

Clinical Investigation

Elective Nodal Irradiation and Patterns of Failure in Head and Neck Cancer After Primary Radiation Therapy



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Summary

A large cohort of patients with head and neck cancer treated with curative radiation therapy was investigated with emphasis on the pattern of nodal failure. Using failure analysis, we found that recurrence outside the elective volumes was rare, and recurrence in the level IB and retropharyngeal regions was very rare, supporting the exclusion of these levels from the elective volumes, except under specific indications. The p16 status was included in the pattern of failure analysis.

Purpose: The delineation of elective clinical target volumes in head and neck cancer (HNC) is important; however, the extent of lymph node levels necessary to include is debated. A comprehensive analysis of recurrence patterns in a large cohort of patients with HNC was performed, with an emphasis on recurrence in the retropharyngeal region and level IB.

Methods and Materials: From 2005 to 2012, 942 patients with oropharyngeal, hypopharyngeal, laryngeal or oral cavity carcinomas were curatively treated with primary radiation therapy. The median follow-up period was 34 months, and 77% of the patients underwent intensity modulated radiation therapy. The retropharyngeal region was only routinely included in cases of involvement of the posterior pharynx wall and level IB only in cases of involvement of the oral cavity. In patients with regional recurrence, the anatomic site of the recurrence was assessed from the surgical descriptions or computed tomography scans and compared with the original radiation treatment plan (available from 2007 onward). The p16 status was available for 282 oropharynx carcinoma cases, with 65% p16-positive.

Results: Of the 942 patients, 376 (40%) developed recurrences: 228 (24.2%) local, 123 (13.1%) regional, and 109 (11.6%) distant. In 700 patients with available treatment plans, retropharyngeal and level IB recurrence was observed in 2 and 7 patients, respectively. Eight patients (1.1%) had recurrence in a lymph node level not included in their primary treatment plan. For oropharynx carcinoma, the locoregional control rate (90% vs 70%) but not distant control rate (92% vs 87%), was significantly better in the p16-positive than in the p16-negative patients. Although fewer recurrences developed in the p16-positive group, patients with recurrence of p16-positive tumors were more likely to develop recurrence in distant sites.

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Conclusions: Retropharyngeal or level IB recurrence after primary HNC radiation therapy is rare. Thus, inclusion of these regions in the elective treatment volumes should be limited to patients with involvement of the posterior pharyngeal wall or oral cavity. © 2016 Elsevier Inc. All rights reserved.

Introduction

Radiation therapy (RT) is evolving rapidly. Just in the past decade, highly conformal intensity modulated RT (IMRT) has replaced conventional 3-dimensional conformal RT as the standard treatment modality for non-resectable head and neck cancer (HNC). Multiple retrospective studies have suggested that IMRT does not compromise the outcome (rates of failure and survival) and that IMRT has a superior toxicity profile compared with conventional RT (1-4). These results have been reproduced in prospective studies for both survival (5) and treatment morbidity (6, 7). However, owing to the precision of IMRT, malignant tissue that would have been included in the treatment field with conventional RT, could be missed. This issue has led to increasing efforts to obtain a more precise definition of the target volumes in the treatment planning process.

The delineation of clinical target volumes (CTVs) is important to account for subclinical spreading of cancer and to treat areas that might harbor micrometastases, such as relevant lymph node regions. However, significant differences exist in the CTV definition. One example of the disparity is the inclusion of lymph node level IB in the treatment of oropharyngeal squamous cell carcinoma (OPSCC) (8), which is commonly practiced in some institutions. Another example is the decision to include high retropharyngeal (RP) lymph nodes routinely in non-nasopharyngeal carcinomas (9, 10). If included, the risk of recurrence might be decreased; however, studies have shown that it is at the expense of the patient's quality of life (11).

During the past 2 decades, a shift in head and neck cancer etiology has occurred, with an increase in human papillomavirus-associated OPSCC and a parallel decrease in traditional smoking-associated HNC (12, 13). Patients with p16-positive OPSCC have had superior overall survival and locoregional control compared with patients with p16-negative OPSCC, with recurrent disease predominantly distant metastases (DMs) (14).

Elective volumes in HNC RT has traditionally been determined from observational studies from the pre-human papillomavirus era; thus, precise failure analyses that incorporate p16 status are valuable. In Denmark, the national treatment guidelines for RT for HNC are specified by The Danish Head and Neck Cancer Group (DAHANCA), including detailed guidelines for the delineation of elective volumes (15).

Treated curatively with RT and in accordance with these guidelines, the present study explored a large cohort of patients and their patterns of failure. Specifically, the

distribution of local, regional, and distant failure in patients with p16-positive and p16-negative HNC was investigated. Furthermore, we determined whether the regional recurrence occurred at a lymph node level included in the original treatment plan.

Methods and Materials

Patient selection

The project was designed as a retrospective database study based on information from DAHANCA, a clinical database that continuously registers all patients with HNC in Denmark. Using the database, patients with SCC HNC treated with curative intent at Rigshospitalet, Copenhagen from 2005 to 2012 were identified. We included patients with primary oral cavity, pharyngeal, or laryngeal SCC and excluded patients with metastatic disease at diagnosis, patients not residing in Denmark, patients with follow-up data for <3 months, those with a history of HNC, those with stage T1 glottic larynx cancer, postoperative patients, and patients with primary cancer of the nasopharynx. The final cohort consisted of 942 patients. Information from the DAHANCA database was validated by reviewing each patient's file.

Treatment and patient evaluation

The target volumes consisted of a gross tumor volume (GTV) with tumor tissue verified by imaging data and clinical examination, including the macroscopically involved lymph nodes. This was encompassed by a clinical target volume with a 10-mm margin from GTV (CTV1), accounting for uncertainties in target delineation. The CTV2 encompassed CTV1 with a concentric margin of 2 mm and included additional areas at high risk of subclinical spread. CTV3 encompassed the CTV2 with an additional 2-mm margin and the low-risk regional elective lymph node regions. The final plans were reviewed daily at planning meetings with the staff oncologists. In the present study, curative intent was defined as treatment of ≥ 30 fractions corresponding to a total dose of ≥ 60 Gy. Of the 942 patients, 99% were treated with 33 to 34 fractions (to a total of 66-68 Gy). Accelerated treatment with 6 fractions/wk was standard. If the macroscopic tumor was >4 cm, the CTV1 received 68 Gy, otherwise it received 66 Gy, and a minimum of 60 Gy was prescribed to CTV2 and 50 Gy to CTV3. Initially, IMRT (implemented in 2003) was used only to treat patients with bilateral lymph node metastases. However, gradually, IMRT replaced conventional 3-dimensional

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