

JOURNAL SCAN FOR IJHNS

Meta-analysis of Chemotherapy in Head and Neck Cancer (MACH-NC): An Update on 93 Randomized Trials and 17,346 Patients

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On behalf of the MACH-NC

BACKGROUND

Our previous individual patient data (IPD) meta-analysis showed that chemotherapy improved survival in patients curatively treated for non-metastatic head and neck squamous cell carcinoma (HNSCC), with a higher benefit with concomitant chemotherapy. However the heterogeneity of the results limited the conclusions and prompted us to confirm the results on a more complete database by adding the randomized trials conducted between 1994 and 2000.

METHODS

The updated IPD meta-analysis included trials comparing locoregional treatment to locoregional treatment + chemotherapy in HNSCC patients and conducted between 1965 and 2000. The log-rank test, stratified by trial, was used to compare treatments. The hazard ratios of death were calculated.

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RESULTS

Twenty-four new trials, most of them of concomitant chemotherapy, were included with a total of 87 trials and 16,485 patients. The hazard ratio of death was 0.88 ($p < 0.0001$) with an absolute benefit for chemotherapy of 4.5% at 5 years, and a significant interaction ($p < 0.0001$) between chemotherapy timing (adjuvant, induction or concomitant) and treatment. Both direct (6 trials) and indirect comparisons showed a more pronounced benefit of the concomitant chemotherapy as compared to induction chemotherapy. For the 50 concomitant trials, the hazard ratio was 0.81 ($p < 0.0001$) and the absolute benefit 6.5% at 5 years. There was a decreasing effect of chemotherapy with age ($p = 0.003$, test for trend).

CONCLUSION

The benefit of concomitant chemotherapy was confirmed and was greater than the benefit of induction chemotherapy.

Phase 3 Randomized Trial on Larynx Preservation Comparing Sequential vs Alternating Chemotherapy and Radiotherapy

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For the EORTC Head and Neck Cancer Cooperative Group and the EORTC Radiation Oncology Group

BACKGROUND

Both induction chemotherapy followed by irradiation and concurrent chemotherapy and radiotherapy have been reported as valuable alternatives to total laryngectomy in patients with advanced larynx or hypopharynx cancer. We report results of the randomized phase 3 trial 24954 from the European Organization for Research and Treatment of Cancer.

METHODS

Patients with resectable advanced squamous cell carcinoma of the larynx (tumor stage T3 – T4) or hypopharynx (T2 – T4), with regional lymph nodes in the neck staged as N0 – N2 and with no metastasis, were randomly assigned to treatment in the sequential (or control) or the alternating (or experimental) arm. In the sequential arm, patients with a 50% or more reduction in primary tumor size after two

cycles of cisplatin and 5-fluorouracil received another two cycles, followed by radiotherapy (70 Gy total). In the alternating arm, a total of four cycles of cisplatin and 5-fluorouracil (in weeks 1, 4, 7, and 10) were alternated with radiotherapy with 20 Gy during the three 2-week intervals between chemotherapy cycles (60 Gy total). All nonresponders underwent salvage surgery and postoperative radiotherapy. The Kaplan – Meier method was used to obtain time-to-event data.

RESULTS

The 450 patients were randomly assigned to treatment (224 to the sequential arm and 226 to the alternating arm). Median follow-up was 6.5 years. Survival with a functional larynx

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was similar in sequential and alternating arms (hazard ratio of death and/or event = 0.85, 95% confidence interval = 0.68 to 1.06), as were median overall survival (4.4 and 5.1 years, respectively) and median progression-free interval (3.0 and 3.1 years, respectively). Grade 3 or 4 mucositis occurred in 64 (32%) of the 200 patients in the sequential arm who received radiotherapy and in 47 (21%) of the 220 patients in the alternating arm. Late severe edema and/or fibrosis was observed in 32 (16%) patients in the sequential arm and in 25 (11%) in the alternating arm.

CONCLUSION

Larynx preservation, progression-free interval, and overall survival were similar in both arms, as were acute and late toxic effects.

Management of the Neck after Chemoradiotherapy for Head and Neck Cancers in Asia: Consensus Statement from the Asian Oncology Summit, 2009

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The addition of a planned neck dissection after radiotherapy has traditionally been considered standard of care for patients with positive neck-nodal disease. With the acceptance of chemoradiotherapy as the new primary treatment for patients with locally advanced squamous-cell head and neck cancers, and the increasing numbers of patients who achieve a complete response, the role of planned neck dissection is now being questioned. The accuracy and availability of a

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physical examination or of different imaging modalities to identify true complete responses adds controversy to this issue. This consensus statement will address some of the controversies surrounding the role of neck dissection following chemoradiotherapy for squamous-cell carcinomas of the head and neck, with particular reference to patients in Asia.

Larynx Preservation Clinical Trial Design: Key Issues and Recommendations: A Consensus Panel Summary

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On Behalf of the Larynx Preservation Consensus Panel

PURPOSE

To develop guidelines for the conduct of Phase III clinical trials of larynx preservation in patients with locally advanced laryngeal and hypopharyngeal cancer.

METHODS AND MATERIALS

A multidisciplinary international consensus panel developed recommendations after reviewing results from completed Phase III randomized trials, meta-analyses, and published clinical reports with updates available through November, 2007. The guidelines were reviewed and approved by the panel.

