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CLINICAL INVESTIGATION **Head and Neck Cancer**

THE ROLE OF COMPUTED TOMOGRAPHY IN THE MANAGEMENT OF THE NECK AFTER CHEMORADIOTHERAPY IN PATIENTS WITH HEAD-AND-NECK CANCER

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Purpose: The aim of this study was to describe the outcome in patients with head-and neck-squamous cell carcinoma (HNSCC) followed up without neck dissection (ND) after concomitant chemoradiotherapy (CRT) based on computed tomography (CT) response. The second objective was to establish CT characteristics that can predict which patients can safely avoid ND.

Methods and Materials: Between 1998 and 2007, 369 patients with node-positive HNSCC were treated with primary CRT at our institution. After a clinical and a radiologic evaluation based on CT done 6 to 8 weeks after CRT, patients were labeled with a complete neck response (CR) or with a partial neck response (PR).

Results: The median follow-up was 44 months. The number of patients presenting with N3, N2, or N1 disease were 54 (15%), 268 (72%), and 47 (13%), respectively. After CRT, 263 (71%) patients reached a CR, and 253 of them did not undergo ND. Ninety-six patients reached a PR and underwent ND. Of those, 34 (35%) had residual disease on pathologic evaluation. A regression of the diameter of ≥80% and a residual largest diameter of 15 mm of nodes had negative pathologic predictive values of 100% and 86%, respectively. The 3-year regional control and survival rates were not different between patients with CR who had no ND and patients with PR followed by ND.

Conclusion: Node-positive patients presenting a CR as determined by CT evaluation 6 to 8 weeks after CRT had a low rate of regional recurrence without ND. This study also suggests that lymph node residual size and percentage of regression on CT after CRT may be useful criteria to guide clinical decisions regarding neck surgery. Those results can help diminish the number of ND procedures with negative results and their associated surgical complications. © 2012 Elsevier Inc.

Head-and-neck cancer, Chemoradiation, Neck dissection, Computed tomography.

INTRODUCTION

Concurrent chemotherapy and radiotherapy (CRT) has become the standard of care for most cases of locally advanced head-and-neck squamous cell carcinoma (HNSCC) (1). Controversies remain concerning the role of surgery for the management of the neck with bulky lymph node involvement (2–4). Patients with a partial regional response after CRT should undergo neck dissection (ND). However, there is no consensus on the treatment of patients with a complete regional response after treatment, and we are unaware of any well-designed randomized trials available. CRT is associated with a high rate of clinical and pathologic (CR), with a low rate of relapse in the neck (5). Thus, systematic ND may expose patients to unwarranted complications with little benefit.

A critical issue in the management of the neck is the absence of universally acknowledged criteria to determine which patients can safely avoid ND. Although there are emerging data on the use of physiologic imaging modality, such as positron emission tomography (PET) (6–8), data are sparse and conflicting on the role of computed tomography (CT) scan after RT (9–11) or CRT (12–15).

At the Centre hospitalier de l'Université de Montréal (CHUM), the policy is to perform a ND in patients receiving CRT only if there is demonstration of residual disease by clinical or radiologic findings. The purpose of this study was to describe the outcome in patients who are followed up without ND based on posttreatment CT response. The second objective was to establish CT characteristics that predict which patients can safely avoid ND.

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METHODS AND MATERIALS

Study design

In this single-institution retrospective study, the files of all consecutive patients receiving CRT between January 1998 and December 2007 for HNSCC were reviewed under institutional board approval. Inclusion criteria were as follows: (*1*) Stage III or IVA–B according to the staging criteria in the 6th edition of the American Joint Committee on Cancer; (*2*) oropharynx, larynx, hypopharynx, oral cavity, or unknown primary; (*3*) presence of cervical lymph node metastasis (levels I–V); (*4*) concomitant platinum-based chemotherapy every 3 weeks. Patients were excluded if they had been treated for a recurrence, postoperatively or with neoadjuvant chemotherapy. The results are based on a final review of charts as of December 2009.

