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Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer

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from *The New England Journal of Medicine*, August 2015

D'Cruz and colleagues report the findings of a prospective, randomized, controlled trial comparing elective neck dissection to therapeutic neck dissection in patients with early-stage, node-negative oral cavity squamous cell carcinoma. Patients were randomized to elective neck dissection vs. close surveillance and therapeutic neck dissection in those who develop nodal metastases. The major finding from this study is that elective neck dissection at the time of the primary tumor resection is associated with a significant overall and disease-free survival advantage. The strengths of this study include a prospective, randomized study design and a large number of patients with appropriate follow-up. Limitations of this study include the use of ultrasound to detect nodal metastases and the lack of data on treatment morbidity associated with neck dissection. Additionally, this study addresses a clinical management question that has largely been answered previously, particularly for oral tongue cancers. Elective neck dissection, based on depth of invasion, is already the standard of care for early stage oral cavity cancers in many centers across the United States. Although the authors demonstrate a survival advantage in the elective surgery group, the high rate of pathologically negative dissections in this group (70%) should not be ignored. As the authors mention, future translational studies should focus on identifying subgroups in which a neck dissection could be avoided without compromising oncologic outcomes.



A Prospective Phase II Trial of De-intensified Chemoradiotherapy for Favorable-Risk HPV-associated Oropharyngeal Squamous Cell Carcinoma

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from The International Journal of Radiation Oncology, August 2015

This is a two-institution, prospective phase II trial to assess the efficacy and morbidity of a de-intensified chemoradiation regimen for favorable risk, HPV associated OPSCC. The primary treatment was 60 Gy IMRT with concurrent weekly IV cisplatin @ 30mg/m². Low-risk HPV OPSCC was defined as T0-T3, N0 - N2c, MO, p16+ disease in a patient with only minimal or remote smoking history. The primary study endpoint was pathologic complete response rate based on required biopsy of the primary site and dissection of pretreatment positive lymph node regions within 6-14 weeks after treatment completion, regardless of radiographic response. Secondary endpoint measures included physician reported toxicity (CTCAE), patient reported symptoms (PRO-CTCAE), and modified barium swallow studies.

Forty-three subject were enrolled with the majority of patients (95%) having never-smoked or <10 pack years tobacco use. There were no toxicity related treatment delays. All patients received 60 Gy and 93% received at least 4 of the weekly cisplatin doses.

With a median follow up of 14.6 months, the complete clinical response rate was 64% at 6 weeks post CRT with a 98% complete clinical response at the primary site and 60% in the neck. The overall pathologic response rate was 98% and 84% for the primary site and the neck, respectively. In 4 of the patients with residual disease, the focus was microscopin (<1mm). The incidence of CTCAE Grade 3/4 toxicity and PRO-CTCAE severe/very severe symptoms were: mucositis 34%/45%, general pain 5%/48%, nausea 18%/52%, vomiting 5%/34%, dysphagia 39%/55%, and xerostomia 2%/75%. Grade 3/4 hematological toxicities were 11%. 39% of patients required a feeding tube for a median of 15 weeks (5 - 22 weeks). No patient required a long-term feeding tube.

Strengths

- prospective design
- clinical response confirmed with pathologic examination through post-treatment biopsy and neck dissection
- strong historical basis for de-intensified regimen

Limitations

- non-randomized, two-institution design with a small subset of patients
- short follow up (median = 14.6 months)
- no direct comparison group to compare toxicity rates

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Microscopic Positive Margins in Differentiated Thyroid Cancer Is Not an Independent Predictor of Local Failure.

Wang LY, Ghossein R, Palmer FL, Nixon JJ, Tuttle RM, Shaha AR, Shah JP, Patel SG, Ganly I.

from *Thyroid*, September 2015

This study is a single institution, retrospective review to determine the impact of a histologically positive margin in patients undergoing total thyroidectomy for well-differentiated thyroid cancer. The primary endpoint was local recurrence free survival (LRFS) at 5 years.

