Original Article

Adherence to National Comprehensive Cancer Network Guidelines for Time to Initiation of Postoperative Radiation Therapy for Patients With Head and Neck Cancer

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BACKGROUND: Adherence to evidence-based treatment guidelines has been proposed as a measure of cancer care quality. The objective of this study was to determine the rate and predictors of care that does not adhere to National Comprehensive Cancer Network guidelines regarding commencing postoperative radiation therapy (PORT) within 6 weeks of surgery for patients with head and neck squamous cell carcinoma (HNSCC). **METHODS:** The National Cancer Data Base was reviewed from 2006 to 2014, and patients with HNSCC who underwent curative-intent surgery followed by PORT were identified. Multivariable logistic regression analysis was used to determine the factors associated with nonadherence to guidelines regarding the timing of initiating PORT. **RESULTS:** In total, 47,273 patients were included in the study. 55.7% of patients (26,340/47,273) failed to commence PORT within 6 week of surgery. The percentage of patients who failed to initiate PORT within 6 week of surgery increased over time. On multivariable analysis, the factors associated with failure to initiate timely, guideline-adherent PORT included black race, public insurance [Medicare, Medicaid] or uninsured status, lower levels of education, increased severity of comorbidity, increased postoperative length of stay, 30-day unplanned hospital readmission, treatment at an academic medical center, and the receipt of surgery and PORT at different facilities. **CONCLUSIONS:** Over 50% of patients with HNSCC who undergo surgery and PORT receive care that does not adhere to National Comprehensive Cancer Network guidelines with regard to initiating PORT within 6 weeks of surgery. Sociodemographic, oncologic, treatment, and hospital factors are all associated with failure to receive guideline-directed care and should be explored in future studies. ***Cancer* 2017;123:2651-60**. © *2017 American Cancer Society*.

KEYWORDS: adherence to guidelines, head and neck quality, National Cancer Data Base, National Comprehensive Cancer Network (NCCN), NCNN guidelines, quality of care.

INTRODUCTION

In recent years, several leading national organizations, including the American Society of Clinical Oncology, the American Cancer Society, the National Quality Forum, and the Institute of Medicine, have issued reports, guidelines, and consensus statements regarding the quality of cancer care in America.[1-7] Timeliness of care is recommended as 1 indicator of quality care.[3] The only measure of timely care incorporated into guidelines for patients with head and neck squamous cell carcinoma (HNSCC) is the interval between surgery and postoperative radiation therapy (PORT). According to the National Comprehensive Cancer Network (NCCN) Treatment Guidelines, version 2.2016, the "preferred interval between resection and postoperative radiotherapy is $\leq$6 weeks."[8] To date, no large studies have documented how often patients with HNSCC initiate PORT in a manner that adheres to NCCN guidelines or which patients are at the highest risk for receiving substandard care.

In the current study of patients with HNSCC undergoing surgery and PORT, we sought to answer the following questions: 1) How frequently do patients receive treatment that does not adhere to NCCN guideline recommendations to initiate PORT within 6 weeks of surgery? 2) What factors are associated with failure to initiate timely, guideline-adherent PORT?

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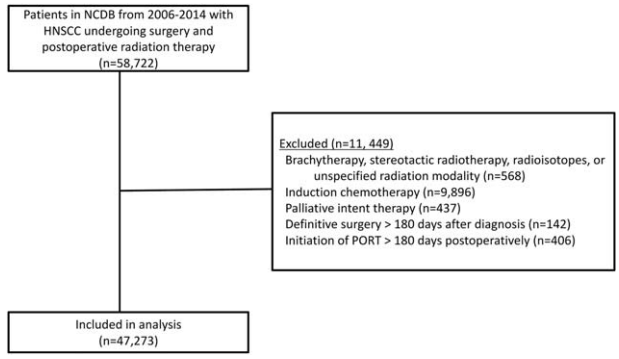

Figure 1. This chart illustrates the derivation of the current study cohort. HNSCC indicates head and neck squamous cell carcinoma; NCDB, National Cancer Data Base; PORT, postoperative radiation therapy.

MATERIALS AND METHODS

Data Source

The National Cancer Data Base (NCDB) is a hospital-based cancer registry that is a joint program of the American College of Surgeons Commission on Cancer, and the American Cancer Society. The NCDB annually collects high-quality and internally appraised cancer data from more than 1500 Commission on Cancer-accredited hospitals in the United States. It captures approximately 70% of cancer diagnoses annually in the United States, making it the world's largest clinical cancer registry.[9]

