

Scientific Article

Premature discontinuation of curative radiation therapy: Insights from head and neck irradiation

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Abstract

Purpose: Factors related to premature discontinuation of curative radiation therapy (PDCRT) are understudied. This study aimed to examine causes and clinical outcomes of PDCRT at our institution by investigating the most common anatomical site associated with PDCRT.

Methods and materials: Among the 161 patients with PDCRT of various anatomic sites at our institution between 2010 and 2017, 36% received radiation to the head and neck region. Pertinent demographic, clinical, and treatment-related data on these 58 patients were collected. Survival was examined using the life-table method and log-rank test.

Results: The majority of patients were male (81%), white (67%), ≥60 years old (59%), living ≥10 miles away from the hospital (60%), single (57%), with Eastern Cooperative Oncology Group score ≥1 (86%), experiencing significant pain issues (67%), and had treatment interruptions in radiation therapy (RT; 66%). The most common reasons for PDCRT were discontinuation against medical advice (33%), medical comorbidity (24%), and RT toxicity (17%). Of the comorbidities leading to PDCRT, 50% was acute cardiopulmonary issues and 43% was infection. The mean follow-up time was 15.9 months, and the 2-year overall survival and disease-specific survival rates were 61% and 78%, respectively. Patients with illicit substance abuse, cardiovascular disease, and Eastern Cooperative Oncology Group score ≥2 had worse survival. A trend toward improved survival with total completed dose ≥50 Gy versus <50 Gy existed (74% versus 44%, respectively; $P = .07$).

Conclusions: In this largest-to-date, modern analysis of PDCRT, the most common cause of discontinuation was discontinuation against medical advice, which underscores the importance of patient education, optimization of RT symptoms, involvement of social work, and integration of other sup-

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portive services early in treatment. Survival remains suboptimal after PDCRT for H&N tumors, with a 2-year overall survival rate of 61%. Completing >50 Gy appears to confer a relative therapeutic benefit.

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Introduction

Radiation therapy (RT) is 1 of the 3 principal modalities in the management of cancer and is delivered with curative intent in approximately 40% of cases.¹ A long RT treatment course is often considered a limitation because the majority of definitive RT cases require 5 to 9 weeks of daily treatments. This becomes particularly relevant for patients with head and neck (H&N) malignancies. External beam RT is a cornerstone of curative treatment for a variety of H&N cancers and offers significant long-term locoregional control and survival.

However, successful completion of a full course of RT can prove challenging for many patients with H&N malignancies. Acute untoward radiation effects, including dermatitis, mucositis, xerostomia, and dysphagia, can lead to a dramatic compromise in patients' physical and psychosocial functioning. Additionally, a prolonged RT course, logistical treatment demands, considerable nutritional deficits, and toxicities of commonly received concomitant chemotherapy further affect quality of life in this group of patients. Therefore, it is not surprising that some patients are unable to complete the prescribed therapeutic regimen. Moreover, other non-RT-related factors may contribute to early treatment withdrawal, including progression of disease or non-cancer-related comorbidities.

Understanding the sociodemographic and clinical characteristics of this subset of patients and identifying the causes of premature discontinuation of curative RT (PDCRT) are important to improving care for patients with H&N cancer and increasing treatment completion rates. However, very few studies have addressed these questions.²⁻⁵ Furthermore, little is known about the clinical impact of PDCRT on H&N tumors. Although the adverse effects of prolonging the RT course on treatment efficacy in H&N cancers have been shown in several studies,⁶⁻⁸ including clinical trials of split-course RT,⁹ very limited data are available to counsel patients on the impact on survival of PDCRT for H&N malignancies.

In such a context, we present the largest single-institution analysis of PDCRT for H&N malignancies to date. By examining 58 cases of early RT treatment withdrawal, we aimed to identify its principal causes as well as potentially important underlying sociodemographic and clinical elements to suggest strategies for improvement in patient care and treatment completion rates. Furthermore, we aimed to assess clinical outcomes after PDCRT.