Treatment

Chemotherapy. Two regimens were primarily used at the CHUM during the study period. One was carboplatin 70 mg/m^2/day in bolus for 4 days, with 5-fluorouracil 600 mg/m^2/day as a continuous infusion for 4 days every 3 weeks, generally used for oropharyngeal cancers. The other was cisplatin 100 mg/m^2 in bolus every 3 weeks. Chemotherapy started with the first day of radiation therapy. Most patients were scheduled to receive three cycles of chemotherapy during radiation therapy.

Radiation therapy. Patients received 70 Gy in daily fractions of 1.8 to 2.12 Gy each to the primary tumor and the involved nodes. The prophylactic dose to adjacent nodal regions was 50 to 60 Gy. Patients were treated either with a standard fractionation consisting of 70 Gy in 35 fractions over 7 weeks, or with a concomitant boost of 72 Gy in 42 fractions over 6 weeks, or with intensity-modulated radiation therapy consisting of 70 Gy in 33 fractions over 6.5 weeks. Treatment was delivered with a 4- or 6-MV linear accelerator.

Surgery. Response to treatment was assessed using clinical examination and CT 6 to 8 weeks after completion of CRT for all patients. The locoregional response was considered to be a clinical CR if there was no evidence of residual disease at the primary site or in the neck. If any residual tissue or node was noted on the posttreatment CT scan, it was considered benign if the node was <10 mm (except <15 mm for jugulodigastric nodes or <8 mm for retropharyngeal nodes), oval with smooth borders, with no imaging evidence of extracapsular spread, necrotic center, or enhancing area (16). If one of the above criteria was not met, the response was classified as a clinical partial response (PR). An ND was considered only for those patients with a PR, except for 10 patients who were registered on a research protocol in which a planned ND after CRT was mandated.

Surgery was performed 8 to 12 weeks after the end of treatment if patients were eligible and accepted the surgery. The extent of ND was decided by the surgeon. The type of ND—selective (SND), modified radical (MRND), or radical (RND)—was defined according to the operative note based on the revised classification system of the American Head and Neck Society and the American Academy of Otolaryngology/Head and Neck Surgery (17). Pathologic response was assessed in patients who underwent ND and was considered complete if no residual viable tumor cells were found. Residual nodes, ND, and pathology results were tabulated by side of neck and level.

Correlation of posttreatment CT evaluation to ND pathology results

Posttreatment response of the neck was assessed by physical examination and CT as previously described. Between 2003 and 2007, sets of contrast-enhanced CT images were retrieved for patients known to have ND data available for correlation. The images were reviewed by the same experienced neuroradiologist (MB) blinded to the pathology results. All suspected lymph nodes based on size ≥10 mm on pretreatment CT were graded both qualitatively and quantitatively. Qualitative grading consisted of noting the presence or absence of extracapsular spread and the presence or absence of focal heterogeneity (focal lucency, enhancement, or necrotic center, round shape). Quantitative grading consisted of pre- and posttreatment measurements of maximum lymph node diameters in axial, lateral, and coronal views for all suspected abnormal lymph nodes on pretreatment CT and then for the same nodes on posttreatment CT. Lymph node volume was estimated by the ellipsoid approximation evaluated from the maximum dimension in each axis (volume = $(4\pi*x*y*z)/3$). Percentage volume reduction was then calculated so that a 100% reduction corresponded to

Table 1. Characteristics of patients and treatments

Characteristic	*n*	%
Total population	369	
Mean age (y)	57	
Sex		
M	287	78
F	82	22
Primary tumor site		
Oropharynx	285	77
Larynx	37	10
Hypopharynx	20	5
Unknown primary	18	5
Oral cavity	9	2
T (tumor stage)		
TX	18	5
T1	76	21
T2	100	27
T3	88	24
T4	87	24
N (lymph node stage)		
N1	54	15
N2	268	72
N3	47	13
Stage		
III	40	11
IVa	274	74
IVb	55	15
Chemotherapy		
Carboplatin/5FU	264	71
Cisplatin	105	29
Number of cycles		
1	4	1
2	135	37
3	222	60
Unknown	8	2
Radiation therapy		
IMRT	118	32
Conventional	233	63
Concomitant boost	18	5
Neck dissection	106 (112 heminecks)	29
Selective	62	55
Modified radical	30	27
Radical	6	5
Unknown	14	13

Abbreviations: 5FU = 5-fluorouracil; IMRT = intensity-modulated radiation therapy.