Study Cohort

The Medical University of South Carolina Institutional Review Board deemed this study exempt from review. The NCDB was reviewed from 2006 through 2014 to identify patients with upper aerodigestive tract HNSCC who had not received prior radiation and underwent curative-intent surgery followed by postoperative radiation with or without chemotherapy (Fig. 1). HNSCC diagnoses were filtered using *International Classification of Disease for Oncology, Third Edition* topography codes for the oral cavity (including lip; codes C00.0-C00.6, C00.8, C00.9, C02.0-C02.3, C02.8, C0.2.9, C03.0, C03.1, C03.9-C04.1, C04.8-C05.0, C06.0-C06.2, C06.8, and C06.9), the oropharynx (codes C01.9, C02.4, C05.1, C05.2, C5.8, C5.9, C09.0, C09.1, C09.8-C10.4, C10.8, C10.9, C14.0, C14.2, and C14.8), the hypopharynx (codes C12.9-C13.2, C13.8, and C13.9), and the larynx (codes C32.0-C32.3 and C32.8-C32.9) as well as histology codes for squamous cell carcinoma (SCC) or relevant variants (codes 8032, 8050, 8052, 8070-8075, and 8083-8084). In total, 58,722 patients met the inclusion criteria. The following patients were excluded (n = 11,449): patients who received brachytherapy, stereotactic radiosurgery, or an unspecified radiation modality (n = 568); received induction chemotherapy (n = 9896); received palliative therapy (n = 437); underwent definitive surgery >180 days after diagnosis (n = 142); and initiated PORT >180 days after surgery (n = 406). We excluded patients who underwent definitive surgery >180 days after diagnosis and initiated PORT >180 days after surgery because of presumed clinical dissimilarity and concern about curative intent. The final study cohort was composed of 47,273 patients. Because the study evaluated the time to initiation of PORT, patients with pathologic T3 and T4 or lymph node-positive HNSCC who should have received adjuvant therapy but did not were not analyzed.

Outcome Measures

The primary outcome measure was nonadherence to the NCCN recommendation to initiate PORT within 6 weeks of surgery. Time to initiation of PORT was calculated as the difference between the time from diagnosis to definitive surgery and the time from diagnosis to the beginning of radiation. Time to initiation of PORT was dichotomized into care that was adherent to NCCN guidelines (initiation of PORT ≤6 weeks postoperatively) or nonadherent (initiation of PORT >6 weeks postoperatively).

Study Variables

Patient covariates included sociodemographics (age, sex, race, ethnicity, urban/rural status, educational attainment, median household income), patient distance from treatment facility, insurance type, comorbidity, oncologic characteristics (tumor site, clinical and pathologic American Joint Committee on Cancer [AJCC] stage, surgical margins), and treatment characteristics (postoperative length of stay [LOS], 30-day hospital readmission, receipt

of adjuvant concurrent chemotherapy). Age was grouped into categories (<50, 50-59, 60-69, and ≥70 years). Race was classified as white, black, Asian, and other. Urban/rural status was based on 2013 data and is classified by the NCDB as metropolitan, urban, and rural based on population size and degree of urbanization.[10] Educational attainment is estimated within the NCDB by matching the patient's zip code to data from 2008 through 2012 regarding the number of adults in the zip code who did not graduate from high school and is categorized into quartiles (<7%, 7%-12.9%, 13%-20.9%, and ≥21%).[10] The median household income is estimated within the NCDB by matching the patient's zip code to data from 2008 through 2012, adjusting for 2012 inflation, and is then categorized into quartiles (<$38,000, $38,000-$47,999, $48,000-$62,999, and ≥$63,000).[10] Distance from the treatment facility is calculated as the distance in miles from the patient's zip code centroid and treatment facility address.[10] Comorbidity was assessed with the Charlson/Deyo comorbidity score[11] and is categorized as 0, 1, or ≥2 within the NCDB.[10] Patients were staged according to the sixth or seventh edition of the AJCC staging system, depending on the year of diagnosis. Thirty-day hospital readmissions are categorized as unplanned or planned within the NCDB but only include readmission to the treating hospital.[10] Radiation modality was categorized as external beam (which included external beam no otherwise specified, photon and/or electron, and neutron), intensity-modulated radiation therapy (IMRT), conformal or 3-dimensional therapy, proton therapy, or other. Extent of surgery is available in the NCDB but is site specific, which makes it challenging to clinically interpret comparisons across tumor subsites; therefore, extent of surgery is not presented in this report. The number of lymph nodes examined is available in the NCDB, allowing inferences about neck dissections, but the extent or laterality of neck dissection is not recorded.

Covariates related to care delivery included treatment facility type, treatment at more than 1 facility, surgery and radiation at the same facility, and region of the United States. Treatment facility type is classified in the NCDB as community cancer program, comprehensive community cancer program, academic program, integrated network cancer program, and other. An academic cancer program is defined by training residents in at least 4 specialties. Nonacademic facility types are differentiated based on annual case volume for all cancers (community vs comprehensive community) or whether they belong to a network of facilities that provide integrated and comprehensive cancer care (integrated network).[12] Treatment at more than 1 facility was calculated using the class of case codes and was categorized as all treatment at 1 facility, treatment at more than 1 facility, and unknown whether treatment was received at 1 or more facilities. Surgery and radiation at the same facility were calculated using the codes for surgery at this facility and radiation at this facility. Geographic region of the United States was recategorized from the 9 NCDB codes into 4 regions: Northeast, South, Midwest, and West.[10]

