Symptom-related emergency department visits and hospital admissions during ambulatory cancer treatment

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Background People with cancer experience symptoms related to the disease and treatments. Symptom distress has a negative impact on quality of life (QoL). Attending to symptoms and side effects of treatment promotes safe and effective delivery of therapies and may prevent or reduce emergency department visits (EDVs) and unplanned hospital admissions (HAs). There is limited evidence examining symptom-related EDVs or HAs (sx-EDV/HAs) and interventions in ambulatory oncology patients.
Objective To examine factors associated with sx-EDV/HAs in ambulatory oncology patients receiving chemotherapy and/or radiation.
Methods This secondary analysis used data from a randomized controlled trial of ambulatory oncology patients (n = 663) who received the web-based Electronic Self-Report Assessment – Cancer intervention (symptom self-monitoring, tailored education, and communication coaching) or usual care with symptom self-monitoring alone. Group differences were described by summary statistics and compared by *t* test. Factors associated with the odds of at least 1 sx-EDV/HA were modeled using logistic regression.
Results 98 patients had a total of 171 sx-EDV/HAs with no difference between groups. Higher odds of at least 1 sx-EDV/HA were associated with socioeconomic and clinical factors. The multivariable model indicated that work status, education level, treatment modality, and on-treatment Symptom Distress Scale-15 scores were significantly associated with having at least 1 sx-EDV/HA.
Limitations This is a secondary analysis not sized to determine cause and effect. The results have limited generalizability.
Conclusion Most patients did not experience a sx-EDV/HA. Demographic and clinical factors predicted a sx-EDV/HA.
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People with cancer can experience distress associated with symptoms stemming from the disease itself and/or symptoms resulting from treatments and associated side effects. Symptom distress has a negative impact on patient quality of life (QoL), affecting the physical, psychological, social, and spiritual domains of life.[1] Managing cancer symptoms and QoL issues are high priorities for oncology clinicians.[2] Furthermore, attending to symptoms and side effects of treatment promotes safe and effective delivery of cancer therapies and may prevent or reduce the use of emergency department (ED) services and unplanned hospital admissions (HAs).

The results of several descriptive, retrospective studies examining the clinical factors associated with emergency department visits (EDVs) and hospital admissions (HAs) in people with cancer suggest that relevant factors include symptoms and diagnoses.[3-5] Common symptoms associated with EDVs and HAs in people with cancer include pain, gastrointestinal symptoms, fever, dyspnea, and nausea and vomiting.[3,5-7] Patients who have had a recent hospitalization are at increased risk of another HA.[4] In addition, people with lung cancer[3,5,6] and those with respiratory and other comorbid conditions may also be at increased risk of an EDV or HA.[4,8]

In summary, symptoms, cancer diagnoses, and comorbid conditions are associated with EDVs and HAs. Fever alone or fever with neutropenia is a strong predictor of an EDV or HA in people receiving chemotherapy or with newly diagnosed cancers, including hematologic malignancies.[6,7] Other symptoms including pain, problems related to the gastrointestinal and respiratory systems, and specific cancer diagnoses are also associated with EDVs and HAs. Attending to symptoms and problems before presentation to the ED may prevent or reduce use of ED services and the number of HAs.

We found 4 studies that examined cancer symptom management and EDVs and HAs: one in women with gynecologic cancer,[9] a second in ambu-

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latory patients with breast or lung cancer receiving chemotherapy or radiation therapy,[10] a third in patients with head and neck cancer receiving concurrent chemo-radiotherapy,[11] and a fourth based on a sample of patients receiving chemotherapy for the first time.[8] EDV and HA outcomes reported in those studies were mixed, suggesting that further investigation is needed.

Most studies that have focused on EDVs and HAs in people with cancer were retrospective and medical record reviews; intervention studies have been mostly limited to patients receiving chemotherapy alone. Therefore, we planned an analysis of prospective trial data from patients with various diagnoses and therapies. The purpose of this study was to examine the factors associated with symptom-related EDV/HAs (sx-EDV/HAs) in ambulatory oncology patients who were receiving chemotherapy and/or radiation therapy.