Methods and materials

Patient selection and radiation treatment

Approval from our institutional review board was obtained prior to the initiation of the study. A total of 161 patients treated with curative irradiation of various anatomic sites at our institution did not complete a full course of RT between 2010 and 2017 (Fig 1). A total of 58 patients who received incomplete RT to the H&N region were included in the present analysis. A total of 1001 patients were treated with curative intent for H&N cancers during the study period. Radiation was delivered with intensity modulated RT by means of a conventional fractionation regimen. The median dose per fraction was 2.0 Gy. PDCRT was defined as a failure to receive a full radiation dose as prescribed by the treating physician. The Radiation Therapy Oncology Group (RTOG) toxicity criteria were used to grade RT side effects.¹⁰

Study endpoints and statistical analysis

The primary endpoints of the study were causes of PDCRT as well as demographic, clinical, and treatment-related characteristics of the analyzed cohort. PDCRT causes were classified into 5 categories, including discontinuation against medical advice (DAMA), medical comorbidity, RT toxicity, disease progression, and social factors. DAMA was defined as a patient's refusal to continue treatment that, per the treating radiation oncologist, would have no clinical indication for interruption or discontinuation. Medical comorbidity was defined as a medical condition other than H&N cancer that warranted early treatment withdrawal. Discontinuation due to RT toxicity was defined as a patient's inability to continue treatment due to significant radiation effects and on the advice of the treating physician. Discontinuation due to disease progression was defined as symptomatic progression of either locoregional disease or development of distant metastases that resulted in the early termination of RT and conversion of the patient's care to palliative/supportive care only. The social factors category included discontinuation due to nonmedical issues and/or family emergencies.

For each patient, we collected data on the following sociodemographic and clinical characteristics: age, sex, race, distance from the hospital (<10 miles vs. ≥10 miles), living situation (living alone vs. with family), marital status (single

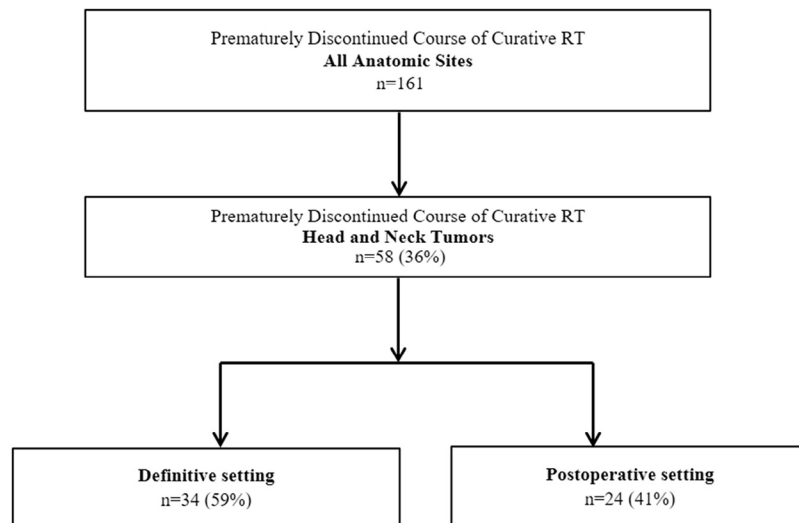


Figure 1 CONSORT diagram. Patients who received curative radiation therapy at our institution between January 2010 and January 2017 but had an incomplete course (ie, ≥ 1 fraction but $<$ prescription dose) were included in the analysis.

vs. married), insurance status (Medicaid vs. Medicare vs. private insurance), Eastern Cooperative Oncology Group (ECOG) score prior to initiation of RT, smoking status, alcohol use, illicit substance abuse, comorbid conditions, primary site of H&N cancer, and RTOG toxicity scores. Smoking status was defined as either current smoking or a significant pack-year smoking history (>10 pack-years).¹¹ Alcohol use and illicit substance abuse were defined as ongoing use of alcohol and recreational substances during treatment. Comorbid conditions included depression, diabetes, hypertension, cardiovascular disease, or history of other cancers. Treatment-related factors included significant pain issues during RT (defined as pain requiring opioid analgesics), radiation treatment interruptions (defined as ≥ 1 day of missed treatment during the incomplete RT course), use of percutaneous endoscopic gastrostomy during RT, receipt of concurrent chemotherapy, inpatient admission as a result of acute RT or chemotherapy toxicities, and cumulative completed RT dose. The secondary endpoints of the study were locoregional recurrence-free survival (LRRFS), distant metastases-free survival, disease-specific survival, and overall survival (OS).

