

**Original Article**

# Risk of Unplanned Hospital Encounters in Patients Treated With Radiotherapy for Head and Neck Squamous Cell Carcinoma



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**Abstract**

**Context.** Radiotherapy is highly effective for treating squamous cell carcinoma of the head and neck but is often associated with significant toxicities and severe morbidity. Unplanned emergency department (ED) visits and hospitalizations are common during treatment and come with a substantial financial and health burden as well as the potential for impaired long-term outcomes due to treatment disruption.

**Objectives.** The objective of this study was to identify patient, disease, and treatment characteristics that were associated with ED encounters and admissions.

**Methods.** A cohort of 462 patients with cancer of the head and neck treated with radiotherapy at UT Southwestern between 2010 and 2015 was retrospectively analyzed. The risks of ED visits, admissions, multiple admissions, and extended admissions were determined. Risk factors for an unplanned hospital encounter were analyzed using univariate and multivariate logistic regression.

**Results.** Overall, 36% of patients had an unplanned hospital encounter during the treatment window. Patients with advanced disease, those with high comorbidity score, and those treated with concurrent chemotherapy were more likely to have unplanned admissions/ED visits. Social factors such as marital status, smoking status, and registration in the public hospital system were also strongly associated with admissions and multiple encounters.

**Conclusion.** The high rate of admissions and ED visits emphasizes the importance of anticipating and managing toxicities during treatment. Social factors have a strong association with unplanned encounters and may present opportunities for targeted interventions to reduce admissions for patients at highest risk. *J Pain Symptom Manage* 2019;57:738–745. © 2018 Published by Elsevier Inc. on behalf of American Academy of Hospice and Palliative Medicine.

**Key Words**

*Hospitalizations, head and neck cancer, radiation therapy, chemoradiation, complications*

**Introduction**

Treatment for head and neck cancer is commonly associated with toxicities that may lead to unplanned emergency room visits and hospital admissions.<sup>1</sup> Although concurrent chemoradiotherapy (CRT) regimens have been clearly shown to improve overall

survival, they also significantly increase the risk of high-grade toxicities.<sup>2</sup> The majority of patients treated with CRT experience severe mucositis and dysphagia, and nausea and vomiting are other frequent side effects that can result in malnutrition and weight loss.<sup>3</sup> The natural history of pretreatment disease

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progression can also contribute to these complications. In one study, 19% of patients had already experienced critical weight loss at presentation before treatment due to disease-related symptoms.<sup>4</sup> Reduced physiologic reserve in these patients likely makes them more susceptible to treatment-associated toxicities.<sup>5</sup>

Admissions and emergency department (ED) visits reflect treatment-associated morbidities and are also a financial burden for patients. They may have direct effects on outcomes as well because long-term hospital stays can result in treatment breaks and extending the length of treatment has been associated with higher rates of local failure.<sup>6</sup> Treatment interruptions pose an even greater challenge for uninsured and economically disadvantaged patients, for whom coordination of care and access to health care resources is often compromised. In this population, treatment breaks have been shown to be associated with poorer long-term outcomes including disease control and even overall survival.<sup>7</sup>

Prior studies have suggested that both radiation dose and particular patient comorbidities, such as pulmonary disease and diabetes, are associated with an increased risk of hospitalization during treatment.<sup>8</sup> Identifying patients who are at increased risk of hospitalization during treatment would allow clinicians to target interventions such as prophylactic nutritional support and swallowing therapy that may reduce the incidence or severity of toxicities and thereby avoid treatment interruptions. Utilizing a large retrospective database of patients treated for head and neck cancer with definitive or adjuvant radiotherapy, we sought to identify characteristics associated with admissions and ED encounters during and soon after the completion of treatment. The large size of this single institution database, granular data on comorbidities, and inclusion of both insured and uninsured patients provided the opportunity to evaluate more potential risk factors for patients in a wider range of socioeconomic standing than was possible in prior studies.

## Methods and Materials

Medical records of 462 patients with squamous cell carcinoma of the head and neck who underwent radiotherapy at the University of Texas Southwestern Medical Center (UTSW) from 2010 to 2015 were analyzed under an IRB-approved protocol. Although all patients were irradiated at UTSW, many received the remainder of their oncologic and primary care at Parkland Hospital, Dallas's public safety net institution.