Methods

Study design and sample

This secondary analysis used data from a randomized controlled trial of the Electronic Self-Report Assessment for Cancer (ESRA-C).[12] The trial was conducted in 2 comprehensive cancer centers during April 2009-June 2011 with approval by the Institutional Review Boards of the Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium and the Dana-Farber/Harvard Cancer Center. A total of 752 eligible adult, ambulatory patients with any type of cancer, who had started a new therapeutic regimen, were enrolled and randomized. The web-based ESRA-C intervention is an easy-to-use, patient-centered technology with patient-self-report assessments plus education tailored to moderate and severe symptom and quality of life reports, and provides patient-to-provider communication coaching. Participants in both trial groups used ESRA-C to self-report symptoms and quality of life (sx-QoL) once at each of the following study time points: T1, before starting a new cancer therapy; T2, at 3-6 weeks; T3, 6-8 weeks after T2; and T4, at the end of the therapy regimen. Randomized trial outcomes resulted in significantly lower symptom distress over the course of treatment and significantly more frequent detailed patient communication of sx-QoL.[12,13]

Most of the sx-EDV/HAs (58%) occurred within the first 2 months on study, therefore only the sx-QoL reports at T1 (baseline) and T2 (first on-treatment time point) were used for this analysis. Treatment and EDV/HA data from a medical record review were available for 663 participants (327 control, 336 intervention) who received chemotherapy and/or radiation therapy. A sx-EDV/HA was defined as an EDV or HA that was initiated with a patient-reported symptom. All reported EDVs and HAs were documented as mutually exclusive events; an EDV that resulted in an HA was coded as an HA.

Analysis

The number of sx-EDV/HAs were described with summary statistics and compared between the study groups with a 2-group, unequal variance *t* test. A *t* test was deemed appropriate given the large sample size of the study.[14] In addition, the odds of having at least 1 sx-EDV/HA were modeled using logistic regression considering a list of preselected variables including study group, financial difficulties, work status, education level, minority status, gender, age, stage, emotional functioning, Symptom Distress Scale-15 score (SDS-15), depression, months on study, age-adjusted comorbidity, and treatment type (radiation, chemotherapy, or both). Sociodemographic characteristics were collected at baseline only. Covariates were first assessed with univariate analyses and then adjusted in a multivariable analysis. The backwards elimination method was used with the Akaike information criterion (AIC) for variable selection in the multivariable model. Type III *P* values were used to assess the overall significance and variables with a *P* value of .1 or less were retained in the model. All analyses were conducted in SAS (version 9.2) and R (version 2.15.2).

Results

Baseline sociodemographic, clinical, and environmental characteristics for the total sample (N = 663; 327 control and 336 intervention) are provided in Table 1. Of the total number of patients, 49 of the 327 control patients had a least 1 sx-EDV/HA, accounting for 96 total sx-EDV/HAs. Of the 336 intervention patients, 49 had at least 1 sx-EDV/HA, for a total of 75 sx-EDV/HAs. The most common reasons for a sx-EDV/HA were pain, fever, and nausea. Forty-seven patients presented with pain for a total of 74 EDV/HAs, 37 presented with a fever for a total of 52 EDV/HAs, and 23 presented with nausea for at total of 40 EDV/HAs (Table 2). A majority of the patients (85%) did not have any sx-EDV/HAs during the analytic period. Of the patients with at least 1 sx-EDV/HA, 58% had only 1, 28% had 2, 7% had 3, 4% had 4, and 3% had 5 or more (data not shown). On average, each patient had 0.26 sx-EDV/HA overall, which corresponds to about 1 sx-EDV/HA in 4 patients. There was no statistically significant group difference in the mean number of sx-EDV/HAs (*P* = .28); 0.22 sx-EDV/HA per patient (roughly 1 in 5) in the intervention group, and 0.29 sx-EDV/HA per patient (roughly 1 in 4) in the control group.

The results from univariate analyses (Figure 1) suggest that higher odds of at least 1 sx-EDV/HA were associated with not working (*P* = .001, OR = 2.13, 90% CI, 1.46-3.13), lower education (*P* = .008, OR = 1.92, 90% CI, 1.29-2.90), stage IV disease (*P* < .0001, OR = 2.40, 90% CI,

TABLE 1 Patient baseline sociodemographic, clinical, and environmental characteristics (N = 663)

