 |
| Pregabalin/gabapentin | 33 | 31 | | | | 32 | 35 | | | | 0.55 |
| Antihistamine | 29 | 27 | | | | 30 | 33 | | | | 0.4 |
| Anticholinergic | 1 | 0.9 | | | | 2 | 2.2 | | | | 0.6 |
| PPI | 60 | 56 | | | | 63 | 68 | | | | 0.073 |
| Diuretic | 12 | 11 | | | | 17 | 18 | | | | 0.15 |
| Alpha blocker | 12 | 11 | | | | 10 | 11 | | | | 0.94 |
| Beta blocker | 32 | 30 | | | | 21 | 23 | | | | 0.26 |
| Alpha-2 adrenergic agonist | 10 | 9.3 | | | | 26 | 28 | | | | **< 0.001** |
| Angiotensin II receptor blocker | 18 | 17 | | | | 13 | 14 | | | | 0.6 |
| ACE inhibitor | 10 | 9.3 | | | | 8 | 8.7 | | | | 0.87 |
| Ca channel blocker | 23 | 21 | | | | 21 | 23 | | | | 0.82 |
| Vasodilator | 8 | 7.5 | | | | 3 | 3.3 | | | | 0.19 |
| Hospital LOS | | | | 24 | 19-38 | | | | 29 | 22-37 | 0.13 |
| IPR LOS | | | | 10 | 7-14 | | | | 12 | 8-15 | 0.056 |

OH, orthostatic hypotension; SD: Standard deviation; BMI, body mass index; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin norepinephrine reuptake inhibitor; PPI, proton pump inhibitor; ACE, angiotensin converting enzyme; LOS, length of stay; IPR, inpatient rehabilitation.

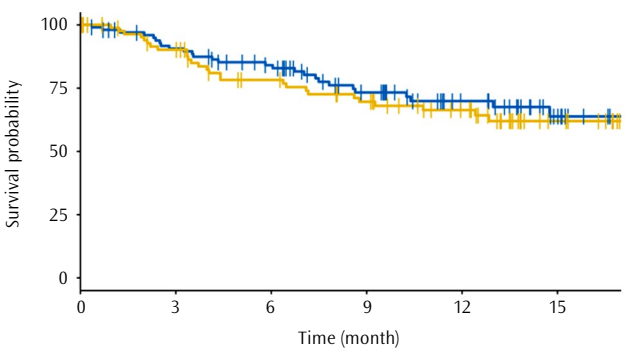
hypertension, arrhythmias, and diabetes also demonstrated similar between-group prevalences (Table 2). Additionally, there was no significant difference in the FIM scores at admission compared to discharge in patients with and without OH. Patients in the OH group were treated with compression stockings (47/92, 51%), abdominal binder (36/92, 39%), hydration (22/92, 24%), midodrine (11/92, 12%), discontinuation of antihypertensive medication (15/92, 16%) and fludrocortisone (4/92, 4%) (Table 3).

Figure 1 depicts the impact of OH on OS. There was no statistically significant difference in survival between those who were admitted to IPR with OH and those who were admitted without OH ($p$ = 0.57). The data used for the Kaplan-Meier analysis in Figure 1 includes 100 patients from the non-OH group, and 88 patients from the OH group. Seven patients from the original non-OH group and four patients from the original OH group were excluded from this analysis due to missing data from chart review.

**Table 3. Treatment of OH during IPR (n = 92)**

| Management | n | % |
|---|---|---|
| Discontinue anti-HTN meds | 15 | 16 |
| Hydration | 22 | 24 |
| Compression stocking | 47 | 51 |
| Abdominal binder | 36 | 39 |
| Fludrocortisone | 4 | 4 |
| Midodrine | 11 | 12 |
| Internal medicine consult | 13 | 14 |

OH, orthostatic hypotension; IPR, inpatient rehabilitation; HTN, hypertension.




| Number at risk | | | | | | |
|---|---|---|---|---|---|---|
| IPR adm. OH = N | 100 | 85 | 71 | 50 | 33 | 15 |
| IPR adm. OH = Y | 88 | 72 | 56 | 47 | 35 | 13 |

**Figure 1.** Impact of OH during IPR on overall survival.
OH, orthostatic hypotension; IPR, inpatient rehabilitation; adm., admission.

## DISCUSSION

In the present study, we evaluated the prevalence of OH in IPR and identified the associated risk factors, treatment applied and its association with LOS and OS. Our study results showed that there was insufficient statistical evidence to connect OH diagnosis with rehabilitation outcomes in the IPR setting. These findings suggest that additional multi-center, large-scale, prospective studies with standardized orthostatic vitals assessment are needed to further investigate the effect of OH and its management in the IPR setting.