Patients were either treated with definitive radiotherapy or CRT, or they were treated with adjuvant RT

or CRT after transoral surgery for oropharyngeal cancer; this population was included because of their favorable performance status after surgery. Treatment with transoral surgery was used as a covariate and found to be unrelated to the risk of admission. Demographic, clinical, and treatment data were extracted from the electronic medical record. Modified ACE-27 comorbidity scores were calculated for each patient based on the initial radiation oncology consultation note.<sup>9</sup> Briefly, the severity of a patient's comorbidities were scored on a 0–3 scale based on the highest ranked single ailment, with 0 representing no comorbid conditions and 3 representing severely a decompensated comorbidity, such as a recent pulmonary embolism or myocardial infarction. A score of 1 represents mild decompensation such as adequately treated hypertension, congestive heart failure responsive to treatment, or diabetes well-controlled with oral medications. Grade 2 includes compensated hepatic failure, insulin-dependent diabetes, and morbid obesity. The cancer section of the score was not counted. If sufficient information about the severity of a comorbid condition was not available in the radiation oncology note, the most proximal medical oncology note was cross-referenced.

Unscheduled hospital admissions and ED encounters at Parkland Hospital and UT Southwestern that occurred during the course of radiotherapy or in the one month immediately after treatment completion were recorded. Planned hospital admissions for elective gastrostomy placement and chemotherapy infusions were not included.

Primary outcomes included any unplanned hospitalization or ED encounter, unplanned hospitalization only, multiple admissions, and length of admission, the latter of which was dichotomized at the median length of stay. Univariate analysis was performed using chi-squared test and univariate logistic regression, and multivariate logistic regression was performed using backward selection for all variables with a *P* variable 0.20 or less. Because Parkland Hospital affiliation was collinear with other candidate covariates, two sensitivity analyses were performed. First, a separate multivariable analysis was performed for patients treated at Clements University Hospital (CUH) alone. Second, a stratified logistic regression was performed, in which Parkland treatment was the stratifying variable. There was no correction for multiple comparisons. All statistics were calculated using SAS (Cary, NC).

## Results

### Patient Characteristics

Of the patients analyzed, 53% were registered in the Parkland Memorial Hospital electronic health record system, the public hospital for Dallas County. The

median patient age was 57 years, 81% were male, and most patients had an ACE-27 comorbidity score of 0 or 1. Twenty-three percent were currently smoking, and 31% had never smoked. The majority had cancer of the oropharynx (68%), and most patients presented with clinically advanced cancer: 67% had clinical Stage IVA-B disease. The majority of patients (81%) received concurrent chemotherapy during their radiation treatment course. The median radiation treatment time was 42 days (interquartile range, IQR 39–45). Patient characteristics are shown in [Table 1](#).

Overall, 36% of patients had at least one unplanned hospital encounter in the form of an ED visit alone or hospital admission preceded by an ED encounter during the treatment window. A total of 17.5% of patients experienced at least one ED visit without a subsequent admission, and 26% of patients were admitted to the hospital at least once during their treatment. Out of the 121 admitted patients, 65 patients (14% of the entire cohort, 54% of patients who were admitted) experienced more than one inpatient encounter. The mean longest length of stay for each patient was 6 days (median 5 days, IQR 3–7). The most common reasons for admission were dehydration/failure to thrive and gastrointestinal symptoms, including nausea, vomiting, constipation, or diarrhea. Other common causes for ED encounters and hospital admissions are shown in [Supplemental Table 1](#).

#### Unplanned ED Visits/Admissions

Univariate predictors of unplanned hospital encounters are shown in [Table 2](#). Increasing age was associated with an increased risk of hospital encounters, especially among patients in the highest age quartile of over 64 years (OR 1.78, 95% CI 1.04–3.06). The ACE-27 score was a potent predictor of hospital encounters, with a rise in OR observed with increasing ACE-27 scores. Patients with Stage IVA-B disease were more likely to have an admissions or ED visit (OR 4.79, 95% CI 1.01–22.70), but there was no significant effect seen from tumor site. Certain treatment factors were also associated with unplanned encounters, with more encounters occurring in patients with a PEG feeding tube (OR 2.96, 95% CI 1.94–4.53) and in those who were treated with concurrent chemotherapy (OR 2.44, 95% CI 1.41–4.22).