Characteristic	No. of patients (%)
Median age: 58 y (range, 19-88)	—
Gender	
Male	333 (50)
Female	330 (50)
Disease stage	
IV	221 (33)
Other	442 (67)
Race/ethnicity	
Minority[a]	61 (9)
Non-minority[b]	553 (80)
Unknown	69 (10)
Treatment type	
Chemotherapy	370 (56)
Radiation	151 (23)
Both	138 (21)
Unknown	4 (<1)
Work status	
Working	392 (59)
Not working	203 (31)
Unknown	68 (10)
Education level	
≥ Some college[c]	530 (80)
High school or less	131 (20)
Unknown	2 (<1)
Study group	
Intervention	336 (51)
Control	327 (49)

[a]Hispanic, Asian, Native Hawaiin or Pacific Islander, black or African American, American Indian/native Alaskan. [b]Caucasian, white, non-Hispanic. [c]Not necessarily a graduate – includes anyone with some college education, as well as graduates and postgraduates.

TABLE 2 The total number of EDV/HAs with presenting symptoms, and the number of patients with at least 1 EDV/HA with presenting symptom (n = 98 patients)

Symptom	No. of EDV/HAs[a]	No. of patients (%) with ≥ 1 EDV/HA[b]
Anxiety	2	2 (2)
Anorexia	3	3 (3)
Bowel-related	15	10 (10)
Breathing-related	22	15 (15)
Cough	13	12 (12)
Delirium	1	1 (1)
Depression	2	1 (1)
Fatigue	11	10 (10)
Fever	52	37 (38)
Nausea	40	23 (23)
Neuropathy	0	0 (0)
Pain	74	47 (48)
Skin-related	5	5 (5)
Weak	8	8 (8)
Other	28	26 (26)

EDV/HA, emergency department visit/hospital admission

[a]The sum of the number of EDV/HA visits overall; a patient could have had an EDV/HA for more than 1 symptom in a visit and more than 1 EDV/HA is possible per patient. bThe number of patients with at least 1 EDV/HA for the given symptom; the percentage, out of 98 patients, with at least 1 EDV/HA, for the given symptom.

1.67-3.46), receiving chemotherapy alone compared with radiation alone (P = .003, OR = 5.25, 90% CI, 2.56-10.79), and receiving chemotherapy and radiation compared with radiation alone (P = .004, OR = 5.61, 90% CI, 2.59-12.16). Higher odds of a sx-EDV/HA also were associated with a higher SDS-15 score at T1 (P < .0001) and a higher SDS-15 score at T2 (P < .0001), with an odds ratio of 1.83 (90% CI, 1.45-2.33) at T1 and 1.83 (90% CI, 1.43-2.34) at T2 per 10-point increase on SDS-15. In addition, higher odds of a sx-EDV/HA were associated with higher depression at T1 (P = .02, OR = 1.8, 90% CI, 1.20-2.71) and T2 (P = .0002, OR = 2.64, 90% CI, 1.71-4.07), and longer time on study (P = .02, OR = 1.52, 90% CI, 1.13-2.04). Comparatively, a 10-point decrease in emotional functioning was associated with higher odds of a sx-EDV/HA at T1 (P = .003, OR = 1.16, 90% CI, 1.08-1.27) and T2 (P = .001, OR = 1.19, 90% CI, 1.08-1.30). The odds of at least 1 sx-EDV/HA was not significantly different by gender (P = .41).

Emotional functioning, depression, and SDS-15 scores, at both T1 and T2, were highly correlated (data not shown). Working status and stage of disease also were strongly associated (P < .0001). Each of the correlated sxQoL scores were modeled separately and the backwards elimination method yielded three possible models involving T1 SDS-15, T2 SDS-15, and T2 depression. The common significant variables in each of the models were education and treatment modality. By the AIC criterion, the selected multivariable model indicated that work status (P = .0003), education level (P = .008), treatment modality (P = .03), and the T2 SDS-15 score (P = .0003) were significantly predictive of having at least 1 sx-EDV/HA. Similar to that in the univariate analyses, the higher odds of at least 1 sx-EDV/HA were associated with not working (OR = 2.22, 90% CI, 1.39-3.57), lower education (OR = 2.33, 90% CI, 1.37-3.85), chemotherapy versus radiation (OR = 5.27, 90% CI, 1.90-14.59), chemotherapy and radiation versus radiation (OR = 5.82, 90% CI, 2.00-16.88), and an increase in T2 SDS-15 (OR = 1.07, 90% CI, 1.04-1.10). When adjusting for other factors, the study group was not

