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Pre-treatment tumor-specific growth rate as a temporal biomarker that predicts treatment failure and improves risk stratification for oropharyngeal cancer

Colin T. Murphy, Karthik Devarajan, Lora S. Wang, Ranee Mehra, John A. Ridge, Christopher Fundakowski, Thomas J. Galloway

from ***Oral Oncology, November, 2015***

The goal of this study was to investigate the ability of tumor specific growth rate (TSGR) as a prognostic factor in oropharyngeal squamous cell carcinoma (OPSCCA) treated with non-surgical modalities. The authors hypothesized that the primary tumor growth rate could be estimated by exploiting the time between a diagnostic and RT-planning scan (which is on average 34 days) to provide a simple and inexpensive maneuver to further risk stratify OPSCCA patients. The inclusion criteria were: OPSCCA, known p16 status, known smoking status, treatment withprimary RT or chemoradiation (CRT), and measurable primary tumor on an RT planning scan and on prior diagnostic imaging (with no interval therapy). Patients were excluded for the following criteria: tumors originating from another site in the upper aerodigestive tract, non-squamous histology, unknown p16 status, unknown smoking status, treatment with palliative intent, <7 days between interval scans, and treatment with primary surgery. TSGR was incorporated into RTOG 0129 risk grouping (0129RG) to assess whether TSGR could improve prognostic accuracy.

Results:
The 0129RG classification was: 56% low, 25% intermediate, and 19% high risk. Median TSGR was 0.74%/day (range 0.01–4.25) and increased with 0129RG low (0.41%), intermediate (0.57%) and high (1.23%) risk, respectively (p = 0.015). TSGR independently predicted for tumor recurrence (TSGR: HR (95%CI) = 2.79, 1.67–4.65, p < 0.001) in the Cox model. On CPE, prognostic accuracy for TF, disease-free survival and overall survival was improved when 0129RG was combined with TSGR. Dichotomizing 0129RG by median TSGR yielded no observed recurrences in low risk patients with TSGR < 0.74% and demonstrated significant difference for intermediate risk (8% vs. 50%) for TSGR < 0.74% vs. P0.74%,

respectively, p < 0.001). For TSGR < 0.74% vs. >74% the estimated 3-yr FFTF was 95.0% (95%CI 88–100%) vs. 61.1% (95%CI 47.3–78.9%), 3-yr DFS 86.5% (95%CI 76.2–98.4%) vs. 55.6% (95%CI 42–73.6%), and 3-yr OS 86.5% (95%CI 76.2–98.4%) vs. 67.2% (95% CI 53.9–83.9%). On multivariate analysis, TSGR was the strongest predictor of treatment failure and of DFS.

Strengths

- Well-executed study which utilizes a readily available and inexpensive technique for better prognosticating p16 + postivie OPSCCA patients
- Sound statistical and study methodology
- Novel approach to taking existing literature regarding tumor growth and applying these results to clinical outcomes

Weaknesses

- heterogeneous scanning technique for measuring volume
- differences in p16, treatment (induction vs concurrent, cetuximab vs cisplatin)
- small numbers (85 patients)
- Single center outcomes leading to need for external validity investigation

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Impact of the multi-gene ThyroSeq next-generation sequencing assay on cancer diagnosis in thyroid nodules with atypia of undetermined significance/follicular lesion of undetermined significance cytology

Yuri E. Nikiforov, Sally E. Carty, Simon I. Chiosea, Christopher Coyne, Umamaheswar Duvvuri, Robert L. Ferris, William E. Gooding, Shane O. LeBeau, N. Paul Ohori, Raja R. Seethala, Mitchell E. Tublin, Linwah Yip, and Marina N. Nikiforova

from ***THYROID, October 2015***

This was a single institution study from the University Pittsburgh that was designed to analyze the performance of a large multi-gene panel noted as ThyroSeq V2 in nodules with atypia of undetermined significance or follicular lesion of undetermined significance cytology (AUS/FLUS). Patients who had undergone fine-needle aspirate biopsies with the cytologic diagnosis of (AUS/FLUS) also had their tissue evaluated using the molecular analysis. For those patients that underwent surgical resection of their thyroid lesions, the final surgical histopathology was used to determine the performance of the molecular analysis. The molecular analysis was performed prospectively prior to surgery and the availability of the final surgical pathology. The initial histopathological diagnosis was established by pathologists who were not blinded to the results of the molecular testing.

465 samples with (AUS/FLUS) cytology were taken from 441 patients from May 2014 to March 2015. Out of the 465 nodules, 3 were found to be of parathyroid origin. Of the remaining 462 nodules 6.7% tested positive for thyroid point mutations or gene fusions whereas the rest were mutation negative. Mutations affecting the NRAS and HRAS genes were most common. 90 patients with 96 nodules underwent surgery. This included patients with 26 mutation-positive nodules and with 70 nodules that had tested negative for mutations. Total thyroidectomy was performed on 45 in these patients and hemithyroidectomy or lobectomy on 44. One patient underwent thyroidectomy and parathyroid gland exploration. On histopathological examination, 22 (22.5%) of the aspirated nodules were malignant and 74 were benign. Among the 31 mutation positive nodules, 26 or 84% were surgically removed. Of those 77% were malignant and 23% were benign. 2 of the 6 benign nodules had NRAS mutations, and single nodules harbored HRAS, EIF1AX or PTEN mutation or THADA fusion. Among the 20 malignant nodules, 2 were classic papillary carcinomas and 18 follicular variant papillary carcinomas. Among the 70 mutation negative nodules, 68 were benign and 2 were malignant at surgical resection. The 2 malignant tumors were a 1.4 cm follicular variant papillary carcinoma and a 1.9 cm encapsulated follicular variant papillary carcinoma.