The role of social factors was also examined in this analysis. Patients who were enrolled in the public Parkland Hospital system and unmarried patients had odds ratios for admissions or ED visits of 3.22 and 2.00, respectively ([Table 2](#)). Current smokers also had a higher rate of admissions/ED encounters (OR 2.33, 95% CI 1.37–3.97).

On multivariate regression, increasing age was associated with a higher rate of unplanned encounters, up

*Table 1*  
**Patient Characteristics**

Value	Number (%)
Number of patients	462
Age	
Min	27
25% quartile	51
Median	57
75% quartile	64
Max	93
ACE-27 score	
0	162 (35)
1	180 (39)
2	87 (19)
3	33 (7)
Tumor site	
Oropharynx	312 (68)
Larynx	95 (21)
Hypopharynx	19 (4)
Nasopharynx	36 (8)
Ethnicity	
Caucasian	323 (70)
African American	76 (16)
Hispanic	36 (8)
Asian	20 (4)
Other	2 (0.4)
Unknown	5 (1)
Sex	
Male	373 (81)
Female	89 (19)
Marital status	
Married	260 (56)
Single	118 (26)
Unknown	32 (7)
Smoking	
Never smoker	141 (31)
Ever smoker	214 (46)
Current smoker	106 (23)
Hospital system	
UTSW	219 (47)
Parkland	243 (53)
PEG	
Not present	180 (39)
Present	282 (61)
Elective PEG	
Not present	268 (58)
Present	194 (42)
p16 status	
Negative	47 (15)
Positive	188 (60)
Unknown	77 (25)
Clinical stage	
I	13 (3)
II	21 (5)
III	94 (20)
IVA	210 (45)
IVB	101 (22)
Unknown	23 (5)
Concurrent chemo	
No (%)	90 (19)
Yes (%)	372 (81)

ACE = adult comorbidity evaluation; PEG = percutaneous endogastric gastrostomy (feeding tube).

to an OR of 3.13 for patients in the highest age quartile ([Table 2](#)). Consistent with the univariate results, female gender, concurrent chemotherapy, and enrollment in the Parkland hospital system (OR 3.89, 95% CI 2.51–6.04) were significantly associated

Table 2  
Unplanned Admissions or ED Encounters

Characteristic	Encounters (%)	UVA OR (CI)	MVA OR (CI)	MVA <i>P</i>	CUH OR (CI)	CUH <i>P</i>
Age						
First quartile	30	REF	REF	0.0017		
Second quartile	37	1.33 (0.77–2.31)	1.44 (0.80–2.58)			
Third quartile	34	1.17 (0.67–2.04)	1.28 (0.71–2.31)			
Fourth quartile	43	1.78 (1.04–3.06)	3.13 (1.70–5.75)			
ACE-27						
0	29	REF			REF	0.0454
1	35	1.32 (0.83–3.12)			2.18 (0.97–4.90)	
2	43	1.81 (1.05–3.12)			1.86 (0.66–5.21)	
3	58	3.32 (1.54–7.16)			9.62 (1.76–52.41)	
Tumor site						
Oropharynx	36	REF				
Larynx	33	0.87 (0.53–1.41)				
Hypopharynx	37	1.04 (0.40–2.72)				
Nasopharynx	44	1.43 (0.71–2.87)				
Gender						
Male	33	REF	REF	0.0164	REF	0.0049
Female	48	1.90 (1.19–3.04)	1.85 (1.12–3.06)		3.24 (1.43–7.35)	
Marital status						
Married	29	REF				
Single	45	2.00 (1.34–3.00)				
Smoking						
Never smoker	27	REF			REF	0.0169
Ever smoker	37	1.59 (1.00–2.52)			1.95 (0.89–4.24)	
Current smoker	46	2.33 (1.37–3.97)			5.20 (1.66–16.37)	
Hospital system						
CUH	22	REF				
Parkland	48	3.22 (2.15–4.83)	3.89 (2.51–6.04)	<0.0001		
PEG						
Absent	22	REF				
Present	45	2.96 (1.94–4.53)				
Elective PEG						
Absent	31	REF				
Present	42	1.60 (1.09–2.36)				
p16 status						
Negative	49	REF				
Positive	31	0.47 (0.24–0.89)				
TOS						
0	39	REF				
1	21	0.42 (0.24–0.72)				
cT1-2						
No	42	1.71 (1.16–2.51)				
Yes	30	REF				
cN2-3						
No	40	REF				
Yes	28	1.66 (1.10–2.53)				
Stage						
I	15	REF				
II	33	2.75 (0.47–15.96)				
III	31	2.45 (0.51–11.78)				
Iva	36	3.06 (0.66–14.15)				
IVb	47	4.79 (1.01–22.70)				
Chemo						
No	31	REF	REF	0.0006		
Yes	41	2.44 (1.41–4.22)	2.77 (1.55–4.96)			