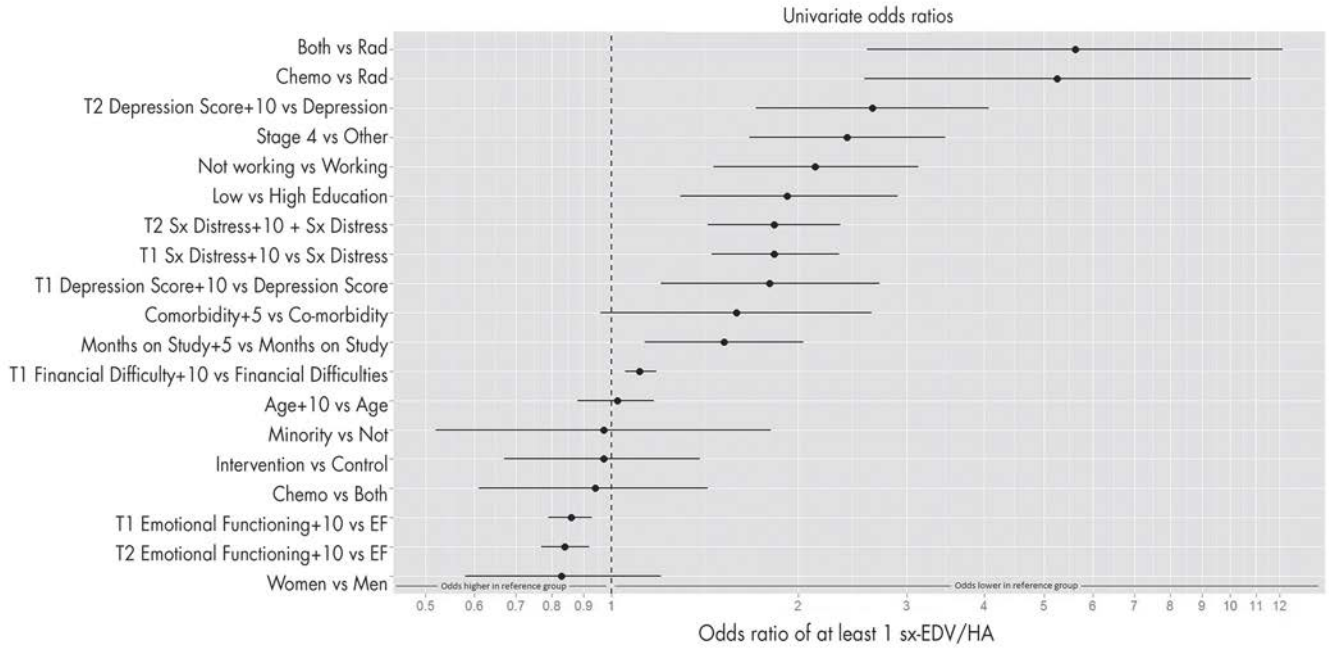

FIGURE Univariate logistic regression to evaluate the odds of at least 1 symptom-related EDV/HA for various predictors.

EDV/HA, emergency department visit/hospital admission; sx, symptom-related; T1, baseline (before starting a new cancer therapy); T2, first on-treatment time point (3-6 weeks after therapy initiation)

Note: The displayed continuous variables represent a 10-point increase for age, Symptom Distress Scale-15 score, emotional functioning, depression, financial difficulties; a 5-point increase for months on study and age adjusted comorbidity index.

TABLE 3 Logistic multivariable regression to evaluate the association between various predictors and the odds of a patient experiencing at least 1 sx-EDV/HA (n = 466)

	Selected model			Containing study group	
Variable	**OR estimate**	***P* value**	**90% CI, OR**	**OR estimate**	***P* value**
Intervention vs control	—	—	—	1.08	.7784
T2 SDS-15 score[a]	1.07	.0003	(1.04, 1.10)	1.07	.0003
Low vs high education level	2.23	.0081	(1.37, 3.87)	2.31	.0080
Not working vs working	2.30	.0048	(1.37, 3.56)	2.23	.0050
Treatment type					
Chemotherapy vs radiation	5.27	.0342	(1.90, 14.59)	5.27	.0339
Chemotherapy+ radiation vs radiation alone	5.82	.0215	(2.00, 16.88)	5.81	.0218

CI, confidence interval; OR, odds ratio; SDS-15, Symptom Distress Scale-15; sx-EDV/HA, symptom-related emergency department visit/hospital admission; T2, first on-treatment time point (3-6 weeks after therapy initiation)

[a]466 patients of the 663 total had a T2 Symptom Distress Scale-15 score

significantly associated with the odds of at least 1 sx-EDV/HA (Table 3).

