The Role of Computed Tomographic Scans in the Management of the N-Positive Neck in Head and Neck Squamous Cell Carcinoma After Chemoradiotherapy

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Objective: To determine the sensitivity and specificity of computed tomographic (CT) scanning in predicting residual cervical metastatic disease (N-positive neck) in patients undergoing curative radiotherapy and chemoradiotherapy for squamous cell carcinoma (SCC) of the upper aerodigestive tract.

Design: Retrospective case series (1995-2002) of patients undergoing radiotherapy and chemoradiotherapy for advanced head and neck SCC.

Methods: Study entry criteria included N-positive neck disease, a complete response to treatment at the primary tumor site, posttreatment CT scan, posttreatment neck dissection, and correlation of posttreatment CT scan with pathologic neck specimen. We calculated the sensitivity and specificity of the CT scan to predict the presence of residual cervical metastatic disease after curative radiotherapy and chemoradiotherapy.

Results: Forty-three patients (including 10 with bilateral N-positive necks) met the study criteria for analysis. Twenty (38%) of the 53 neck dissection specimens were positive for residual cervical metastatic disease. The sensitivity of the CT scan was 85%, while the specificity was only 24%. The positive predictive value of the CT scan was 40%.

Conclusions: While the role of the posttreatment neck dissection remains controversial, the surgeon must rely on clinical examination and imaging studies. Our practice has been to perform planned staged neck dissections on all N2/N3 necks as well as N1 necks with an incomplete response to treatment. Based on our results, it appears that the CT scan technique lacks adequate sensitivity and specificity to reliably predict the presence of residual metastatic disease.

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SQUAMOUS CELL CARCINOMA (SCC) is the most common malignancy of the head and neck region in adults. Control of local and regional disease as well as distant metastases is the primary goal in the treatment of these patients, with an emphasis on functional preservation and decreased morbidity. Over the past 15 years, multiple chemoradiotherapy regimens have been advocated in an attempt to preserve organ function (eg, larynx or tongue) while achieving adequate locoregional control.1-10

Combination therapy (including concurrent chemotherapy and radiotherapy) has emerged as a viable treatment option in many patients with advanced head and neck SCC.1-3,8 In many cases, the primary tumor site responds well to the treatment regimen and is free of disease at the completion of therapy. On the other hand, cervical metastatic disease is generally less responsive, and it is often necessary to perform a posttreatment neck dissection (cervical lymphadenectomy) to remove any residual disease. Several authors have shown that planned early salvage neck dissection may improve survival, particularly in patients with a less than complete clinical response to the chemoradiotherapy regimen.2,6,10 Lavertu et al2 have demonstrated persistent pathologically positive neck disease in 7 (23%) of 30 patients initially staged N2-N3 despite a complete response to a concurrent chemoradiotherapy protocol. Other authors have advocated a selective approach to planned staged neck dissection, recommending neck dissections only in the setting of advanced neck disease (N2-N3) and less than a complete clinical response.1,7,11,12 The complete clinical response is typically assessed using a combination of physical examination and imaging studies (computed tomography [CT] or magnetic resonance imaging [MRI]).13,14 The role of cervical lymphadenectomy after organ preservation protocols remains controversial.
To ascertain the need for a posttreatment cervical lymphadenectomy, CT scans are often obtained to assess for residual cervical metastatic disease.\textsuperscript{15-18} Our philosophy has been to perform posttreatment neck dissections in all advanced neck disease (N2-N3) as well as any N1 neck with a less than complete clinical response as measured by CT imaging. To date, there is insufficient evidence to define the sensitivity or specificity of the CT scan in assessing the presence of residual metastatic disease in patients undergoing chemoradiation treatment protocols. The purpose of this study was to ascertain the sensitivity and specificity of preoperative CT scans vs histopathologic specimens in predicting residual metastatic disease after cervical lymphadenectomy.

### METHODS

A retrospective study of all records for patients diagnosed with cancer of the head and neck from 1995 to 2002 and treated at the University Health System Hospital (University of Texas Health Science Center of San Antonio) and at the San Antonio Veterans Affairs Hospital was undertaken. Patient records were identified through the tumor registry database of each institution. Institutional review board approval was obtained for the project. A total of 681 medical records were reviewed, and those patients who met the study criteria were selected for further review. The study criteria for entrance into the study group included (1) biopsy-proven SCC of the upper aerodigestive tract; (2) N-positive neck disease (N1, N2, N3) using American Joint Committee on Cancer (AJCC) criteria; (3) completion of chemoradiotherapy and radiotherapy treatment protocol; (4) complete response at the primary tumor site; (5) completion of posttreatment CT scan of the neck with contrast; and (6) completion of posttreatment neck dissection.

The primary site of SCC of all patients was confirmed free of disease by clinical examination and direct laryngoscopy, with biopsies performed as indicated. Posttreatment CT scans were obtained on all patients to assess the neck for residual disease after completion of treatment. In cases of bilateral neck dissections, each neck side was evaluated independently. These CT scans were evaluated by 2 of us (R.A.V. and F.R.M.) and rated as positive, negative, or indeterminate for the presence of residual neck metastatic disease. The CT criteria for the presence of residual cervical metastatic disease included nodal size (>1 cm), the presence of multiple nodes or confluent nodes (>8 mm), central necrosis, and extracapsular spread.\textsuperscript{15-17} An indeterminate CT scan resulted when the 2 reviewers were unable to reach consensus. The results of the CT scan review were compared with the final histopathologic findings of the neck dissections, and calculations of sensitivity, specificity, and positive and negative predictive values were performed.