UVA = univariable analysis; MVA = multivariable analysis; OR = odds ratio; CUH = Clements University Hospital cohort multivariable analysis; ACE = adult comorbidity evaluation; PEG = percutaneous endoscopic gastrostomy (feeding tube); TOS = transoral surgery.

The odds ratios (ORs) and 95% CIs for hospital admissions and emergency department encounters are shown from univariable analysis along with the significant results ( $P < 0.05$ ) from the multivariate model (MVA). Encounters (%) is the percent of patients within the category who had an unplanned hospital encounter.

with hospital encounters. Notably, the occurrence of admissions or ED encounters was higher for Parkland patients who did not receive chemotherapy (31%) than in University Hospital patients who did receive chemotherapy (25%). However, there was no statistically significant interaction in the odds ratios in the chemotherapy effect between hospital sites.

Multivariate analysis of the results from the private CUH yielded significant associations for ACE-27 score, female gender, and current smokers (Table 2).

#### Unplanned ED Visits Only

A total of 81 patients (17.5%) experienced an ED visit that did not also result in an admission, and these

Table 3  
Unplanned Hospital Admissions

Characteristic	Encounters (%)	UVA OR (CI)	MVA OR (CI)	MVA <i>P</i>	CUH OR (CI)	CUH <i>P</i>
Age						
First quartile	19	REF	REF	0.0059	REF	0.0328
Second quartile	25	1.44 (0.77–2.70)	1.47 (0.77–2.81)		0.88 (0.23–3.38)	
Third quartile	28	1.70 (0.92–3.14)	1.89 (1.00–3.59)		2.33 (0.69–7.85)	
Fourth quartile	32	2.03 (1.10–3.72)	3.12 (1.62–5.99)		3.52 (1.17–10.57)	
ACE-27						
0	19	REF				
1	26	1.49 (0.89–2.50)				
2	34	2.22 (1.23–4.01)				
3	39	2.75 (1.23–6.12)				
Tumor site						
Oropharynx	26	REF				
Larynx	24	0.91 (0.53–1.55)				
Hypopharynx	37	1.66 (0.63–4.37)				
Nasopharynx	28	1.10 (0.51–2.37)				
Gender						
Male	25	REF				
Female	31	1.38 (0.83–2.29)				
Marital status						
Married	22	REF			REF	0.0405
Single	31	1.65 (1.06–2.56)			2.87 (1.25–6.60)	
Smoking						
Never smoker	18	REF				
Ever smoker	29	1.85 (1.10–3.13)				
Current smoker	33	2.29 (1.27–4.14)				
Hospital system						
CUH	17	REF				
Parkland	34	2.47 (1.59–3.83)	2.92 (1.83–4.66)	<0.0001		
PEG						
Absent	17	REF				
Present	32	2.38 (1.50–3.79)				
Elective PEG						
Absent	23	REF				
Present	32	1.52 (1.00–2.31)				
p16 status						
Negative	34	REF				
Positive	22	0.54 (0.27–1.08)				
TOS						
0	29	REF				
1	13	0.38 (0.20–0.72)				
cT1-2						
No	31	1.65 (1.08–2.50)				
Yes	22	REF				
cN2-3						
No	29	1.49 (0.94–2.35)				
Yes	21	REF				
Stage						
I	15	REF				
II	19	1.29 (0.20–8.31)				
III	24	1.78 (0.37–8.64)				
IVA	25	1.86 (0.40–8.65)				
IVB	35	2.92 (0.61–13.90)				
Chemo						
No	20	REF	REF	0.0002	REF	0.0060
Yes	31	3.40 (1.70–6.81)	3.96 (1.94–8.10)		8.31 (1.83–37.67)	