RESULTS

According to the recommendations, the trial population should include patients with T2 or T3 laryngeal or hypopharyngeal squamous cell carcinoma not considered for partial laryngectomy and exclude those with laryngeal dysfunction or age greater than 70 years. Functional assessments should include speech and swallowing. Voice should be routinely assessed with a simple, validated

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instrument. The primary endpoint should capture survival and function. The panel created a new endpoint: laryngo-esophageal dysfunction-free survival. Events are death, local relapse, total or partial laryngectomy, tracheotomy at 2 years or later, or feeding tube at 2 years or later. Recommended secondary endpoints are overall survival, progression-free survival, locoregional control, time to tracheotomy, time to laryngectomy, time to discontinuation of feeding tube, and quality of life/patient-reported outcomes. Correlative biomarker studies for near-term trials should include estimated glomerular filtration rate, excision repair cross-complementary-1 gene, E-cadherin and b-catenin, epiregulin and amphiregulin, and TP53 mutation.

CONCLUSION

Revised trial designs in several key areas are needed to advance the study of larynx preservation. With consistent methodologies, clinical trials can more effectively evaluate and quantify the therapeutic benefit of novel treatment options for patients with locally advanced laryngeal and hypopharyngeal cancer.

Clinical Implications of Human Papillomavirus in Head and Neck Cancers

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Human Papillomavirus (HPV) is now recognized to play a role in the pathogenesis of a subset of head and neck squamous cell carcinomas (HNSCCs), particularly those that arise from the lingual and palatine tonsils within the oropharynx. High-risk HPV16 is identified in the overwhelming majority of HPV-positive tumors, which have molecular-genetic alterations indicative of viral oncogene

function. Measures of HPV exposure, including sexual behaviors, seropositivity to HPV16, and oral, high-risk HPV infection, are associated with increased risk for oropharyngeal cancer. HPV infection may be altering the demographics of HNSCC patients, as these patients tend to be younger, nonsmokers, and nondrinkers. There is sufficient evidence to conclude that a diagnosis of HPV-

positive HNSCC has significant prognostic implications; these patients have at least half the risk of death from HNSCC when compared with the HPV-negative patient.

J. Clin Oncol, 24:2606-11.

The HPV etiology of these tumors may have future clinical implications for the diagnosis, therapy, screening, and prevention of HNSCC.

Neuroectodermal Neoplasms of the Head and Neck with Emphasis on Neuroendocrine Carcinomas

Stacey E Mills

Tumors exhibiting neuroectodermal differentiation occur throughout the body, and the diverse tissues of the head and neck give rise to a wide assortment of these neoplasms. Neuroectodermal neoplasms may be divided into lesions showing primarily epithelial differentiation (Group I, neuroendocrine carcinomas) and a more diverse group (Group II) of nonepithelial neoplasms.

This article reviews these neuroectodermal tumors of the head and neck with emphasis on the neuroendocrine carcinomas and their nomenclature. The author believes that with regard to Group I tumors, the older terminology of carcinoid, atypical carcinoid, and small cell carcinoma should be replaced by subclassifications of well-differentiated, moderately differentiated, and poorly differentiated neuroendocrine carcinoma.

The latter category should be further subdivided into small cell and large cell variants. Neuroendocrine carcinomas, particularly the moderately differentiated

Mod Pathol 2002;15(3):264-78.

subtype, are often underdiagnosed in the head and neck region. In the larynx, these tumors are the most common form of nonsquamous carcinoma. Poorly differentiated neuroendocrine carcinoma of small cell type is most common in the salivary glands but can occur elsewhere in the region. The large cell subtype of poorly differentiated neuroendocrine carcinoma has not been well documented in this region. However, the most likely candidate for this tumor category is the so-called sinonasal undifferentiated carcinoma. Group II tumors discussed include olfactory neuroblastoma, malignant melanoma, and Ewing's sarcoma. In addition, differential diagnostic problems related to Group I and II tumors are reviewed in detail. This article reviews and updates our understanding of neuroectodermal neoplasms arising in the head and neck. The focus is on tumors that exclusively involve this region or show a strong predilection to occur here.

Comparison of Two Prognostic Scores for Patients with Parotid Carcinoma

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ABSTRACT

Background: Salivary glands present a wide diversity in histopathologic types and biologic behaviors, thus complicating the search for prognostic factors.

METHODS

We compared 2 prognostic scores that were previously published for patients with parotid carcinoma in a

retrospective series of 175 patients treated in a single institution.

RESULTS

Cox multivariate analysis indicated clinical skin invasion, facial nerve function, and perineural growth as the most significant recurrent disease-related prognostic factors. According to the Vander Poorten score, 148 patients were

divided into 4 groups, with the 5-year disease-free survival of 76%, 81%, 69%, and 35%, respectively. In the Carrillo's score, the patients were divided into 3 groups: low-risk, intermediaterisk, and high-risk, with the 5-year disease-free survival of 84%, 73%, and 34%, respectively.

Head-Neck; 2009;31:1188-95.

CONCLUSION

Carrillo's score showed more distinct survival curves, and determination of groups with a more favorable prognosis was difficult for both scores. Therefore, both scores were not totally reproducible for our group of patients.