Statistical Analysis

Univariable logistic regression analysis was performed on covariates to identify factors associated with the failure to initiate PORT within 6 weeks of surgery. The variables that were associated with failure to initiate timely, guideline-adherent PORT on univariable analysis ($P < .05$) with perceived clinical relevance were entered into the multivariable logistic regression model. In cases of collinearity, clinical relevance was used to select which covariates to include in the model. Multivariable logistic regression analysis was performed using a backward stepwise manual-removal approach in which covariates were removed based on the P values (ie, the covariate with the largest P value was removed) until we arrived at the final model, in which the P values for regression coefficients for each covariate were $< .01$. For categorical variables with unknown or missing information, the unknown groups were included throughout for data analysis but were omitted from the final multivariable analysis for clarity of presentation. Data analysis was performed using SPSS version 24 (IBM SPSS Inc., Chicago, Ill). All statistical tests were 2-sided. Given the large sample size, statistical significance was set at a P value of $< .01$, and measures of precision of point estimates are presented as 99% confidence intervals (CIs).

RESULTS

Patient Population and Characteristics

We identified 47,273 patients with HNSCC who underwent surgery and PORT from 2006 through 2014 and met study inclusion criteria. Of these, 55.7% (26,340 of 47,273 patients) failed to start PORT within 6 week of surgery, as recommended; and 40.9%, 29.4%, 15.9%, and 9% of patients failed to commence PORT within 7, 8, 10, and 12 weeks of surgery, respectively. Data on the patients' sociodemographic, oncologic, and treatment characteristics and their relation to the failure to initiate timely, guideline-adherent PORT are presented in Tables 1 and 2. In the entire cohort of patients, most were men (76%), white (88%), and had private insurance

TABLE 1. Patient Demographics and Comorbidities

Patient Variable	No. of Patients (%)			
	Total Patients, n = 47,273	Initiation of PORT ≤6 Weeks, n = 20,933	Initiation of PORT >6 Weeks, n = 26,340	OR [99% CI]
Age, y				
<50	9500 (20.1)	4245 (20.3)	5255 (20)	1.00 [Ref]
50-59	16,727 (35.4)	7203 (34.4)	9524 (36.2)	1.07 [1.00-1.14]
60-69	13,056 (27.6)	5729 (27.4)	7327 (27.8)	1.03 [0.96-1.11]
≥70	7990 (16.9)	3756 (17.9)	4234 (16.1)	0.91 [0.84-0.99]
Sex				
Men	35,762 (75.6)	16,352 (78.1)	19,410 (73.7)	1.00 [Ref]
Women	11,511 (24.4)	4581 (21.9)	6930 (26.3)	1.29 [1.21-1.35]
Race				
White	41,505 (87.8)	18,855 (90.1)	22,650 (86)	1.00 [Ref]
Black	4020 (8.5)	1428 (6.8)	2592 (9.8)	1.51 [1.38-1.65]
Asian	1053 (2.2)	381 (1.8)	672 (2.6)	1.47 [1.24-1.74]
Other/unknown	695 (1.5)	269 (1.3)	426 (1.6)	1.32 [1.08-1.61]
Ethnicity				
Non-Hispanic	43,036 (91)	19,107 (91.3)	23,929 (90.8)	1.00 [Ref]
Hispanic	1973 (4.2)	704 (3.4)	1269 (4.8)	1.44 [1.27-1.63]
Unknown	2264 (4.8)	1122 (5.4)	1142 (4.3)	0.81 [0.73-0.91]
Insurance type				
Private	23,203 (49.1)	11,289 (53.9)	11,914 (45.2)	1.00 [Ref]
Medicare	15,207 (32.2)	6683 (31.9)	8524 (32.4)	1.21 [1.15-1.28]
Medicaid	4741 (10)	1448 (6.9)	3293 (12.5)	2.16 [1.97-2.35]
Uninsured	2459 (5.2)	858 (4.1)	1601 (6.1)	1.77 [1.58-1.98]
Other	994 (2.1)	380 (1.8)	614 (2.3)	1.53 [1.29-1.82]
Unknown	669 (1.4)	275 (1.3)	394 (1.5)	1.36 [1.11-1.67]
Urban/rural				
Metropolitan	37,520 (79.4)	16,543 (79)	20,977 (79.6)	1.00 [Ref]
Urban	7574 (16)	3412 (16.3)	4162 (15.8)	0.96 [0.90-1.03]
Rural	930 (2)	447 (2.1)	483 (1.8)	0.85 [0.72-1.01]
Unknown	1249 (2.6)	531 (2.5)	718 (2.7)	1.07 [0.92-1.24
Education				
Highest quartile	10,613 (22.5)	5260 (25.1)	5353 (20.3)	1.00 [Ref]
Second highest quartile	15,531 (32.9)	6936 (33.1)	8595 (32.6)	1.22 [1.14-1.30]
Second lowest quartile	12,707 (26.9)	5442 (26)	7265 (27.6)	1.31 [1.23-1.40]
Lowest quartile	8001 (16.9)	3131 (15)	4870 (18.5)	1.53 [1.42-1.65]
Unknown	421 (0.9)	154 (0.8)	257 (1)	1.54 [1.19-2.00]
Median household income				
Highest quartile	12,807 (29.2)	6466 (30.9)	7341 (27.9)	1.00 [Ref]
Second highest quartile	12,746 (27)	5780 (27.6)	6966 (26.4)	1.06 [1.00-1.13]
Second lowest quartile	11,609 (24.6)	5058 (24.2)	6551 (24.9)	1.14 [1.07-1.22]
Lowest quartile	8658 (18.3)	3449 (16.5)	5209 (19.8)	1.33 [1.24-1.43]
Median household income				
Highest quartile	12,807 (29.2)	6466 (30.9)	7341 (27.9)	1.00 [Ref]
Second highest quartile	12,746 (27)	5780 (27.6)	6966 (26.4)	1.06 [1.00-1.13]
Second lowest quartile	11,609 (24.6)	5058 (24.2)	6551 (24.9)	1.14 [1.07-1.22]
Lowest quartile	8658 (18.3)	3449 (16.5)	5209 (19.8)	1.33 [1.24-1.43]
Unknown	453 (1)	180 (0.9)	273 (1)	1.34 [1.04-1.72]
Distance from treatment facility, miles				
≤10	20,686 (45.8)	9548 (47.8)	11,138 (44.2)	1.00 [Ref]
11-20	8774 (19.4)	3941 (19.7)	4833 (19.2)	1.05 [0.98-1.12]
21-50	8987 (19.9)	3817 (19.1)	5170 (20.5)	1.16 [1.09-1.24]
51-100	3764 (8.3)	1492 (7.5)	2272 (9)	1.31 [1.19-1.43]
>100	2529 (5.6)	1031 (5.2)	1498 (6)	1.25 [1.12-1.39]
Unknown	421 (0.9)	161 (0.8)	260 (1)	1.38 [1.07-1.80]
Charlson/Deyo comorbidity score				
0	37,304 (78.9)	16,941 (80.9)	20,363 (77.3)	1.00 [Ref]
1	7883 (16.7)	3194 (15.3)	4689 (17.8)	1.22 [1.15-1.30]
≥2	2086 (4.4)	798 (3.8)	1288 (4.9)	1.34 [1.19-1.51]