Survival intervals were calculated from the date of the last RT treatment to the date of last contact or first occurrence of the event of interest. Survival estimates with corresponding 95% confidence intervals were measured for the study endpoints using the life-table method. The log-rank test was used to compare distributions of OS stratified by various demographic and clinical factors. A χ^2 analysis was performed to assess differences in patients' treatment-related characteristics between the definitive and adjuvant groups. Hypothesis testing was 2-sided and conducted at the 5% level of significance. All statistical analyses were performed using StataIC version 14 (StataCorp LP, College Station, TX).

Results

Patient demographic and clinical characteristics

Among the 58 identified patients who were unable to complete an initially planned RT course for H&N tumors, the majority were ≥ 60 years old (59%), male (81%), white (67%), living ≥ 10 miles away from the hospital (60%), single (57%), and had ECOG score ≥ 1 (86%; Table 1). Twenty-one percent of patients had ECOG score ≥ 2 prior to the initiation of RT. In addition, 47% of patients were smokers, 24% reported active alcohol use, and 12% disclosed active illicit substance abuse. Twenty percent of patients had depression, and 25% had a history of other cancers. The most common primary sites were oropharynx (38%), larynx (21%), and oral cavity (12%). A total of 84% of the tumors were squamous cell carcinomas.

Causes of premature discontinuation of curative radiation therapy

The most common causes of PDCRT were DAMA (33%; $n = 19$), medical comorbidity (24%; $n = 14$), RT toxicity (17%; $n = 10$), and disease progression (9%; $n = 5$; Fig 2). Of the medical comorbidities leading to PDCRT, 50% ($n = 7$) was acute cardiopulmonary issues and 43% ($n = 6$) was infection. Acute cardiopulmonary issues included acute heart failure exacerbation ($n = 2$), cardiopulmonary arrest ($n = 2$), ventricular fibrillation ($n = 1$), pulmonary embolism ($n = 1$), and severe respiratory distress ($n = 1$). Cases of infection included pneumonia complicated by sepsis ($n = 2$), *Clostridium difficile* infection complicated by sepsis ($n = 1$), and sepsis of other etiologies ($n = 3$).

Table 1 Patient demographic and disease characteristics—entire cohort (n = 58)

Characteristic	Number of patients	Proportion of patients (%)
Age (years)		
<60	24	41
≥60	34	59
Sex		
Male	47	81
Female	11	19
Race		
White	39	67
Hispanic	12	21
Other	7	12
Distance from Hospital		
<10 miles	23	40
≥10 miles	35	60
Living Situation		
Lives alone	21	36
Lives with family	37	64
Marital Status		
Single	33	57
Married	25	43
Insurance Status		
Medicaid	9	16
Medicare	19	33
Private	30	52
ECOG Score		
0	8	14
1	38	65
≥2	12	21
Smoker		
Yes	27	47
No	31	53
Alcohol Use		
Yes	14	24
No	44	76
Illicit Substance Abuse		
Yes	7	12
No	51	88
Depression		
Yes	12	21
No	46	79
Diabetes		
Yes	13	22
No	45	78
Hypertension		
Yes	32	55
No	26	45
Cardiovascular Disease		
Yes	15	26
No	43	74
History of Other Cancer		
Yes	15	26
No	43	74
Primary Site		
Oropharynx	22	38
Larynx	12	21
Oral cavity	7	12
Other	17	29

ECOG, Eastern Cooperative Oncology Group.

Treatment-related characteristics

At the time of treatment discontinuation, 59% (n = 34) of patients were undergoing definitive RT, and 41% (n = 24) were undergoing postoperative RT. Of patients, 48% (n = 28) received concurrent chemotherapy, and 21% (n = 12) had received induction chemotherapy. More than one-third of all patients experienced RTOG grade ≥2 toxicities (Table 2): 36% of patients had grade ≥2 dermatitis, 44% had grade ≥2 mucositis, and 64% had grade ≥2 dysphagia. In addition, 24% of patients had severe dysphagia (grade ≥3). The majority of patients (67%) experienced significant pain requiring opioid analgesics during RT. Furthermore, 66% of patients had treatment interruptions in RT, and 33% required an inpatient admission due to acute treatment effects. There were no statistically significant differences in toxicities, pain, or other treatment-related factors between the definitive and adjuvant cohorts.