Discussion

In a sample of ambulatory oncology patients with various cancer diagnoses, we found that pertinent sociodemographic and clinical factors were associated with sx-EDV/HAs, which included education level, work status, symptom distress, and treatment with chemotherapy with or without radiation compared with radiation alone. Our participants had a lower rate of sx-EDV/HAs than the rates reported in retrospective medical record review studies examining factors associated with the frequencies of EDVs and HAs.[6,7,15]

In other studies of ambulatory oncology patients who were receiving chemotherapy, frequencies varied widely for any type of EDV or HA.[6,7] Livingston and colleagues[6] reported 772 of 2,380 oncology outpatients (32.5%) used the ED at least once, with a range of 1-15 visits per patient; more than half of the EDVs required an HA. In McKenzie and colleagues,[7] 233 of 316 (73.7%) patients who had received chemotherapy within six months made an EDV and 87.6% of all EDVs resulted in an HA. Our data were from patients who had enrolled in a clinical trial and may have been more conscious of care and symptom management at home. All the patients were receiving active treatment and reporting symptoms regularly; all of the providers were given patient report summaries before each outpatient visit. The self-reporting in the intervention group and provider reports may have increased early recognition, awareness, and treatment of symptoms before they escalated to problems that would warrant an EDV or HA. Also, we limited our analysis to sx-EDV/HAs, whereas other studies reported all EDVs or HAs, including, for example, comorbidities and cancer diagnoses; the visits or admissions were not reported separately by associated factors.

Not surprisingly, we found that greater symptom distress while on treatment was associated with the higher odds of a sx-EDV/HA. The 3 common presenting symptoms, pain, fever and nausea, in our data, are similar to several retrospective reviews addressing common symptoms or diagnoses[3-5] associated with EDVs or HAs. Barbera and colleagues3 conducted a large, retrospective review of administrative health care data in Ontario from patients with cancer who had died between 2002-2005 (N = 76,759) and reported that patients made 194,017 EDVs during the last 6 months of life. Abdominal pain was the most common symptom recorded for the sx-EDVs. Other common symptoms associated with sx-EDVs included dyspnea, malaise and fatigue, chest pain, and nausea and vomiting.[3] Swenson, and colleagues[5] also reported gastrointestinal symptoms and pain as the 2 most common symptoms in people with cancer who made an EDV.

In a sub analysis using a randomly selected sample (n = 443) from a retrospective medical record review (N = 2,380) of 2007 data, Livingston and colleagues[6] reported that fever and neutropenia were the most frequent EDV diagnoses followed by nausea and vomiting, dehydration and abdominal pain for ambulatory patients with cancer. In a sample of patients (N = 363) receiving outpatient chemotherapy, McKenzie and colleagues[7] reported that fever or fever and neutropenia, and pain were the most common reasons for unplanned hospital presentations.

Our original randomized trial was not planned to detect a significant difference in the rate of sx-EDV/HAs; we observed a lower, though statistically insignificant, rate for the ESRA-C intervention group compared with the control group. In studies examining in-person and telephone nursing interventions that targeted symptoms in people receiving chemotherapy with or without radiation therapy for cancer, differences in rates of EDVs and HAs have been reported for those receiving the intervention compared with those who did not.[8,9,11] Kurz and colleagues[8] used a cognitive behavioral nursing intervention over a 20-week period in a sample in which the majority of patients (65%) had late stage disease; symptom severity and the number of comorbidities were predictive of EDVs. The frequency of EDVs was lower in the intervention group, there was a trend toward fewer HAs, and when only those patients with greater symptom severity were examined, there was a reduction in the number of HAs in the intervention group.[8] McCorkle and colleagues[9] tested an advance practice nurse (APN) intervention in women with ovarian cancer and found that the intervention group reported more EDVs and there was no difference in HAs between the 2 groups. The authors suggested that the APN may have instructed the women in the intervention group to make an after-hours EDV for evaluation before symptom escalation.[9] In a retrospective medical record review comparing HAs, in patients who received concurrent chemo-radiotherapy before and after a nurse practitioner-led clinic was established, the patients who were seen regularly in the NP-led clinic experienced fewer HAs.[11]

In our sample, we found that late-stage disease, highly correlated with not working, was a predictor of sx-EDV/HAs. However, we did not have a sufficient number of patients to analyze the subset of late-stage patients who were likely to have greater symptom severity compared with all other patients for an intervention effect on sx-EDV/HAs.

