Completion of Radiotherapy for Local and Regional Head and Neck Cancer in Medicare

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Objective: To identify factors associated with interruption or early discontinuation of treatment in patients receiving radiotherapy for head and neck cancer, because it is believed that such treatment interruption or early discontinuation increases the risk of disease relapse and adversely influences survival.

Design, Setting, and Patients: Using the Surveillance, Epidemiology, and End Results (SEER)–Medicare linked database, we identified Medicare beneficiaries 66 years or older who were diagnosed as having local or regional head and neck cancer from January 1, 1997, through December 31, 2003. For each case, we calculated the timing and duration of radiotherapy using Medicare claims data. We then performed logistic regression analyses to estimate the association between tumor and clinical characteristics and early discontinuation of and/or interruptions in radiotherapy.

Main Outcome Measure: Completion of uninterrupted radiotherapy.

Results: A substantial proportion of patients (39.8% overall) had interruptions in radiotherapy and/or incomplete therapy. Altogether, 70.4% of surgical patients completed radiotherapy with no interruptions compared with 52.0% of nonsurgical patients ($\chi^2 = 78.17; P < .001$). Surgery was associated with an increased likelihood of completing uninterrupted radiotherapy for all tumor sites. Comorbidity, chemotherapy, and regional disease were all associated with a decreased likelihood of completing radiotherapy at a subset of sites.

Conclusions: Failure to complete uninterrupted radiotherapy is common among Medicare enrollees with head and neck cancer. Surgery before radiotherapy is associated with an increased likelihood of completing radiotherapy. At a subset of sites, chemotherapy is associated with a decreased likelihood of completing radiotherapy. Further research is needed to identify factors associated with noncompletion of radiotherapy among nonsurgical patients and patients who receive chemotherapy.


HEAD AND NECK CANCERS are a complex group of tumors that involve the ethmoid sinus, maxillary sinus, lip, oral cavity, nasopharynx, oropharynx, hypopharynx, supraglottic larynx, and glottic larynx. Radiotherapy alone or as an adjuvant to surgery and/or chemotherapy has been shown to be curative in patients with local or regional head and neck cancers.5-6 Clinical evidence suggests that the radiation dose and duration of treatment is correlated with tumor control and survival.5,7 Breaks in radiotherapy have been associated with inferior tumor control in the larynx, pharynx, and oral cavity.8,9 Common causes for treatment discontinuation and complications include mucositis, xerostomia, dysphagia, and aspiration.10-12

Although radiotherapy can be an important part of treatment for head and neck cancer, to our knowledge, the incidence of incomplete and/or interrupted radiotherapy, as well as factors that put patients at risk of not completing therapy, has not been studied in a large, population-based sample. To determine the extent to which patients with head and neck cancer discontinue or experience interruptions in radiotherapy, we evaluated patterns of radiotherapy among Medicare enrollees 66 years or older who were diagnosed as having local or regional head and neck cancer. We also estimated the associations between several clinical and demographic variables and early discontinuation and/or interruptions in radiotherapy.

Methods

Databases and Study Population

Patients with head and neck cancer were identified from the Surveillance, Epidemiology, and End Results (SEER)–Medicare database, which consists of linked records from the SEER cancer registries data and the Medicare enrollment and claims files. The SEER registry collects demographic information, tumor-specific clinical and pathologic infor-
Data on radiotherapy were extracted from the Medicare National Claims History or the Carrier File and outpatient Statistical Analysis File using the *Current Procedural Terminology, Fourth Edition*, *ICD-9, International Classification of Diseases, Ninth Revision*. Radiotherapy may be recorded in either of the following 2 ways: as an element of a claim representing a single date of service, or as part of bundled claims records in which treatments are entered as a single claim spanning multiple days.