The median prescribed dose was 69.96 Gy (range, 50-72 Gy). The median completed radiation dose was 50.4 Gy (range, 2-68 Gy), and 55% of all patients were able to complete ≥50 Gy of the prescribed dose. The majority of patients within the definitive cohort were able to complete ≥50 Gy (65%), whereas the majority within the adjuvant cohort (58%) received <50 Gy of radiation ($P = .08$). Eighty-six percent of all patients had neck irradiation as part of the prescribed therapy; of these, 82% had bilateral neck RT.

Clinical outcomes

The mean follow-up time was 15.9 months (range, 0-81.9 months). At the time of analysis, 9% (n = 5) of patients developed locoregional failure, and 7% (n = 4) had developed distant metastases. A total of 20 (34%) deaths were recorded. The median completed dose among the deceased patients was 39 Gy. Fifty-five percent (n = 11) of deaths were due to the underlying H&N cancer, of which 55% (n = 6) were due to disease progression, 27% (n = 3) to distant metastases, and 18% (n = 2) to locoregional recurrence. The 2-year rates for OS, disease-specific survival, LRRFS, and distant metastases-free survival were 61%, 78%, 93%, and 95%, respectively (Table 3). Patients with illicit substance abuse, cardiovascular disease, and ECOG score ≥2 had worse survival (Table 4). A trend toward improved survival with a total completed dose of ≥50 Gy versus <50 Gy was found (74% versus 44%, respectively; $P = .07$). The 2-year OS rates were the lowest among patients with ECOG score ≥2 (18%) and those who had depression (37%), required an inpatient admission (36%), had a history of another cancer (43%), received <50 Gy of the prescribed dose (44%), or had substance abuse issues (45%).

Discussion

To the best of our knowledge, this is the largest modern study to examine the clinical outcomes after PDCRT. H&N

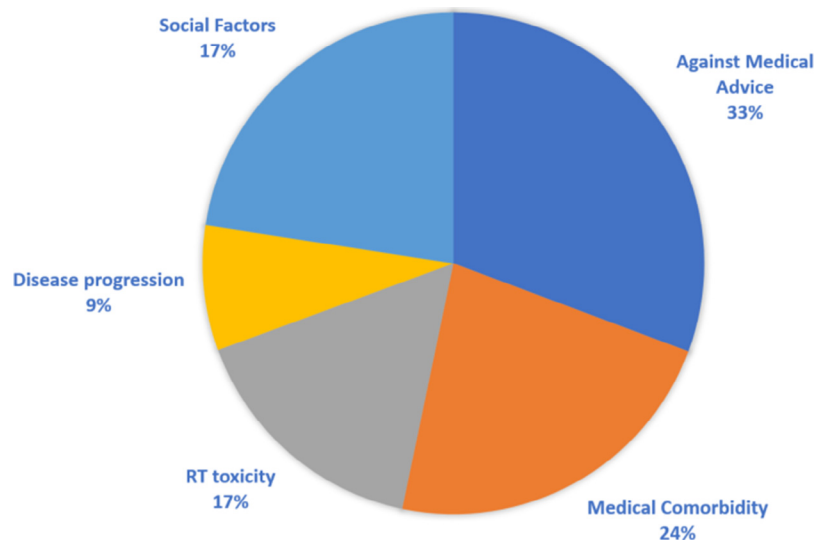


Figure 2 Causes of premature discontinuation of curative radiation therapy.

irradiation accounted for more than one-third of all cases of early treatment withdrawal in our institution. In this analysis, a high proportion of patients who discontinued treatment were older, white, male, and single; lived far from the hospital; had poor performance status; experienced significant

pain issues; had treatment interruptions; and were undergoing definitive RT. Thirty percent of patients discontinued treatment against medical advice, and 24% stopped due to non-cancer-related comorbidity. RT toxicity accounted for 17% of early treatment withdrawals. The short-term

Table 2 Radiation toxicities and treatment-related factors stratified by setting of radiation therapy (definitive versus adjuvant; n = 58)