Abbreviations: CI, confidence interval; OR, odds ratio; PORT, postoperative radiation therapy; Ref, reference category.

(49%). The most common primary site was the oropharynx (42%), the most common stage was AJCC pathologic stage IV (45%), and the most common radiation modality was IMRT (53%). Most patients received concurrent chemoradiation (53%). The hospital-level characteristics are provided in Table 3. The most common type of treatment

TABLE 2. Patient Oncologic and Treatment Characteristics

Patient Variable	No. of Patients (%)			OR [99% CI]
	Total Patients, n = 47,273	Initiation of PORT ≤6 Weeks, n = 20,933	Initiation of PORT >6 Weeks, n = 26,340	
Cancer primary site				
Oral cavity	15,037 (31.8)	4298 (20.5)	10,739 (40.8)	1.00 [Ref]
Oropharynx	19,771 (41.8)	10,138 (48.4)	9633 (36.6)	0.38 [0.36-0.40]
Hypopharynx	1214 (2.6)	438 (2.1)	776 (2.9)	0.71 [0.60-0.83]
Larynx	11,251 (23.8)	6059 (28.9)	5192 (19.7)	0.34 [0.32-0.37]
AJCC clinical stage grouping				
I	6123 (13)	3681 (17.6)	2442 (9.3)	1.00 [Ref]
II	5743 (12.1)	2621 (12.5)	3122 (11.9)	1.80 [1.63-1.98]
III	7683 (16.3)	3353 (16)	4330 (16.4)	1.95 [1.78-2.13]
IV	18,204 (38.5)	7160 (34.2)	11,044 (41.9)	2.33 [2.15-2.51]
Unknown	9520 (20.1)	4118 (19.7)	5402 (20.5)	1.98 [1.82-2.15]
AJCC pathologic stage grouping				
I	3154 (6.7)	1801 (8.6)	1353 (5.1)	1.00 [Ref]
II	3310 (7)	1433 (6.8)	1877 (7.1)	1.74 [1.53-1.98]
III	6282 (13.3)	2563 (12.2)	3719 (14.1)	1.93 [1.72-2.16]
IV	21,153 (44.7)	7475 (35.7)	13,678 (51.9)	2.44 [2.20-2.69]
Unknown	13,374 (28.3)	7661 (36.6)	5713 (21.7)	1.00 [0.90-1.10]
Surgical margin status				
Negative	28,245 (59.7)	10,806 (51.6)	17,439 (66.2)	1.00 [Ref]
Positive	11,760 (24.9)	5643 (27)	6117 (23.2)	0.67 [0.63-0.71]
Unknown	7268 (15.4)	4484 (21.4)	2784 (10.6)	0.39 [0.36-0.41]
Postoperative LOS, d				
0-3	23,520 (49.8)	12,966 (61.9)	10,554 (40.1)	1.00 [Ref]
4-7	6664 (14.1)	2468 (11.8)	4196 (15.9)	2.09 [1.94-2.25]
8-14	6100 (12.9)	1574 (7.5)	4526 (17.2)	3.53 [3.25-3.84]
15-21	1520 (3.2)	273 (1.3)	1257 (4.7)	5.61 [4.71-6.69]
>21	1289 (2.7)	172 (0.8)	1117 (4.2)	7.98 [6.44-9.88]
Unknown	8180 (17.3)	3480 (16.6)	4700 (17.8)	1.66 [1.55-1.77]
30-Day hospital readmission				
None	42,618 (90.2)	19,133 (91.4)	23,485 (89.2)	1.00 [Ref]
Unplanned	1329 (2.8)	451 (2.2)	878 (3.3)	1.59 [1.36-1.85]
Planned	1246 (2.6)	524 (2.5)	722 (2.7)	1.12 [0.97-1.30]
Unknown	2080 (4.4)	825 (3.9)	1255 (4.8)	1.24 [1.10-1.40]
Radiation modality[a]				
External beam	20,521 (43.4)	9634 (46)	10,887 (41.3)	1.00 [Ref]
IMRT	24,963 (52.8)	10,347 (49.4)	14,616 (55.5)	1.25 [1.19-1.32]
Conformal or 3D therapy	1714 (3.6)	941 (4.5)	772 (2.9)	0.73 [0.64-0.83]
Proton therapy	75 (0.2)	11 (0.1)	64 (0.2)	5.15 [2.20-11.94]
Concurrent chemoradiation				
No	21,785 (46.1)	9588 (45.8)	12,197 (46.3)	1.00 [Ref]
Yes	25,096 (53.1)	11,165 (53.3)	13,931 (52.9)	0.98 [0.94-1.03]
Unknown	392 (0.8)	180 (0.9)	212 (0.8)	0.93 [0.71-1.21]