### Table 1. Medicare Claims Codes Used to Identify Treatment in Patients With Head and Neck Cancer

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT4 codes used to identify radiotherapy</td>
<td>77401-77416, and 77418</td>
</tr>
<tr>
<td>CPT4 codes used to identify surgical resection</td>
<td>15732, 15738, 20680, 21015, 21044, 21084, 21244, 30150, 31200, 31225, 31300, 31360, 31365, 31367, 31368, 31370, 31375, 31380, 31382, 31390, 31395, 31785, 31786, 38700, 38720, 38724, 40510, 40520, 40525, 40527, 40530, 40810, 40812, 40814, 40816, 40818, 41110, 41112, 41113, 41114, 41120, 41135, 41140, 41145, 41150, 41153, 41155, 41204, 42106, 42107, 42120, 42140, 42160, 42410, 42415, 42420, 42423, 42426, 42440, 42450, 42808, 42821, 42826, 42831, 42836, 42842, 42844, 42845, 42870, 42890, 42892, 42894, 42950, 43130, 43135, 60210, 60240, 60605, 69535, 69740, 69745, and 69970</td>
</tr>
<tr>
<td>ICD-9 codes used to identify surgical resection</td>
<td>213, 2130, 2131, 2132, 214, 215, 216, 2161, 2162, 2169, 224, 2241, 2224, 2226, 2260, 2261, 2262, 2263, 2264, 251, 252, 253, 254, 2629, 263, 2631, 2632, 273, 2731, 2732, 274, 2742, 2743, 2749, 2772, 282, 283, 285, 286, 2892, 293, 2933, 2939, 30, 300, 3001, 3009, 301, 302, 3021, 3022, 3023, 303, 304, 315, 404, 4040, 4041, 4042, 762, 763, 7631, 7639, 764, 7641, 7642, 7643, 7644, 7645, and 7646</td>
</tr>
</tbody>
</table>


**RADIOTHERAPY DATA ALGORITHMS**

Medicare administrative claims records of radiotherapy treatment are subject to errors and inaccuracies. To reduce the possibility of labeling administrative coding errors as disruptions in therapy, we developed a 2-step algorithm to exclude patients with a high probability of having errors in the Medicare claims.

First, we calculated the ratio of radiotherapy treatments recorded per RTD codes to the treatments recorded per radiation treatment management (RTM) codes. When used correctly, 1 RTM code, 77427, encompassed 9 treatments. Thus, a patient will have an apparent excess of treatments if RTM codes are recorded for individual treatments. We compared the total number of treatments for each patient according to RTD vs RTM codes to identify such errors. Patients with a ratio of at least 2.5 treatments to each RTM code met the first criterion for exclusion.

The second exclusion criterion was based on identifying patients with too few treatments recorded within the treatment period. Among patients meeting the first exclusion criterion, we identified and excluded patients with extreme values (ie, the highest 2.5%) for the ratio of the total number of treatment days to the total number of treatments per RTD code; thus, a ratio of 2.0 indicates 1 treatment every 2 days, on average. This ratio was less than 3.5 for 97.5% of all patients; the remaining 2.5% with ratios greater than 3.5 (n = 121) were excluded.

**REGRESSION ANALYSES**

Completion of uninterrupted radiotherapy was the outcome of interest for the regression analyses. Medicare claims do not include details of radiation dosage; therefore, we used the number of treatments administered to determine whether a patient completed therapy. We defined a complete course of radiotherapy as follows: at least 30 radiotherapy treatments for patients who did not undergo surgery before completing radiotherapy, or at least 25 treatments for patients who underwent surgery before completing radiotherapy. Patients with fewer treatments were identified as not having completed radiotherapy. These cutoffs are set slightly below the number of treatments for a commonly prescribed course of radiotherapy for head and neck cancer (ie, 2 Gy administered 5 d/wk for 6.5-7.0 weeks for a total of 70 Gy and 35 treatments, as defined by Bourhis et al15) to allow for variations in practice patterns and to avoid mislabeling shorter prescribed courses of therapy as incomplete radiotherapy. As reviewed by Zackrisson et al16, prescribed treatment lengths can vary from 25 to 45 treatments, and patients receiving surgery and radiotherapy often receive fewer treatments than patients receiving radiotherapy alone.
We defined treatment interruptions or gaps as lapses of more than 4 but less than 31 days between radiotherapy treatments. We included interruptions occurring at any point in each patient’s first course of radiotherapy to allow for variations in prescribed therapy involving more than 25 or 30 treatments. Patients with longer gaps between treatments were identified as having a second course of treatment that was not considered in this analysis.

For patients whose therapy was recorded in discrete claims, we defined gaps as 5- to 30-day lapses between claims. However, a more complex approach was required for patients with multiple claims recorded in a single claim spanning several days or weeks. In these claims, we found that the service dates of the claim sometimes exceeded the number of treatments, with no indication of which dates radiotherapy was administered. In those instances, we assumed that the treatments occurred on consecutive days. We adjusted the service dates of claims with at least 5 multiple claims recorded in a single claim spanning several days or weeks. In those instances, we assumed that the treatments occurred on consecutive days. We adjusted the service dates of claims with at least 5 fewer treatments than the number of service dates as follows:

1. The starting date of the first claim was changed to the last date of the claim—x weekdays, where x indicates the number of treatments.
2. The ending date of all other claims was changed to the ending date of all other claims.