Characteristic	Total (n = 58) No. (%)	Definitive (n = 34) No. (%)	Adjuvant (n = 24) No. (%)	P-value
Dermatitis, RTOG Grade				
0	9 (16)	6 (18)	3 (12)	.44
1	28 (48)	18 (53)	10 (42)	
≥2	21 (36)	10 (29)	11 (46)	
Mucositis, RTOG Grade				
0	16 (28)	12 (35)	4 (17)	.20
1	16 (28)	7 (21)	9 (37)	
≥2	26 (44)	15 (44)	11 (46)	
Dysphagia, RTOG Grade				
0	21 (36)	11 (32)	10 (42)	.52
1-2	23 (40)	13 (38)	10 (42)	
≥3	14 (24)	10 (30)	4 (16)	
PEG Use during RT				
Yes	26 (45)	14 (41)	12 (50)	.51
No	32 (55)	20 (59)	12 (50)	
Significant Pain Issues during RT				
Yes	39 (67)	23 (68)	16 (67)	.94
No	19 (33)	11 (32)	8 (33)	
Interruptions in RT				
Yes	38 (66)	22 (65)	16 (67)	.88
No	20 (34)	12 (35)	8 (33)	
Inpatient admission				
Yes	19 (33)	11 (32)	8 (33)	.94
No	39 (67)	23 (68)	16 (67)	

PEG, percutaneous endoscopic gastrostomy; RT, radiation therapy; RTOG, Radiation Therapy Oncology Group.

Table 3 Clinical outcomes (mean follow-up: 15.9 months; range, 0-81.9 months), entire cohort (n = 58)

Variable	LRRFS (95% CI)	DMFS (95% CI)	OS (95% CI)	DSS (95% CI)
1 year	93% (0.80-0.98)	95% (0.83-0.99)	68% (0.53-0.79)	83% (0.68-0.90)
2 year	93% (0.80-0.98)	95% (0.83-0.99)	61% (0.45-0.74)	78% (0.62-0.88)
3 year	93% (0.80-0.98)	86% (0.54-0.96)	61% (0.45-0.74)	78% (0.62-0.88)
4 year	93% (0.80-0.98)	86% (0.54-0.96)	52% (0.30-0.70)	66% (0.37-0.77)

CI, confidence interval; DMFS, distant metastases-free survival; DSS, disease-specific survival; LRRFS, locoregional relapse-free survival; OS, overall survival.

survival after PDCRT was suboptimal, with 2- and 4-year OS rates at 61% and 52%, respectively. Achieving a total dose of at least 50 Gy using standard fractionation may confer a relative therapeutic benefit.

This report is the first to provide data on both the etiology and outcomes of PDCRT in the context of H&N irradiation. Currently, there is a scarcity of valid clinical data on this important topic. In fact, a literature search on PubMed for publications related to early treatment withdrawal from curative irradiation for H&N tumors revealed only 3 reports written in English and published in the last 15 years.^{4,12,13} None of these papers specifically addressed the question of PDCRT.

The present study identified DAMA as the primary cause of PDCRT. Therefore, it is critical that involvement of social work, enhancement of pre- and on-treatment patient education, optimization of RT symptoms, and active integration of supportive services (ie, mental health professionals, pastoral counselors, support groups) be considered early in treatment by the radiation oncologist. Recognizing the logistical issues of the treatment process, as well as psychosocial and quality of life aspects, may help increase completion rates of this often lifesaving treatment. Notably, a recent publication on the challenges of patients with H&N cancer¹⁴ highlighted that the impact of RT on social activities and interactions is often underdiscussed by the treating physician and of key concern to patients. The authors also suggested that there is a significant gap in addressing the communication and informational needs of patients' caregivers and family members. One may hypothesize that a significant proportion of PDCRT cases could be avoided by addressing some of these issues. Ultimately, more efforts focused on providing support to both patients and their families should be made to meet the unique needs of this challenging patient population.

The finding that non-treatment-related comorbidities resulted in a quarter of all RT treatment withdrawals stresses the importance of improving interdisciplinary communication between oncology and non-oncology services. Although some of the comorbidities that resulted in PDCRT in this study were acute in nature (eg, acute heart failure exacerbation) and therefore often difficult to foresee, it may be important for the treating radiation oncologist to discuss RT treatment risks with the non-oncological specialist (eg, cardiologist) of a high-risk patient prior to initiating treat-

ment. This would help the radiation clinician assess the likelihood of treatment withdrawal and hence warrant closer monitoring of the patient during the course of RT. On the other hand, high-risk patients with significant comorbidities should be strongly advised to continue follow-up for their respective chronic medical condition throughout the RT treatment.