A total of 2616 patients were included in the study; 90% had negative margins and 10% had positive margins. Microscopic positive margin status was defined as tumor present at the specimen edges on pathological analysis. Local recurrence was determined by clinical examination supplemented with fine needle aspiration of lesions in the thyroid bed or on imaging. Biochemical recurrence defined by elevated thyroglobulin levels alone was not considered robust enough to indicate local recurrence. Details of the use of radioactive iodine and external beam radiation therapy were also studied.

As expected patients with positive margins were more likely to have larger tumors, extrathyroidal extension (ETE), multicentric disease, nodal disease and were most likely to receive adjuvant radiation therapy either in the form of iodine (RAI) or external beam. Patients with positive margin status received high-dose RAI (> 100 mCi) in 60.5% of cases, compared with 36.2% of patients with negative margins. This compared with patients with negative margins of whom 50% received no RAI compared to 23.6% with positive margins. LRFS at 5 years for patients with positive margins was slightly poorer but clinically similar compared with patients with microscopically negative margins (98.9% versus 99.5%, $p=0.018$). When considering level of risk as defined by the ATA (www.liebertpub.com/thy), positive margins were uncommon in the ATA low risk (2.6% incidence) and intermediate risk (11.6% incidence) groups, the majority of which were treated without radioactive iodine. Neither low nor intermediate risk groups had any patient with local recurrence. On univariate analysis, other predictors of LRFS were gender and gross ETE. To determine if positive margins were associated with poor LRFS after considering ETE and T stage, unadjusted and adjusted hazard ratios for margin status were performed. When adjusting for gross ETE and T stage, margin status was not predictive. This seemed to indicate that the prognostic relevance of margin status appears secondary to more clinically relevant variables such as ETE and tumor stage. The authors concluded that in the absence of ETE and other adverse pathological features it is possible that highly selective patients with a microscopically positive margin may be observed without radioactive iodine.

Strengths:

- a relatively large population with complete demographic information available

Limitations:

- lack of information on location of the positive margin (i.e. anterior versus posterior)
- inherent selection bias by treating physicians and surgeons with regard to the use of radioactive iodine as adjuvant therapy

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Characteristics and significance of minimal and maximal extrathyroidal extension in papillary thyroid carcinoma

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from Oral Oncology, August 2015

This is a single institution retrospective study of 967 patients with papillary thyroid carcinoma undergoing thyroidectomy over a 11 year period. Each case was stratified based on presence or absence of extrathyroidal extension (ETE) and correlated with other risk factors as well as disease specific and overall survival. ETE was based on pathologic examination and defined as absence of ETE, minimal ETE defined as extension of the primary tumor to the perithyroidal soft tissues or strap muscles (divided into 2 subgroups in relation to strap muscle invasion, STI + or STI negative), and maximal ETE defined as extension of the primary tumor to the trachea, esophagus, recurrent laryngeal nerve, larynx, subcutaneous soft tissues, skin, internal jugular vein, or carotid artery.

The objective of this study was to investigate the prognostic significance of minimal vs maximal ETE in PTC. Aside from the subgroups of minimal ETE this followed the TNM staging system. The authors demonstrated that maximal ETE was significantly associated with larger tumor size, bilateral tumors, and lateral neck metastasis. Recurrence rates (27.4% in the maximal group vs 2.5% in the minimal group), disease free survival (96.5% min vs 59.1% max at 10 years), and overall survival (94.6% min vs 75.2% max) were significantly ($p < 0.001$) decreased in patients with maximal vs minimal ETE whereas there was no statistical difference in minimal (STI+ or STI -) and absence of ETE. Thus minimal ETE, even with strap muscle involvement, did not adversely affect outcomes.

These results largely support the current TNM staging system (see Table 1). They also support ATA guidelines for recommending post operative I131 in patients with T4 tumors and cautionary discretion with T3 tumors (minimal ETE, see Table 2). This study supports that minimal ETE with or without strap muscle involvement does not affect clinical outcomes including overall prognosis and that maximal ETE results in decreased long term prognosis and outcomes.

Strengths:

- large series of patients at a single institution (n = 967)
- consistent pathological assessment and grading system to access for ETE

Weakness:

- retrospective study
- short mean follow up 74.6 +/- 33.8 months.

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