Patients who failed to complete the required number of radiotherapy treatments and/or who had gaps in treatment were identified as having failed to complete uninterrupted therapy. We used the χ² test to compare the frequency of completing uninterrupted therapy between surgical vs nonsurgical patients.

We used logistic regression models to estimate odds ratios and 95% confidence intervals (CIs) for the association between clinical and tumor characteristics and early discontinuation of and/or gaps in radiotherapy. We constructed separate models for each of the following 5 head and neck tumor sites: larynx, nasal cavity (including the nose and middle ear), oral cavity (consists of lips, tongue, floor of mouth, other oral cavity and pharynx, and gum and other mouth), pharynx (consists of the oropharynx, nasopharynx, hypopharynx, and tonsils), and salivary gland. Each model included the following independent variables: surgery relative to the initiation of radiotherapy (<30 days, ≥30 days, or no surgery), tumor stage (local or regional), chemotherapy (yes or no), and comorbidity measured via the Charlson Comorbidity Index. This index provides a single measure (the Charlson score) of comorbidity based on 19 medical conditions, each weighted according to its association with mortality.17,18 All models were adjusted for categorical age, sex, race, and urban vs rural residence.

RESULTS

A total of 5086 patients met the inclusion criteria for this study. In all tables, cells with fewer than 5 patients were suppressed to protect patient confidentiality. Demographic characteristics and Charlson score stratified by tumor site are detailed in Table 2. Compared with men, women were more likely to receive surgery before radiotherapy (41.8% vs 50.3%). Early discontinuation and/or interruptions in therapy were less frequent in patients who underwent surgery before radiotherapy than in those who did not; 48.0% of nonsurgical patients had gaps in treatment and/or incomplete therapy compared with only 29.6% of surgical patients ($\chi^2 = 78.17; P < .001$). Overall, 21.7% of patients had a Charlson score of 0 (ie, no comorbidities), and 30.2% of patients had a Charlson score of 3 or higher.

The site-specific frequency of SEER summary stage and treatment are detailed in Table 3. The proportion of patients with regional cancer was smallest among those with
laryngeal tumors (39.6%) and greatest among those with pharyngeal tumors (83.8%). Overall, 14.8% of patients had chemotherapy in addition to radiotherapy, and 44.6% of patients underwent surgery before completing radiotherapy. Among surgical patients, 33.6% underwent surgery within 30 days before the initiation of radiotherapy or before the last radiotherapy treatment, and 63.3% underwent surgery 30 days or more before the initiation of radiotherapy.

Figure 1 shows the distribution of time elapsed between the diagnosis and the initiation of radiotherapy.
therapy in patients with regional and local tumors, stratified by surgery status. The stage-specific distributions were similar, and long lapses between the diagnosis and initiation of radiotherapy were more common among surgical patients. On average, surgical patients started radiotherapy 74.4 days after diagnosis, compared with 52.8 days for nonsurgical patients. As shown in Figure 2, the total number of radiotherapy treatments received was similar between patients with local and regional tumors. In all patients combined, surgical patients had an average of 30.8 treatments, and nonsurgical patients had an average of 31.6 treatments.

Table 4 lists the prevalence of interrupted and/or incomplete radiotherapy treatment for each tumor site, stratified by treatment received. Although the prevalence of interrupted and/or incomplete treatment varies across tumor sites, at all sites the prevalence was lowest among patients receiving surgery and radiotherapy.

The results of the logistic regression of patient characteristics associated with interruptions in planned radiotherapy are presented in Table 5. Patients with oral cavity tumors who underwent surgery within 30 days before the initiation of radiotherapy were 2.43 (95% CI, 1.69-3.48) times more likely to complete planned therapy. Patients with oral cavity tumors and a Charlson score of 2 or higher were 29% (95% CI, 6%-45%) less likely to complete planned therapy compared with patients with a Charlson score of 0, and patients undergoing chemotherapy for oral cavity tumors were 40% (18%-56%) less likely to complete planned therapy compared with patients having no chemotherapy.