Abbreviations: 3D, 3 dimensional; AJCC, American Joint Committee on Cancer; CI, confidence interval; IMRT, intensity-modulated radiation therapy; LOS, length of stay; OR, odds ratio; PORT, postoperative radiation therapy; Ref, reference category.
[a] Certain rows and columns may not sum to the total if 1 of the categorical variables has a cell size <10 to protect patient identity, according to National Cancer Data Base policy.

facility was an academic medical center (44%), and most patients did not receive surgery and PORT at the same facility (51%).

Temporal Trends in Nonadherence to Guidelines for Time to Initiation of PORT

From 2006 through 2014, there was an increase in the percentage of patients who had their PORT initiated more than 6 weeks after surgery (52.9% of patients in 2006 vs 58.7% of patients in 2014; $P < .001$) This increase in the percentage of patients who experienced delayed PORT initiation mirrors the increasing use of IMRT over time (Fig. 2).

Factors Associated With Nonadherence to Guidelines for Time to Initiation of PORT

Multivariable logistic regression analysis was used to identify factors associated with failure to initiate PORT within 6 weeks of surgery. Forest plots generated for the adjusted odds ratios (ORs) from the regression analysis are

TABLE 3. Hospital Characteristics

Hospital Variable	No. of Patients (%)			OR [99% CI]
	Total Patients, n = 47,273	Initiation of PORT ≤6 Weeks, n = 20,933	Initiation of PORT >6 Weeks, n = 26,340	
Treatment facility type				
Community	4058 (8.6)	2070 (9.9)	1988 (7.5)	1.00 [Ref]
Comprehensive community	16,465 (34.8)	8266 (39.5)	8199 (31.1)	1.03 [0.94-1.13]
Academic	20,635 (43.7)	7834 (37.4)	12,801 (48.6)	1.70 [1.56-1.86]
Integrated network	4700 (9.9)	2131 (10.2)	2569 (9.8)	1.26 [1.12-1.40]
Other/unknown	1415 (3)	632 (3)	783 (3)	1.29 [1.10-1.51]
No. of facilities involved in treatment				
All treatment at 1 CoC facility	11,698 (24.7)	5308 (25.4)	6390 (24.3)	1.00 [Ref]
Treatment at >1 CoC facility	12,745 (27)	5192 (24.8)	7553 (28.7)	1.21 [1.13-1.29]
Unknown	22,830 (48.3)	10,433 (49.8)	12,397 (47.1)	0.99 [0.93-1.05]
Surgery and radiation at same facility				
Yes	23,343 (49.4)	11,034 (52.7)	12,309 (46.7)	1.00 [Ref]
No	23,930 (50.6)	9899 (47.3)	14,031 (53.3)	1.27 [1.21-1.33]
Region of the United States				
Northeast	9058 (19.2)	3252 (16.9)	5526 (21)	1.00 [Ref]
Midwest	13,558 (28.7)	6435 (30.7)	7123 (27)	0.71 [0.66-0.76]
South	16,319 (34.5)	7353 (35.1)	8966 (34)	0.78 [0.73-0.84]
West	6923 (14.6)	2981 (14.2)	3942 (15)	0.85 [0.78-0.92]
Unknown	1415 (3)	632 (3)	783 (3)	0.79 [0.68-0.92]

Abbreviations: CI, confidence interval; CoC, Commission on Cancer; OR, odds ratio; PORT, postoperative radiation therapy; Ref, reference category.