Characterizing clinical outcomes for patients with cancer and OH is critical to identifying prognostic factors and developing protocols to effectively manage the patients most at risk for prolonged hospital admissions or negative rehabilitation outcomes. A meta-analysis conducted by Angelousi et al.[5] reported that OH increased the overall risk of mortality by 36%. Iwański et al.[7] also found that type of cancer played a significant role in the prevalence of OH, and that patients with the most common cancer types such as lung and breast had a two-fold increased risk of having OH. The aforementioned authors also showed that 57.5% of patients with lung cancer and 37.5% of patients with breast cancer had OH compared to 16.5% ($p$ = 0.003) in patients who did not have a cancer diagnosis. The pathophysiology of OH can be classified as neurogenic or non-neurogenic. Neurogenic causes include cases such as Parkinson's disease, Lewy body dementia, multiple system atrophy, and peripheral neuropathy. Non-neurogenic causes include volume depletion, cardiovascular diseases, adrenal insufficiency, and physical deconditioning. The higher prevalence of OH in oncology patients undergoing systemic chemotherapy may be explained by the common side-effects such as chemotherapy-induced peripheral neuropathy (CIPN), physical deconditioning, and volume depletion as demonstrated in the studies by Shaheen et al.[6] and Cortes et al.[8]

In the current study, out of 199 individuals diagnosed with cancer, 92 (46.2%) were diagnosed with OH upon admission to IPR. Those individuals who were diagnosed with OH had a median IPR LOS of 12 days (95% CI: 8-15), and those without OH had a median IPR LOS of 10 days (95% CI: 7-14), although the difference was not statistically significant ($p$ = 0.056). However, this finding warrants further investigation in a larger study population to determine whether a clinically meaningful association exists. The early detection and treatment of OH in our IPR could shorten their IPR stay. We found that the median hospital LOS for participants with OH was 29 (range, 22 to 37) days, and the median hospital LOS for participants without OH was 24 (range, 19 to 38) days. Although this difference was not statistically significant ($p$ = 0.13), further investigation in a larger study population may be warranted.

In our study, OH was strongly associated with the use of alpha-2 adrenergic agonists ($p < 0.001$). While the association between OH and alpha-2 adrenergic agonists has been long established, it is clinically relevant to recognize the role this medication could play in prolonging IPR and hospital LOS in oncology patients.[10]

Furthermore, management of OH in our cohort was predominantly non-pharmacological, with lower-extremity compression, abdominal binders, and oral or intravenous hydration being the most frequently used interventions. This approach is consistent with the multifactorial nature of OH in patients with cancer, in whom contributing factors may include malnutrition, reduced oral intake, and volume depletion. A smaller proportion of patients required pharmacological treatment, including midodrine and fludrocortisone, particularly in the context of associated adrenal insufficiency.[11] However, the present study did not evaluate whether the type or timing of OH interventions was associated with rehabilitation outcomes. Future studies should examine these relationships to determine whether specific management strategies or earlier intervention may influence functional recovery and other rehabilitation outcomes. Prospective, multi-center studies incorporating standardized OH assessment at admission and discharge, together with a standardized management protocol, are warranted to further elucidate the impact of OH and its management on rehabilitation outcomes in patients with cancer.

Nonetheless, there are certain limitations to this study that should be acknowledged. First, this was a retrospective study conducted at a single institution, and the study population was predominantly White. Therefore, the findings may not be generalizable to other hospital settings or to more racially and ethnically diverse populations of patients with cancer. Second, the diagnosis of OH was determined through retrospective chart review and was, therefore, dependent on the completeness of vital-sign documentation during the initial physical and occupational therapy evaluations. Although physical therapists were instructed to perform a complete orthostatic assessment during the initial evaluation of all admitted patients, orthostatic vital-sign data were missing from a substantial proportion of medical records (291/490). Furthermore, patients with symptomatic OH may have been more likely to undergo a complete orthostatic assessment than asymptomatic patients, potentially introducing ascertainment bias. Third, vital-sign measurements from patients with severe symptoms of OH who were unable to tolerate standing were also classified as incomplete data sets and were documented similarly to those of asymptomatic patients with missing orthostatic measurements. Consequently, the prevalence of OH among patients unable to tolerate standing could not be separately assessed. These factors may have influenced the estimated prevalence of OH in our study population. Systematic and standardized documentation of orthostatic vital signs in all patients with cancer at regular intervals may provide more accurate estimates of the prevalence of OH in this population.

In conclusion, OH was common among oncology patients admitted to IPR. Although OH was not significantly associated with FIM transfer scores, IPR LOS, or mortality, its high prevalence indicates the importance of early identification and appropriate management in the rehabilitation setting. The strongest association

observed was between OH and the use of alpha-2 adrenergic agonists, highlighting the importance of careful medication review and blood pressure monitoring in this population. Close monitoring of orthostatic vital signs, volume status, and medications upon admission may facilitate the early identification and management of patients at increased risk for OH. Further multi-center, large-scale, prospective studies using standardized OH assessment and management protocols are warranted to further characterize risk factors and determine the impact of OH and its management on rehabilitation outcomes in patients with cancer.

**Declaration of Conflicting Interests**

The authors declare that there are no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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**Author Contributions**

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**Data Availability**

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

**AI Disclosure**

The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or 'hallucinate' references, and that all references have been carefully verified for accuracy.

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