Patients with pharyngeal tumors who underwent surgery within 30 days before the initiation of radiotherapy

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**Table 4. Proportions of Patients With Incomplete and/or Interrupted Radiotherapy**

<table>
<thead>
<tr>
<th>Treatment Category</th>
<th>Larynx</th>
<th>Nasal Cavity</th>
<th>Oral Cavity</th>
<th>Pharynx</th>
<th>Salivary Gland</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treated, No.</td>
<td>I/I, %</td>
<td>Treated, No.</td>
<td>I/I, %</td>
<td>Treated, No.</td>
<td>I/I, %</td>
</tr>
<tr>
<td>Radiation only</td>
<td>1173</td>
<td>37.3</td>
<td>69</td>
<td>62.3</td>
<td>532</td>
<td>55.6</td>
</tr>
<tr>
<td>Surgery and radiotherapy</td>
<td>646</td>
<td>19.5</td>
<td>146</td>
<td>34.2</td>
<td>721</td>
<td>33.3</td>
</tr>
<tr>
<td>Chemotherapy and radiotherapy</td>
<td>155</td>
<td>51.6</td>
<td>15</td>
<td>60.0</td>
<td>144</td>
<td>59.7</td>
</tr>
<tr>
<td>Chemotherapy, surgery, and radiotherapy</td>
<td>34</td>
<td>52.9</td>
<td>16</td>
<td>37.5</td>
<td>60</td>
<td>53.3</td>
</tr>
<tr>
<td>All</td>
<td>2008</td>
<td>33.0</td>
<td>246</td>
<td>43.9</td>
<td>1457</td>
<td>44.9</td>
</tr>
</tbody>
</table>

Abbreviation: I/I, incomplete/interrupted.
patients good candidates for surgery may also make them more likely to complete radiotherapy. Because comorbidities are known to decrease survival in patients with head and neck cancer,19 healthier patients may be chosen by surgeons to complete more rigorous treatments (eg, surgery in addition to radiotherapy). Although our analyses were adjusted for comorbidity, residual confounding by unmeasured factors such as social support and general health status could explain why patients who receive surgery are more likely to complete radiotherapy. In addition, patients who are willing to undergo major surgery to treat their disease may also be more motivated to complete a full course of uninterrupted radiation therapy, despite any toxic effects of treatment that may occur.

Patients with oral, pharyngeal, and laryngeal tumors who received chemotherapy concurrently with radiotherapy were less likely to complete the expected course of radiotherapy without interruptions. This association could be attributed to the toxic effects of the chemotherapeutic agents commonly administered for head and neck cancers. These agents include carboplatin, cisplatin, docetaxel, fluorouracil, and paclitaxel,20 and common adverse effects are nausea, vomiting, mucositis, neutropenia, thrombocytopenia, neuropathy, and anemia.21,22 The resulting toxic effects of these agents may cause patients to take extended breaks between treatments.10

In addition to our hypothesis that acute chemotherapy-related comorbidity increases the odds of discontinuation of radiotherapy and/or gaps between treatments, we might expect that preexisting comorbidities could reduce the likelihood of completing planned therapy. Indeed, patients with oral and laryngeal tumors with a Charlson score of 2 or higher were significantly less likely to complete uninterrupted radiotherapy than patients with a Charlson score of 0, but we did not observe this association for patients with cancers of the nasal cavity, salivary gland, or pharynx. This could be attributable to our limited sample size for some sites or to site-specific differences in the effect of comorbidity on one’s ability to complete radiotherapy.

### Table 5. Logistic Regression of Patient Characteristics Associated With Completion of Radiotherapy With No Gaps

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Larynx (n=2008)</th>
<th>Nasal Cavity (n=246)</th>
<th>Oral Cavity (n=1457)</th>
<th>Pharynx (n=953)</th>
<th>Salivary Gland (n=442)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical resection &lt; 30 d before initiation of radiotherapy</td>
<td>2.91 (2.16-3.91)</td>
<td>1.85 (0.87-3.93)</td>
<td>2.43 (1.69-3.48)</td>
<td>2.05 (1.27-3.29)</td>
<td>7.16 (3.22-15.94)</td>
</tr>
<tr>
<td>Surgical resection ≥ 30 d before initiation of radiotherapy</td>
<td>2.05 (1.53-2.74)</td>
<td>3.59 (1.94-6.65)</td>
<td>2.23 (1.77-2.82)</td>
<td>1.88 (1.33-2.66)</td>
<td>6.41 (3.06-13.41)</td>
</tr>
<tr>
<td>Charlson score c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.79 (0.58-1.09)</td>
<td>1.37 (0.67-2.80)</td>
<td>1.00 (0.74-1.35)</td>
<td>0.90 (0.62-1.30)</td>
<td>0.92 (0.51-1.66)</td>
</tr>
<tr>
<td>≥ 2</td>
<td>0.62 (0.46-0.83)</td>
<td>1.06 (0.55-2.06)</td>
<td>0.71 (0.55-0.94)</td>
<td>0.78 (0.56-1.10)</td>
<td>1.04 (0.61-1.77)</td>
</tr>
<tr>
<td>Local stage d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.77 (1.44-2.17)</td>
<td>1.38 (0.71-2.65)</td>
<td>1.07 (0.84-1.36)</td>
<td>1.99 (1.37-2.88)</td>
<td>1.30 (0.82-2.06)</td>
</tr>
<tr>
<td>≥ 2</td>
<td>0.58 (0.42-0.79)</td>
<td>1.13 (0.50-2.55)</td>
<td>0.60 (0.44-0.82)</td>
<td>0.69 (0.51-0.93)</td>
<td>1.05 (0.47-2.34)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio.