All neck dissection specimens were evaluated by a staff pathologist (H.S.M.) according to the following protocol: The neck dissections were oriented by the surgeons and submitted to the Pathology Department. The specimens were fixed in 10% neutral buffered formalin. A gross pathologic examination was then performed. Any related anatomic structures including the sternocleidomastoid muscle, external and internal jugular veins, submandibular gland, and spinal accessory nerve were identified. The specimens were separated by anatomic levels and serially sectioned. Identifiable lymph nodes or masses were described and measured in 3 dimensions. Either representative sections or the entire specimen was submitted for processing and preparation of histologic sections. One hematoxylin-eosin-stained glass slide was evaluated for each tissue block submitted. Additional levels were prepared as necessary. The total number of lymph nodes identified and the number and size of lymph nodes containing metastatic tumor were reported by anatomic level. The presence of extracapsular spread and the pathologic stage were also indicated in the pathology report.

### RESULTS

A total of 681 medical records were reviewed between the 2 institutions. Of these, 52 patients met the inclusion criteria for the study. A total of 43 patients (including 10 bilateral neck dissections) had completed preoperative and postoperative data available for analysis, yielding a total of 53 neck dissections. Nine patients were unavailable for analysis secondary to missing medical records or CT scans. The average age of the patients was 57.6 years (range, 40-79 years); 40 (93%) were smokers, and 26 (60%) consumed significant amounts of alcoholic beverages. Most patients (n = 31) presented with primary tumors in the oropharynx, followed by the oral cavity (n = 3), supraglottis (n = 3), and hypopharynx (n = 3). Two patients had tumors of the larynx, and 1 had a primary tumor of unknown location. Four necks were initially staged at N1, 40 at N2, and 9 at N3.

Patients in this study were treated primarily by a combination of radiation therapy and chemotherapy prior to cervical lymphadenectomy. All patients were treated with radiation; 88% received concurrent chemotherapy; and 23% received bilateral neck dissections. Radiation was given as daily fractions of 1.8 to 2.0 Gy, with total doses ranging from 66 to 88 Gy. Various concurrent chemotherapy treatment protocols were used over this interval, including cisplatin/flourouracil, taxotere/cisplatin/flourouracil, paclitaxel/flourouracil, and carboplatin/paclitaxel/Ifosfamide. Chemoradiotherapy consisted of 2 to 4 cycles in conjunction with radiation therapy. The average time between pretreatment completion and neck dissection was 2 months, and CT scans were typically obtained 2 to 4 weeks prior to surgery.

Overall, 43 patients underwent posttreatment cervical lymphadenectomy (including 10 bilateral) for a total of 53 neck dissections. Of the 53 neck dissections, 20 (38%) were positive for residual metastatic neck disease. The CT criteria for the presence of residual neck metastatic disease yielded a total of 9 in the N3 group.

Based on the above data, posttreatment CT scans of the neck with contrast were found to have an 85% sensitivity but only a 24% specificity in predicting residual metastatic neck disease. The positive predictive value of the CT scan was 40%, while the negative predictive value was 73%.

### COMMENT

There are multiple treatment modalities for local, regional, and distant control of head and neck SCC. Protocols involving large surgical resections have often been superseded by combination treatments involving functional preservation with similar rates of regional control and survival. Selective neck dissection has similar regional control rates to more comprehensive operations in appropriately selected patients. On the other hand, the
role of cervical lymphadenectomy after chemoradiotherapy for head and neck SCC remains controversial. Several studies have shown that patients who respond clinically to treatment of their neck disease but who do not undergo neck dissections have regional control rates similar to those of patients treated with salvage surgery. Clayman et al recommended salvage surgery only for patients with partial response or with gross disease 2 to 3 months after completion of chemoradiation.

Usually, CT images are obtained during the preoperative evaluation of patients who will undergo cervical lymphadenectomy. Depending on the dose of radiation given to the N-positive necks, the soft tissue changes can make interpreting these scans difficult. We found that even scans that appear on CT scan positive for persistent disease can be found to be pathologically negative (positive predictive value of 40%). Even more important is the opposite scenario of false-negative results, where viable tumor is found in the pathologic specimen where the CT indicated a complete response. One can presume that if these necks are left untreated, they will later present as recurrences. The negative predictive value of 73% and low specificity of 24% found in the present study preclude the use of CT scans as the sole indicator for determining the need for posttreatment neck dissection in patients with advanced head and neck SCC.

Numerous new imaging techniques have been developed in the last 2 decades: MRI and positron emission tomography (PET) have been used successfully in patients with head and neck carcinomas for radiotherapy planning, evaluation of synchronous lesions, and detection of recurrences. The sensitivity and specificity of PET imaging has been reported to be 96% and 74%, respectively, in recurrent SCC of the head and neck. Given the data, PET with CT/MRI fusion may al-

Figure 1. True-positive finding. Pretreatment (A) and posttreatment (B) contrasted computed tomographic images of a neck found to be positive for squamous cell carcinoma on pathologic evaluation. The evident mass on the left side of the neck represents a true-positive finding.

Figure 2. False-positive finding. Evident masses are seen in the right side of the neck of pretreatment (A) and posttreatment (B) computed tomographic (CT) images of a patient with no identifiable tumor on the neck dissection specimen. The posttreatment image (B) represents a false-positive finding because the CT scan was read as positive but the final pathologic specimen tested negative.
low for more accurate imaging of the posttreatment neck. Ongoing clinical research at our institution is being conducted to further elucidate these possibilities.

In conclusion, CT scans performed prior to cervical lymphadenectomy have a relatively good sensitivity but poor specificity in predicting remaining SCC in the neck of patients treated with chemoradiotherapy. More predictive methods in determining residual neck disease in patients treated with chemoradiotherapy are still needed.

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REFERENCES