Some sx-EDV/HAs may be avoidable. It is necessary to first understand the reasons for sx-EDV/HAs to develop interventions to prevent sx-EDV/HAs related to treatable symptoms and to assess patients for those symptoms that may herald a preventable or potentially more serious problem if they are not addressed early. For example, constipa-

tion, a common symptom that ranked 11th out of 30 of the most common reasons for an EDV in 1 report,[3] can often be prevented when the underlying cause is addressed. Constipation is related to opioid use for pain control in people with cancer and can be prevented when properly managed with laxatives.[16] And, if constipation is the result of other more serious etiologies such as gastrointestinal obstructions, early assessment of the symptom and interventions may prevent sx-EDV/HAs.

Clinicians would be best advised to consider providing greater attention and targeting interventions proactively to those individuals most at risk of a sx-EDV/HA. Our findings indicated that ambulatory oncology patients who have less education, are not working, report greater symptom distress, and are receiving chemotherapy with or without radiation therapy, were more likely to have a sx-EDV/HA. It is not entirely clear why those who were not working were at higher odds of having a sx- EDV/HA; however, work status and disease stage were related. Therefore, it is likely that patients with late-stage cancers were not working, were more burdened by symptoms, and were experiencing worse overall functionality than were those who reported that they were still working.[17] We also found that patients who were receiving chemotherapy or combined chemotherapy and radiation therapy were at higher odds of a sx-EDV/HA than were those who were receiving radiation alone. In a recently published descriptive study of ambulatory oncology patients who were receiving combined chemotherapy and radiation therapy for head and neck cancer, 13 of the 40 patients (33%) required an unplanned hospitalization during treatment; slightly greater than 50% of HAs (7 of 13) were symptom related.[18]

The patients in our study who were receiving radiation therapy alone had lower odds of a sx-EDV/HA. In people who are receiving radiation therapy alone without chemotherapy, the symptoms related to the radiation therapy may be delayed. For example, the severity, frequency,[19-21] and distress[20] associated with fatigue gradually increases during radiation therapy, peaks after therapy is completed, and decreases over several months after therapy. Therefore, the symptom distress in patients receiving radiation therapy alone may not have peaked until after our study period.

Limitations

Our findings cannot be generalized beyond a sample of ambulatory oncology patients who were majority race and ethnicity and college-educated. The original trial sample size was not planned to test differences in sx-EDV/HAs between study groups. All patients in this sample were ambulatory oncology patients with solid tumors who were receiving active treatment. Furthermore, they were all enrolled in a clinical trial and may have been monitored more closely than the general ambulatory oncology population, possibly resulting in better outcomes than in those who would not be enrolled in a clinical trial[22] and/or as a result of the Hawthorne effect.[23] The low number of sx-EDV/HAs limited our ability to study the relationships between EDVs and HAs. In addition, although the symptom-related reason for each EDV/HA was known, the symptom severity was not collected at the time of the sx-EDV/HA. We had no knowledge of other variables that occurred before the study time period.

Future work

There are few intervention studies examining sx-EDV/HAs among ambulatory oncology patients. Future work to confirm that certain groups of individuals, such as ambulatory oncology patients who have greater symptom severity, comorbid conditions, pertinent cancer diagnoses, or those patients who are receiving chemotherapy or who are not working are more likely to have a sx-EDV/HA would be useful information to help plan targeted interventions. Prospective studies that are designed to examine the effects of symptom management interventions and associated use of health care services would be beneficial to assess the impact of interventions and to further identify those who would receive the most benefit.

Conclusions

Overall, most of the patients in this sample of ambulatory oncology patients did not experience a sx-EDV/HA. The predictors associated with having at least 1 sx-EDV/HA were receiving chemotherapy with or without radiation therapy, lower education level, not working, and higher symptom distress scores. The implementation of symptom management strategies for those who are at high risk of sx-EDV/HAs and the evaluation of outcomes related to sx-EDV/HAs is warranted.

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