UVA = univariable analysis; MVA = multivariable analysis; OR = odds ratio; CUH = Clements University Hospital cohort multivariable analysis; ACE = adult comorbidity evaluation; PEG = percutaneous endoscopic gastrostomy (feeding tube); TOS = transoral surgery.

ORs and 95% CIs for unplanned hospital admissions are shown from univariable analysis along with the significant results from the multivariate model ( $P < 0.05$ ). Encounters (%) is the percent of patients within the category who had an unplanned hospital encounter.

encounters were also analyzed separately from hospital admissions. In this analysis, the only significant predictor was Parkland hospital enrollment (OR 5.07, 95% CI 2.80–9.20). In the analysis restricted to CUH patients, only female gender (OR 5.28, 95% CI 1.78–15.7) was associated with ER admissions.

### Hospital Admissions

Similar associations were seen when exploring the associations of these factors with hospital admissions (Table 3). Overall, the patient and disease characteristics followed the same trends as described previously, with advanced age and high ACE-27 score maintaining

a positive association in the univariate analysis. With regard to social factors, current smokers, Parkland patients, and unmarried patients were more likely to have hospital admissions (Table 3). None of the reported characteristics in this analysis were associated with a statistically significant opposing effect compared to the analysis described in Table 2.

After multivariate adjustment, concurrent chemotherapy had the strongest association with hospital admissions, with an OR of 3.96 (95% CI of 1.94–8.10, Table 3). Parkland status and advanced age were still significant in multivariate analysis. However, other factors significant in the univariate analysis, including ACE-27 score, smoking status, and use of a feeding tube, were not significant after multivariate correction. For private CUH patients, concurrent chemotherapy also had the strongest association (OR 8.31, 95% CI 1.83–37.67). However, marital status was also significant in this population (Table 3).

#### *Multiple and Prolonged Admissions*

A total of 14% of patients had multiple admissions or ED encounters and 17% of all patients had extended hospitalizations of greater than three days during the treatment window. In univariate analysis, registration in the Parkland hospital system had the strongest association with multiple admissions or ED encounters (OR 8.08, 95% CI 3.75–17.38, Supplemental Table 2). Patients who identified as current smokers had significantly increased odds for multiple admissions/ED encounters and extended admissions (Supplemental Table 3). Consistent with the overall admission/ED encounter analysis, marital status was a significant factor with regard to multiple admissions, with an OR of 2.48.

With multivariate analysis, concurrent chemotherapy was associated with both extended admissions and multiple admissions with ORs of 3.33 and 3.11, respectively. Parkland hospital registration also had a strong association (Supplemental Tables 2 and 3). The ACE-27 score was a significant component of the multivariate model for extended admissions ( $P = 0.0027$ ) but not for multiple admissions. Unmarried patients had a univariable OR of 2.48 for multiple admissions/ED encounters but showed no significant increased risk for multiple admissions or extended admissions after multivariate correction. However, in the private CUH cohort, marital status was a significant risk factor of both multiple hospital encounters (OR 11.11, 95% CI 2.17–56.98) and extended admissions (OR 3.50, 95% CI 1.39–8.82).

#### *Stratified Analysis*

Since Parkland Hospital carried such a strong effect in all the primary analyses, a stratified analysis of ED encounters and admissions was completed by hospital

system to identify other independent predictors. The combined results after stratified analysis yielded a significant association with concurrent chemotherapy (OR 2.76, 95% CI 1.54–4.93), female gender (OR 1.84, 95% CI 1.12–3.04), and age (OR 3.11, 95% CI 1.70–5.72 for the highest age quartile).