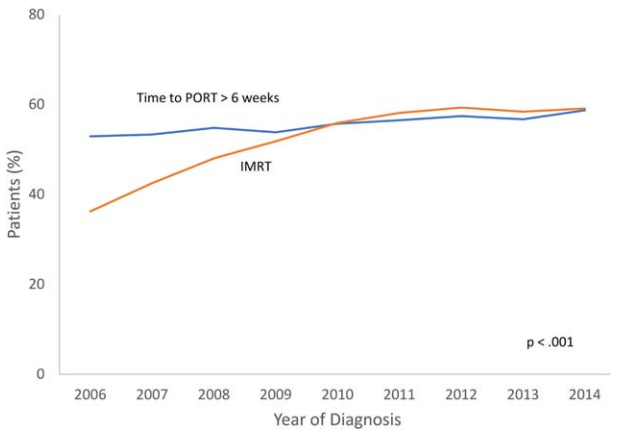

Figure 2. Temporal trends in the failure to initiate postoperative radiation therapy within 6 weeks of surgery are illustrated according to the year of diagnosis and the percentages of patients who received intensity-modulated radiation therapy (IMRT). PORT indicates postoperative radiation therapy.

presented in Figure 3 and Supporting Table 1. Measures of low socioeconomic status correlated with failure to initiate timely, guideline-adherent PORT and included Medicaid enrollment (OR, 1.59; 99% CI, 1.44-1.75) or uninsured (OR, 1.53; 99% CI, 1.35-1.73) and living in a zip code with a high percentage of failure to complete high school (OR, 1.19-1.30; 99% CI, 1.11-1.42 for all quartiles relative to the highest education quartile). Increasing severity of comorbidity, as assessed by the Charlson/Deyo comorbidity score, was also correlated with delayed initiation of PORT (OR, 1.14 [99% CI, 1.06-1.22] for 1 comorbidity; and OR, 1.21 [99% 1.06-1.38] for 2 or more comorbidities).

Various oncologic and treatment variables were associated with failure to initiate timely, guideline-adherent PORT. Relative to patients who had oral cavity primary tumors, those who had tumors in all other subsites were more likely to experience timely, guideline-adherent initiation of PORT. Increasing postoperative LOS correlated with failure to start PORT within 6 weeks, ranging from a 1.4-fold increased risk for patients with an LOS of 4 to 7 days (OR, 1.39; 99% CI, 1.28-1.50) to a 4.9-fold risk for those with a postoperative LOS >21 days (OR, 4.94; 99% CI, 3.96-6.15). Unplanned hospital readmission within 30-days of surgery also increased the risk of delayed initiation of PORT (OR, 1.28; 99% CI, 1.09-1.50). Patients who received IMRT or proton therapy as their radiation modality were more likely to experience delayed care (IMRT: OR, 1.24; 99% CI, 1.17-1.31; proton therapy: OR, 5.18; 99% CI, 2.18-12.31).

Variables related to the hospital system of care delivery were also associated with failure to initiate timely, guideline-adherent PORT. Patients who received some portion of their care at an academic medical center were significantly more likely not to commence PORT within the recommended timeframe (OR, 1.28; 99% CI, 1.16-1.41). Fragmentation of care was correlated with delayed