a Adjusted for age, sex, urban/rural residence, and race.
b Reference category is none.
c Reference category is 0.
d Reference category is regional.

We analyzed patterns of radiotherapy administered for head and neck cancer using population-based SEER-Medicare claims data to determine factors associated with discontinuation and/or interruptions in therapy. We found that surgical patients are more likely to complete uninterrupted therapy than are patients who receive radiotherapy alone or in combination with chemotherapy. Surgical patients may be more likely to complete radiotherapy for several reasons. First, characteristics that make patients good candidates for surgery may also make them more likely to complete radiotherapy. Because comorbidities are known to decrease survival in patients with head and neck cancer,19 healthier patients may be chosen by surgeons to complete more rigorous treatments (eg, surgery in addition to radiotherapy). Although our analyses were adjusted for comorbidity, residual confounding by unmeasured factors such as social support and general health status could explain why patients who receive surgery are more likely to complete radiotherapy. In addition, patients who are willing to undergo major surgery to treat their disease may also be more motivated to complete a full course of uninterrupted radiation therapy, despite any toxic effects of treatment that may occur.

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**COMMENT**

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This analysis provides insight into factors associated with completing uninterrupted radiotherapy, and future investigations of SEER-Medicare data could determine whether deviations from planned therapy are associated with decreased survival times for patients with head and neck cancer. However, limited sample sizes for some combinations of tumor site and stage may inhibit detecting statistically significant survival differences.

Observational retrospective data such as Medicare claims have limitations with regard to accuracy and the scope of information provided. Although patterns of radiotherapy administration may be discerned from claims information, the doses administered to patients are not available from the SEER-Medicare data. In this analysis, the lack of radiation dosage information limited our ability to determine whether patients completed a full course of therapy and to distinguish therapeutic from palliative treatments. In addition, higher treatment doses may increase the toxic effects of treatment and the likelihood of not completing the full course of treatment. Performance status measures such as the Karnofsky Performance Score are typically used to measure quality of life and determine how well a patient can perform basic activities, which may be related to the completion of prescribed therapy. However, it is not possible to calculate performance status using the data contained in Medicare claims.

Although this analysis accounted for urban vs rural residence as a factor influencing the likelihood of completing treatment, it should also be noted that the actual delivery of radiotherapy to patients with head and neck cancer can vary greatly, depending on the medical institution where the patient receives care. Although the SEER-Medicare database is an excellent source of population-based patients with head and neck cancer, we excluded a large number of patients who may have had improperly coded radiotherapy claims. This approach minimized the risk of including incorrect radiation claims data, but also limited sample size in the stratified analyses and may have reduced our ability to detect statistically significant associations. It is also likely that we excluded some patients whose claims were recorded accurately but who were administered an unusual radiotherapy regimen that met our criteria for exclusion.

CONCLUSIONS

Completion of planned radiotherapy is important for disease control and reduction of the risk of disease progression and recurrence. In this retrospective study of Medicare enrollees with head and neck cancer, we find that patients receiving surgery before the initiation of radiotherapy are more likely to complete radiotherapy than are those who do not undergo surgery. This likely reflects selection of patients for surgery who are more likely to complete therapy because of clinical and other patient-specific factors. In contrast, concurrent chemotherapy significantly reduces the likelihood of completion of radiotherapy among patients with oral, pharyngeal, or laryngeal tumors. Further research is needed to identify factors associated with noncompletion of radiotherapy among patients with head and neck cancer who do not undergo surgery. Because chemotherapy appears to reduce the likelihood of completing radiotherapy, future research is needed to identify specific agents, doses, and schedules that specifically reduce the likelihood of completing treatment in community settings.