#### *Discussion*

In this analysis, we have shown that patients receiving head and neck radiotherapy experience a high incidence of unplanned hospital encounters, with over one-third of all patients presenting for acute care. Most ED encounters and hospital admissions were due to the common toxicities of radiotherapy: nausea, vomiting, and the secondary inability to eat and drink exacerbated by pain and mucositis.

Previously reported retrospective studies have explored risk factors for hospitalizations and ED encounters among patients treated with radiotherapy for head and neck cancer. In a large cohort of patients with various types of cancer, unmarried patients and those treated with concurrent chemotherapy had more hospital admissions.<sup>10</sup> However, only 115 patients in that cohort had cancer of the head and neck. In another cohort of 147 patients, pulmonary disease, diabetes, and increased radiation dose were associated with hospital admissions.<sup>8</sup> Analysis from a much larger cohort of patients from the SEER-Medicare database showed that ED encounters and hospitalizations were associated with patient comorbidity, older age, and the use of concurrent chemotherapy.<sup>1</sup> We found associations that are consistent with and expand upon previous reports. Indeed, this study includes substantially more patients ( $n = 462$ ) with head and neck cancer than the first two studies cited, allowing analysis of potential associations across ED encounters, admissions, and extended hospital admissions. Our findings also build upon the SEER-Medicare results by including patients of all ages and with variable insurance status, which emerged as the dominating association in most of our analyses.

It is not surprising that patients with severe comorbidities such as end-stage renal disease and decompensated heart failure are at a higher risk of hospital admissions. However, even patients with less severe medical problems, such as poorly controlled hypertension or diabetes, experienced more unplanned ED encounters or admissions for treatment-related toxicities. The univariate analysis suggests that there is a continuum of risk associated with the severity of patient comorbidities, as seen with a stepwise increase in odds across all the reported analyses except extended admissions with increasing ACE-27 score. However, in the multivariate analysis, ACE-27

score was significant only with respect to extended hospital admissions in the whole cohort and to any hospital encounter in the University subset. Correction for the dominating effect of Parkland status likely plays a large role in reducing the significance of this and several other factors that were significant in univariate analysis, and this is at least partially influenced by the clustering of the patients with many medical comorbidities in the Parkland population as described in the following.

Concurrent chemotherapy has been widely adopted for head and neck cancer treatment because disease control and long-term outcomes are improved despite increased toxicity during treatment.<sup>2</sup> Yet the use of chemotherapy was strongly predictive of admission, despite the potential bias of more frequent administration of chemotherapy in healthier patients. This association was seen across all analyses and the stratified analyses between both hospital systems. Clearly, the addition of chemotherapy to the treatment regimen comes with substantial risk, which shows that the selection of patients who are most likely to benefit and the proactive management of toxicities are critical to prevent unnecessary morbidity.

One aspect of prophylactic intervention intended to reduce malnutrition and dehydration is the early placement of feeding tubes, which has been the subject of multiple prospective studies yielding mixed results.<sup>11–13</sup> However, there is concern from retrospective analysis that percutaneous feeding tubes may be associated with increased late dysphagia and other complications.<sup>14</sup> In this study, the presence of a PEG was associated with an increased occurrence of unplanned hospital encounters, but this result could simply reflect confounding by indication; that is, patients with a higher symptom load were more likely to receive a PEG and also require acute evaluation.

We see that social factors are strongly associated with more hospital admissions and ED encounters, independent of disease characteristics. For example, patients who are unmarried have a substantially greater chance of unplanned hospital encounters, likely due to a weaker social support system to help manage toxicities.<sup>10</sup> Unmarried status is also consistently associated with increased mortality in this population, highlighting the crucial importance of partnership and family in the management of the disease and treatment.<sup>15</sup> This is consistent with a reduced risk of mortality in married patients with head and neck cancer observed in a prior study.<sup>15</sup> One of the strongest and most consistent factors associated with increased ED visits, hospitalizations, extended admissions, and multiple admissions was whether the patient had care established at the county hospital, Parkland. This relationship is complex and likely involves many factors because these patients are more likely to be