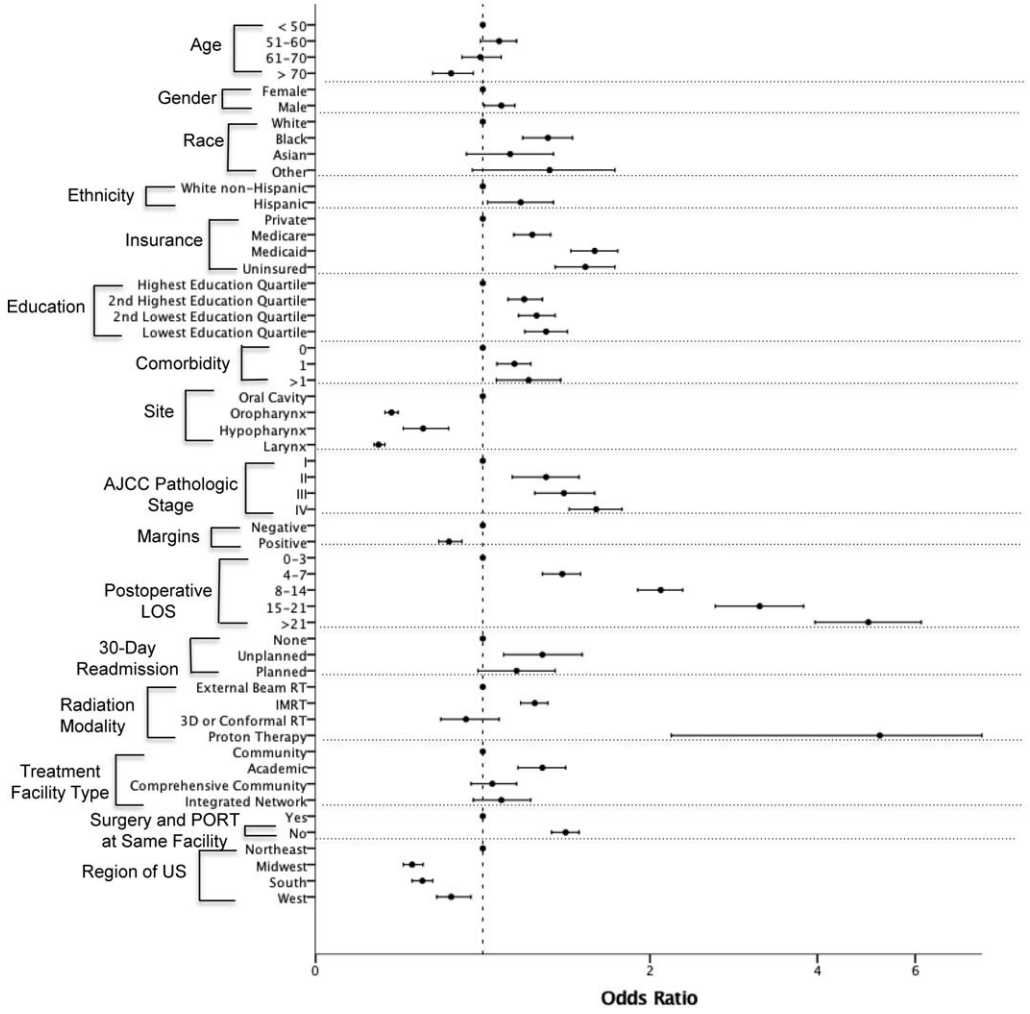

Figure 3. Multivariable analysis of the factors associated with delayed initiation of postoperative radiation therapy is illustrated. The first category in each group is the reference category. 3D indicates 3 dimensional; AJCC, American Joint Committee on Cancer; IMRT, intensity-modulated radiation therapy; LOS, length of stay; RT, radiation therapy.

initiation of PORT, because patients who underwent surgery and received radiation at different facilities were more likely to experience delayed initiation of PORT (OR, 1.41; 99% CI, 1.33-1.49).

DISCUSSION

Variability in the delivery of cancer care with unexplained heterogeneity and deviation from national standards exists across several oncology disciplines.[1] This unexplained variability in care contributes to low-quality care and may impact the cost of care. One manifestation of lower quality cancer care is failing to deliver timely cancer care.[3] In this large, nationally representative, hospital-based cancer registry, we observed that, for patients with HNSCC who receive PORT, care that is not adherent to NCCN guidelines with regard to the timely initiation of PORT is common. Furthermore, nonadherence is related to measures of socioeconomic status and comorbidity, oncologic characteristics, the postoperative hospital course, type of radiation modality, type of facility of treatment, care fragmentation, and region of the United States.

Frequency of Care that Does Not Adhere to NCCN Guidelines

Over 50% of the patients in this study received care that did not adhere to NCCN guidelines with regard to the timely initiation of PORT after surgery. Discrepancies between guideline-directed care and delivered care have been described across the spectrum of pretreatment evaluation, treatment, and posttreatment surveillance for

patients with oral cavity cancer[13] and laryngeal cancer[14,15] and in the receipt of adjuvant therapy for patients who have head and neck cancer with high-risk features.[16] The failure to achieve guideline-directed care has been reported in single-institution studies[17] and in national studies of patients with head and neck cancer.[18] Continued effort will be required to improve the quality of care delivered to these patients.[19]

Temporal Trends in Care that Does Not Adhere to NCCN Guidelines

The frequency of care that did not adhere to NCCN guidelines with regard to commencing adjuvant therapy in a timely fashion increased over the study period (from 52.9% in 2006 to 58.7% in 2014). This finding of worse adherence over time was largely explained by a matching increase in the percentage of patients who received IMRT over the study period. Others have also documented a rise in the receipt of IMRT over time by patients with head and neck cancer.[20] Despite the benefits of IMRT in terms of xerostomia and health-related quality of life for patients with head and neck cancer,[21] the relation between more sophisticated technologies and increasing time to treatment remains an area of tension as providers try to provide high-quality care in a timely fashion.[22]

Factors Associated With Nonadherence to Guidelines for the Timely Initiation of PORT

Numerous patient-level factors were related to the failure to receive PORT in a timeframe that adhered with NCCN recommendations. In the current study, measures of low socioeconomic status were correlated with receipt of care that did not adhere to NCCN guidelines. An increased likelihood of care that does not adhere to NCCN guidelines for patients with low socioeconomic status has been documented in patients with head and neck cancer[16] and in other surgical oncology specialties, such as breast cancer,[23,24] colorectal cancer,[25] lymphoma,[26] and various others.[27]

Increasing severity of comorbidity was correlated with delayed initiation of PORT. In patients with head and neck cancer, the severity of comorbidity affects timing of diagnosis, selection of treatment, prognosis, and quality of life.[28] More severe levels of comorbidity have been associated with lower quality care across a variety measures, including the likelihood of receiving NCCN guideline-adherent care with regard to receipt of adjuvant therapy,[16] the likelihood of receiving high-quality care for laryngeal cancer,[14] increased time to initiation of definitive therapy,[22] and increased duration of radiation therapy.[29]

Increasing postoperative LOS and unplanned hospital readmission with 30 days of surgery also increased the risk of untimely, guideline-nonadherent PORT. Hospital LOS has been suggested as a quality indicator in head and neck cancer care.[30] Unplanned readmissions have received significant attention because of Medicare reimbursement; however, they have also been correlated with worse survival in patients with oral cavity cancer.[13] LOS and hospital readmission are both potentially modifiable risk factors that can be improved through quality-improvement methodology to decrease the rate of nonguideline-directed care.