Among 6 nodules positive for mutations found to be benign after surgical excision, 4 were diagnosed as follicular adenomas and 2 as hyperplastic nodules.

In studying the performance of the molecular analysis in the 96 nodules with known surgical outcome and 2 nodules found have strong expression of PTH gene with clinical evidence of primary hyperparathyroidism, 98 nodules were considered to have definitive outcome information. In this group, molecular analysis with ThyroSeq allowed correct classification of 91 nodules as either benign (n=71) or malignant (n=20) with 6 false positive and 2 false negative tests. The performance characteristics were 90.9% sensitive, 92.1% specific with a 76.9% positive predictive value and a 97.2% negative predictive value and overall accuracy of 91.8%.

The authors compared these results of the ThyroSeqv2 system to the previously reported results of the Afirma GEC system and found the negative predictive value not statistically significantly different however the positive predictive value of ThyroSeq was significantly higher.

The authors concluded that the ThyroSeq molecular testing offers accurate classification of most thyroid nodules with (AUS/FLUS) cytology into benign or malignant groups. This should guide to improve management of a large number patients and will allow clinicians to avoid many of the currently required diagnostic surgeries that are associated with significant cost and potential risks.

Strengths:

- Relatively large number of nodules studied
- Solid methodology and follow up

Limitations:

- Non-randomized, single institution study
- Pathologists were not blinded as to the results of the molecular analysis

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Incidence of Suicide in Patients With Head and Neck Cancer

David Kam, BS; Andrew Salib, BA; George Gorgy, BA; Tapan D. Patel, MD; Eric T. Carniol, MD, MBA; Jean Anderson Eloy, MD; Soly Baredes, MD; Richard Chan Woo Park, MD

from JAMA Otolaryngology Head & Neck Surgery, December, 2015

This is a retrospective cohort study using the SEER program of 350,413 cases of patients with head and neck cancer between 1973- 2011 for a total of 2,263,376 person-years. A total of 857 suicides were identified giving an age-, sex-, and race-adjusted suicide rate of 37.9 per 100 000 person-years. The corresponding suicide rate in the general US population was 11.8 per 100 000 person-years.

Patients with tumors of each head and neck cancer site, except for the thyroid gland, had higher suicide rates than the general US population for at least 10 years after diagnosis. Rates were highest in patients with cancers of the hypopharynx (164.2 per 100 000 person-years), larynx (64.7 per 100 000 person-years), and oral cavity and oropharynx (61.8 per 100 000 person-years). In men, patients with nasopharyngeal cancers (87.3 per 100 000 person-years;) had the second-highest rates, while for women the second-highest rates were seen among those with oral cavity and oropharyngeal cancers (18.4 per 100 000 person-years). Relative suicide risk remained high for longest duration in those with nasopharyngeal cancer, for over 15-30 years. Radiation therapy without surgery was associated with a suicide rate of 60.4 per 100, 000 person-year, while patients treated with surgery alone had a suicide rate of 30.4 per 100,000 person-years.

Suicide rates among patients with head and neck cancer are significantly higher than that of the general population.

Strengths

- In in-depth analysis of suicide in patients with head and neck cancer, not previously discussed in this detail

Limitations

- Possible misclassification of the cause of death
- Could not account for substance abuse and other possible confounders

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Cetuximab and Radiotherapy Versus Cisplatin and Radiotherapy for Locally Advanced Head and Neck Cancer: A Randomized Phase II Trial

Stefano Maria Magrini, Michela Buglione, Renzo Corv`o, Luigi Pirtoli, Fabiola Paiar, Pietro Ponticelli, Alessia Petrucci, Almalina Bacigalupo, Monica Crociani, Luciana Lastrucci, Stefania Vecchio, Pierluigi Bonomo, Nadia Pasinetti, Luca Triggiani, Roberta Cavagnini, Loredana Costa, Sandro Tonoli, Marta Maddalo, and Salvatore Grisanti

from Journal of Clinical Oncology, December, 2015

This study by Magrini et al. compared compliance, toxicity, and efficacy between radiation therapy and cetuximab (CTX) versus radiation therapy and cisplatin for locally advanced head and neck squamous cell carcinoma. This was a phase II, multicenter, randomized trial that included 35 patients in each of the treatment arms. The major findings from this study relate to toxicity and other adverse events in the CTX arm. Patients undergoing treatment with CTX were significantly more likely experience drug dosage reduction, disruption of radiation therapy, or experience serious adverse events as a result of therapy. Although survival and recurrence rates were not the primary endpoints of this study, no significant difference in survival was noted between the treatment arms. Subset analysis of oropharyngeal and oral cavity cancers showed improved oncologic outcomes in the radiation and cisplatin group. This is the first clinical trial comparing radiation therapy and CTX with radiation therapy and weekly cisplatin for locally advanced head and neck cancer. This is an important study because it highlights a significant toxicity profile for a treatment regiment previously considered to be more tolerable.

The strengths of this study include the randomized, prospective study design and detailed data on tolerability, toxicity, and oncologic outcomes.

Limitations include a relatively small number of patients (trial was closed after 70 patients enrolled due to slow accrual).

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