uninsured, living in poverty, and less likely to seek regular medical care. The individual social risk factors identified in this analysis tend to cluster in patients of lower socioeconomic class, and there are presumably other unmeasured characteristics of this population that contribute to an increased probability of hospitalization. Thus, designing individual interventions to mitigate this risk can be difficult, but as a first step, we propose focusing on the key issues that drove many admissions. For example, early nutritional intervention and swallow therapy, smoking cessation resources, and promoting mental health with counseling may prophylactically meet critical needs in this population that influence unplanned hospital encounters.<sup>11,16,17</sup> It remains a challenge to successfully deliver complex medical care to the socially and economically disadvantaged population, so implementing low-cost and convenient strategies to improve proactive management of toxicities is most critical for these patients and this health system.

There are some inherent limitations in this study. For example, the dominating association of admissions with registration in the public hospital system and grouping of patients with unfavorable characteristics in that population makes it challenging to reliably separate the individual contributions of those characteristics in multivariate analysis. The stratified analysis we performed does help address that concern, and moreover, the subset analysis of the University patients notably revealed complementary risk factors for hospital encounters in a private system. Additional factors that could limit this analysis include incomplete description of comorbidities in patient notes and ED encounters and admissions at outside hospitals that were not captured. Although the relatively large number of patients in this study improves the reliability of these analyses, there were still relatively few patients who had only ED visits without subsequent admission, multiple admissions, and extended admissions, which makes the assessment of the wide array of individual characteristics for those outcomes more limited.

In sum, the factors outlined previously contribute to a very high risk of poorly controlled treatment-associated morbidity and hospital admissions during treatment. With 36% of patients experiencing unplanned hospital encounters, the financial cost and resource utilization due to inadequate outpatient management are substantial, with substantial impact on health and long-term outcomes. Future prospective studies could confirm these risk factors and inform providers when the risk is sufficiently high to warrant additional prophylactic interventions for the highest-risk individuals. One example of a tool that could be applied to prevent complications and admissions in high risk patients is patient-reported monitoring of side-effect severity with mobile devices.<sup>18</sup>

Reducing the health and financial burdens of treatment-related morbidity and resulting hospital encounters is a critical goal in improving cost-effective care for patients with head and neck cancer.

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## *Appendix*

*Supplemental Table 1*  
**Causes of Hospital Encounters**

Cause	Number (%)
Dehydration/FTT	51 (22)
GI symptoms	43 (19)
Other	43 (19)
Infection/fever	36 (16)
Pain	24 (10)
Aspiration pneumonia	15 (7)
Neurologic symptoms	12 (5)
Acute cardiopulmonary event	6 (3)

FTT = failure to thrive; GI = gastrointestinal.

Supplemental Table 2  
Multiple Admissions or ED Encounters

Characteristic	Encounters (%)	UVA OR (CI)	MVA OR (CI)	MVA P	CUH OR (CI)	CUH P
Age						
First quartile	15	REF				
Second quartile	16	1.08 (0.53–2.22)				
Third quartile	12	0.80 (0.37–1.71)				
Fourth quartile	14	0.94 (0.45–1.97)				
ACE-27						
0	12	REF				
1	13	1.10 (0.58–2.11)				
2	17	1.57 (0.75–3.27)				
3	24	2.41 (0.95–6.10)				
Tumor site						
Oropharynx	13	REF				
Larynx	17	1.30 (0.70–2.44)				
Hypopharynx	5	0.36 (0.05–2.75)				
Nasopharynx	17	1.29 (0.51–3.28)				
Gender						
Male	13	REF				
Female	17	1.31 (0.70–2.46)				
Marital status						
Married	9	REF			REF	0.0155
Single	19	2.48 (1.40–4.40)			11.11 (2.17–56.98)	
Smoking						
Never smoker	11	REF				
Ever smoker	11	0.99 (0.50–1.93)				
Current smoker	24	2.41 (1.21–4.79)				
Hospital system						
CUH	4	REF				
Parkland	23	8.08 (3.75–17.38)	8.13 (3.77–17.54)	<0.0001		
PEG						
Absent	22	REF				
Present	45	4.12 (2.04–8.32)				
Elective PEG						
Absent	18	REF				
Present	18	1.75 (1.03–2.96)				
p16 status						
Negative	15	REF				
Positive	11	0.68 (0.27–1.72)				
TOS						
0	16	REF				
1	7	0.39 (0.16–0.92)				
cT1-2						
No	17	1.70 (1.00–2.90)				
Yes	11	REF				
cN2-3						
No	16	1.82 (0.98–3.35)				
Yes	10	REF				
Stage						
I	8	REF				
II	5	0.6 (0.03–10.51)				
III	13	1.76 (0.21–14.75)				
IVA	12	1.62 (0.20–13.01)				
IVB	24	3.74 (0.46–30.27)				
Chemo						
No	10	REF	REF	0.0143		
Yes	17	3.27 (1.27–8.40)	3.33 (1.27–8.82)			