Fragmented care, ie, surgery and radiation at different facilities, was correlated with delayed initiation of PORT. Care fragmentation was common in this study, because >50% of patients underwent received surgery at 1 facility and received adjuvant therapy at another. To our knowledge, the role of fragmentation between treatment facilities for surgery and radiation has not been described for patients with head and neck cancer. Significant differences have been described in the quality of radiation therapy and outcomes for patients who undergo surgery and receive radiation at an academic medical center compared with surgery at an academic medical center and radiation at a nonacademic medical center.[31,32] The effect of fragmented care on oncologic outcomes should be explored in the future.

Oncologic Effect of Timely PORT and Treatment Package Time

Despite the NCCN's endorsement of the preferred time to initiation of PORT for HNSCC, the evidence underlying the recommendation is conflicted with regard to its effect on locoregional recurrence and survival. The rationale for timely initiation of radiation therapy is the repopulation and proliferation of residual microscopic disease and tumor clonogens.[29,33] Some studies have reported benefits in terms of locoregional control and survival, whereas other studies have questioned whether recent advances in technology and use of chemotherapy mitigate against the adverse effects of treatment delays.[29,33-40] Although a total treatment package time, from surgery to completion of PORT, is not part of NCCN guidelines, numerous publications have indicated that the total duration of treatment is highly prognostic, with treatment package time goals ranging from <87 to <100 days.[33,37,40,41]

Recommendations to Improve Guideline-Adherent Care

Future research will be required to implement and study different interventions designed to decrease the rate of

delayed initiation of PORT. Attempts to alter modifiable risk factors, such as prolonged LOS and unplanned hospital readmission, already occur at the hospital level; however, understanding their implications on timely PORT and, consequently, potentially on survival might raise awareness and improve outcomes. For nonmodifiable risk factors, such as low socioeconomic status, resource intensification to help these patients understand the importance of timely initiation of PORT and succeed in making it to appointments potentially could help. In addition, global attention to this issue for all patients, including preoperative consultation with radiation oncology, minimization of fragmented care, and nurse navigator assistance with timeline expectations, might mitigate some of the problem. These suggestions merit future prospective study.

Limitations

This study has important limitations. Because it is a retrospective database study, we do not have knowledge of certain patient or tumor characteristics that might affect treatment decisions, such as particularly aggressive tumor behavior, perineural invasion, lymphovascular invasion, tumor board discussion, or patient-physician discussion about the risk/benefit ratio of adjuvant therapy that might affect the time to initiation of PORT. The role of patient preferences, indecisiveness, and the ability to meet the schedule of postoperative appointments necessary for timely initiation of PORT also cannot be discerned from this database. Missing data or coding errors related to patient or treatment characteristics are possible, likely are not random, and may bias the results of this study. This study only examines adherence to NCCN recommendations for the preferred time to initiation of PORT and not whether adherence to these guidelines is associated with improved oncologic outcomes, such as decreased rates of recurrence or improved survival. Future studies should address the relation between adherence to guidelines regarding the timely initiation of PORT and disease-specific oncologic outcomes. Despite these limitations, there are numerous methodological strengths to the study. It captures patients of all adult ages, has a national scope and a large sample size, and analyzes treatment at different types of hospitals.

Conclusions

Over 50% of patients with HNSCC who undergo surgery and PORT receive care that does not adhere to NCCN guidelines with regard to initiating PORT within the 6 weeks of surgery. The number of patients receiving guideline nonadherent care is increasing over time. Sociodemographic, oncologic, treatment, and hospital factors are all associated with care that does not adhere to guidelines. Modifiable risk factors for decreasing the rate of delayed initiation of PORT include postoperative LOS and unplanned hospital readmissions.

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AUTHOR CONTRIBUTIONS

Evan M. Graboyes: Conception and design, acquisition of data or analysis and interpretation of data, writing–initial draft, writing–review and revision, approval of final version, and agree to be accountable for all aspects of the work. **Elizabeth Garrett-Mayer:** Conception and design, acquisition of data or analysis and interpretation of data, writing–initial draft, writing–review and revision, approval of final version, and agree to be accountable for all aspects of the work. **Anand K. Sharma:** Conception and design, acquisition of data or analysis and interpretation of data, writing–initial draft, writing–review and revision, approval of final version, and agree to be accountable for all aspects of the work. **Eric J. Lentsch:** Conception and design, acquisition of data or analysis and interpretation of data, writing–initial draft, writing–review and revision, approval of final version, and agree to be accountable for all aspects of the work. **Terry A. Day:** Conception and design, acquisition of data or analysis and interpretation of data, writing–initial draft, writing–review and revision, approval of final version, and agree to be accountable for all aspects of the work.

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