Radiation toxicities have been cited previously as the major causes of treatment interruptions or noncompletion in H&N and other cancers.^{2,8,15} In this study, this was the third most common cause of PDCRT. This finding highlights once again that successful treatment completion remains a significant challenge for patients who experience severe RT toxicities and often requires a thorough investigation of management options by the treating physician and staff.

Although there is a variety of literature and online resources on the management of radiation side effects, one potential avenue to address this issue could be the development of a smartphone application for radiation clinicians that would unify all the available practical information on the prevention and management of radiation toxicities. Such an application would include data not only on supportive medications but also on alternative remedies, dietary suggestions, and lifestyle modifications. To date, there is only one smartphone application called Rad Onc Reference that provides information solely on commonly used drugs in RT. In the era of technology and active daily use of smartphones by clinicians, the development of a smartphone application for management of radiation sequelae is urgently needed.

In our institution, the interdisciplinary H&N group (including medical, surgical, and radiation oncologists; nursing staff; social workers; and registered dietitians) meets weekly with the goal to address the issues of patients on treatment. This model can certainly be applied in other practices and can serve as one of the avenues for improvement of treatment completion rates. In fact, among all patients treated in our institution with curative RT for H&N cancers between 2010 and 2017, only 6% withdrew from treatment. Additionally, the development of a screening tool to comprehensively assess patients' psychosocial concerns, physical symptoms, and logistical limitations of treatment (eg, transportation, patient transfer, financial constraints) would be useful. The use of such an

Table 4 Two-year overall survival rates (mean follow-up 15.9 months; range, 0-81.9 months), entire cohort (n = 58)

Variable	Two-year overall survival rate (95% CI)	Log-rank P-value
Age (years)		
<60	76% (0.51-0.89)	.26
≥60	52% (0.31-0.70)	
Sex		
Male	64% (0.46-0.77)	.48
Female	53% (0.17-0.80)	
Race		
White	60% (0.40-0.75)	.92
Hispanic	68% (0.31-0.89)	
Other	60% (0.11-0.89)	
Smoker		
No	69% (0.47-0.83)	.54
Yes	51% (0.26-0.71)	
Alcohol Use		
No	61% (0.42-0.75)	.52
Yes	65% (0.32-0.85)	
Illicit Substance Abuse		
No	64% (0.46-0.77)	.05
Yes	45% (0.10-0.78)	
ECOG		
0	83% (0.27-0.97)	<.0001
1	72% (0.51-0.85)	
≥2	18% (0.03-0.44)	
Living situation		
Lives alone	55% (0.35-0.71)	.29
Lives with family	75% (0.48-0.90)	
Marital status		
Single	54% (0.32-0.71)	.40
Married	72% (0.48-0.86)	
Insurance status		
Medicaid	60% (0.20-0.85)	.39
Medicare	57% (0.29-0.77)	
Private	65% (0.40-0.82)	
Depression		
No	68% (0.50-0.81)	.12
Yes	37% (0.09-0.67)	
Diabetes		
No	65% (0.47-0.78)	.61
Yes	48% (0.14-0.76)	
Hypertension		
No	67% (0.39-0.85)	.23
Yes	57% (0.36-0.73)	
Cardiovascular Disease		
No	71% (0.52-0.84)	.01
Yes	33% (0.10-0.61)	
History of Other Cancer		
No	68% (0.49-0.82)	.29
Yes	43% (0.15-0.69)	
Distance from Hospital		
<10 miles	62% (0.37-0.80)	.69
≥10 miles	62% (0.41-0.77)	
Primary Site		
Oropharynx	60% (0.33-0.79)	.48
Larynx	70% (0.33-0.89)	
Oral cavity	50% (0.11-0.80)	
Other	61% (0.28-0.83)	
Completed RT Dose		
<50 Gy	44% (0.20-0.66)	.07
≥50 Gy	74% (0.52-0.87)	
Concurrent Chemotherapy		
No	61% (0.39-0.78)	.92
Yes	61% (0.35-0.79)	
Interruptions in RT		
No	65% (0.38-0.82)	.83
Yes	60% (0.39-0.75)	
PEG during RT		
No	68% (0.45-0.83)	.34
Yes	53% (0.29-0.72)	
Inpatient admission during RT		
No	72% (0.52-0.85)	.11
Yes	36% (0.12-0.62)	

CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; PEG, percutaneous endoscopic gastrostomy; RT, radiation therapy.

instrument may help identify patients at risk for PDCRT and result in early intervention by the treating physician and staff. A National Comprehensive Cancer Network Distress Thermometer that was designed for psychosocial screening in patients with cancer can serve as an excellent sample of such an assessment tool.^{16,17}

The survival rates observed in the present study were surprisingly higher than we expected for an incomplete course of RT. However, OS was still suboptimal: 2- and 4-year OS rates for the entire cohort were 61% and 52%, respectively. One should be particularly careful when interpreting these outcomes given the heterogeneity of the primary tumor locations, stages, and biology, the short follow-up, and the small sample size. Nevertheless, when compared with data from other retrospective series on mixed cohorts of H&N malignancies, the OS after PDCRT appears to be worse than with completed RT. For instance, a University of Florida (UF) study of the outcomes of patients who fully completed a prescribed course of intensity modulated RT for H&N cancers demonstrated a 3-year OS rate of 71%.¹⁸ The corresponding 3-year OS in this study was 61%. Furthermore, the 3-year OS rates for oropharynx cancer (OPC) in the UF study was 84%, whereas the OS rate at 2 years for OPC in this study was 60%. Notably, the UF study was larger than ours (100 patients vs. 58), had a longer follow-up, and consisted mostly of oropharyngeal, nasopharyngeal, and hypopharyngeal cancers (versus mostly oropharyngeal, laryngeal, and oral cavity cancers in this report).

The present study demonstrated that completing a total radiation dose of at least 50 Gy may provide a therapeutic benefit for patients with H&N cancer. Given that there is little consensus on how to counsel patients who wish to discontinue RT prematurely, these data may serve as an essential asset for the practicing radiation oncologist. Advising a patient that reaching at least 50 Gy could offer a better chance for survival could prove vital. In fact, there are promising emerging data from some dose deintensification trials that suggest that for a selected subset of patients with H&N cancer, specifically human papillomavirus-associated OPCs, a lower total dose may in fact be curative. For instance, the most recent findings from the ECOG-American College of Radiology Imaging Network E1308 phase 2 trial of induction chemotherapy followed by reduced-dose RT with weekly cetuximab in patients with human papillomavirus-associated OPCs revealed excellent short-term outcomes. The 2-year overall survival with a total dose of 54 Gy and concurrent cetuximab was 94%.¹⁹

The current study has several important limitations. A short follow-up and small sample size prevented us from making conclusions with regard to the effect of PDCRT on long-term clinical outcomes. Additionally, a follow-up in patients who discontinue treatment early can be challenging; hence it is possible that rates of locoregional recurrence or distant metastases were underestimated.

Furthermore, no data were collected on salvage chemotherapy and/or surgery after treatment withdrawal, which would have potentially overestimated the calculated survival rates.

Another limitation of the current study is that we did not provide data on chemotherapy toxicities and their effect on patients' decisions to discontinue treatment. Also, we did not analyze different American Joint Committee on Cancer stages as a factor contributing to treatment discontinuation and its effect on clinical outcomes. Given the significant variability in staging systems of different H&N cancers, such an analysis would not be appropriate. Additionally, although we observed a prevalence of certain demographic and clinical characteristics among patients who discontinued RT early, we cannot assume a predictive association between those factors and PDCRT. A control cohort of patients with a completed RT course would need to be selected to examine such a relationship. This was beyond the scope of the study.

Finally, although the categories of PDCRT were defined as mutually exclusive in this analysis, it is possible that there were multifactorial reasons for early treatment withdrawal that were not well documented in the patient charts, especially in the context of DAMA.

Conclusions

This study demonstrated that patient noncompliance was the predominant cause of PDCRT for H&N cancers. Older age, male sex, white race, greater distance from the hospital, single marital status, poor performance status, treatment interruptions, and significant pain issues during the RT course represented potential important characteristics of the at-risk patient population. Improving patient education, optimizing pain control, integrating supportive services early, and recognizing and addressing patients' psychosocial challenges are critical for successful treatment completion. Identifying interventions that would help at-risk patients complete a full course of RT is essential and can be best done in the context of a prospective study. Such interventions have the potential to affect overall survival in patients with H&N malignancies.

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