UVA = univariable analysis; MVA = multivariable analysis; CUH = Clements University Hospital cohort multivariable analysis; ACE = adult comorbidity evaluation; PEG = percutaneous endoscopic gastrostomy (feeding tube); TOS = transoral surgery.

Odds ratios (ORs) and 95% CIs for the occurrence of multiple admissions or ED encounters are shown. Encounters (%) is the percent of patients within the category who had an unplanned hospital encounter.

Supplemental Table 3  
Extended Admissions

Characteristic	Encounters (%)	UVA OR (CI)	MVA OR (CI)	MVA p	CUH OR (CI)	CUH p
Age						
First quartile	12	REF				
Second quartile	19	1.72 (0.83–3.56)				
Third quartile	18	1.61 (0.78–3.35)				
Fourth quartile	19	1.72 (0.83–3.56)				
ACE-27						
0	10	REF	REF	0.0027		
1	16	1.57 (0.83–2.99)	1.69 (0.88–3.27)			
2	30	3.64 (1.84–7.18)	3.71 (1.84–7.47)			
3	24	2.73 (1.07–7.00)	2.41 (0.91–6.36)			
Tumor site						
Oropharynx	17	REF				
Larynx	15	0.86 (0.46–1.64)				
Hypopharynx	32	2.31 (0.84–6.35)				
Nasopharynx	19	1.21 (0.50–2.90)				
Gender						
Male	17	REF				
Female	18	1.08 (0.59–1.98)				
Marital status						
Married	14	REF			REF	0.0293
Single	21	1.61 (0.97–2.69)			3.50 (1.39–8.82)	
Smoking						
Never smoker	10	REF				
Ever smoker	19	2.15 (1.12–4.11)				
Current smoker	23	2.66 (1.30–5.43)				
Hospital system						
CUH	10	REF				
Parkland	24	2.96 (1.73–5.06)	2.84 (1.64–4.95)	0.0002		
PEG						
Absent	9	REF				
Present	22	2.70 (1.52–4.80)				
Elective PEG						
Absent	16	REF				
Present	19	1.19 (0.73–1.94)				
P16 status						
Negative	1	REF				
Positive	15	0.74 (0.32–1.70)				
TOS						
0	19	REF				
1	11	0.56 (0.28–1.13)				
cT1-2						
No	20	1.49 (0.92–2.43)				
Yes	14	REF				
cN2-3						
No	19	1.38 (0.81–2.35)				
Yes	14	REF				
Stage						
I	15	REF				
II	14	0.92 (0.13–6.38)				
III	17	1.13 (0.23–5.59)				
IVA	15	0.99 (0.21–4.67)				
IVB	22	1.53 (0.32–7.43)				
Chemo						
Yes	14	REF	REF	0.0078		
No	19	2.85 (1.26–6.42)	3.11 (1.35–7.17)			

UVA = univariable analysis; MVA = multivariable analysis; CUH = Clements University Hospital cohort multivariable analysis; ACE = adult comorbidity evaluation; PEG = percutaneous endoscopic gastrostomy (feeding tube); TOS = transoral surgery.

Odds ratios (ORs) and 95% CIs for admissions of greater than three days are shown. Encounters (%) is the percent of patients within the category who had an unplanned hospital encounter.