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The Effect of Treatment Package Time in Head and Neck Cancer Patients Treated with Adjuvant Radiation Therapy and Concurrent Systemic Therapy

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Purpose/Objective(s): In patients with head and neck squamous cell carcinoma (HNSCC), the "treatment package time" (TPT), defined as the number of days from surgery to end of adjuvant radiation therapy (RT), has been shown to impact outcomes with TPT above 100 days resulting in worse survival. However, these studies were restricted to cases receiving only adjuvant RT with no data for those receiving concurrent systemic therapy (CRT). We analyzed the influence of TPT on survival endpoints for HNSCC treated by surgery followed by CRT.

Materials/Methods: After IRB approval, we used our institutional database to identify HNSCC cases treated with curative surgical resection followed by CRT. The addition of concurrent systemic therapy was due to the presence of positive margins (PM) and/or extracapsular nodal extension (EC). Those with deficient surgical, pathological or follow up data were excluded. For each case we calculated a provisional risk score (RS) based on NCCN defined adverse features; 2 points each were assigned for PM and EC and 1 point for each of the remaining adverse features (T3/4, N2/3, perineural invasion (PNI) and lympho-vascular invasion (LVI). TPT was assessed by calculating the number of days elapsed between surgery date and the last day of CRT for each case. We used %findcut SAS macro tool to search for the cutoff TPT that was associated with significant overall survival (OS) and recurrence free survival (RFS) benefit. According to the TPT optimal cutoff point two groups were formed and Kaplan-Meier curves, log rank tests as well as univariate and multivariate (MVA) analyses were used to assess OS and RFS.

Results: We identified 103 cases that met inclusion criteria treated between 2008 & 2015 with a median follow up time of 59 months. Oropharyngeal tumors (OP) were 43%, oral cavity (OC) 40% and laryngeal 17%. HPV positive disease was detected in 22% of patients (50 % of OP). CRT included platinum and cetuximab that were utilized in 72% & 28%, respectively. Optimal TPT was found to be less than 100 days (n = 62) with significantly better OS ($p = 0.011$) and RFS ($p = 0.043$) compared to TPT ≥100 days (n = 41). Also 2 & 5 years OS and RFS were significantly better for TPT <100 days (91% vs. 68% & 74% vs. 46% for OS; $p<0.05$). Study groups were balanced for all characters except that those with TPT <100 days have more OP location; whereas the other group had higher smoking incidence, OC and T4 tumors ($p<0.05$). On MVA excluding risk score; EC, LVI & PNI were associated with inferior OS. Nevertheless, when RS was included, after excluding its components; TPT <100 days and high RS were independent predictors for worse OS ($p<0.05$). T4, EC and high RS were all significantly related to inferior RFS ($p<0.05$).

Conclusion: Shorter treatment package time <100 days is associated with better survival outcomes in HNSCC with high risk features even when systemic therapy is added to adjuvant RT. Thus, multidisciplinary coordinated care must be provided to ensure the earliest start of CRT with minimal treatment breaks.

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Early (90-Day) Mortality after Radical Radiation Therapy for Head and Neck Squamous Cell Carcinoma: A Population-Based Analysis

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Purpose/Objective(s): A retrospective, population-based analysis of 90-day mortality in patients with squamous cell carcinoma of the head and neck (HNSCC) treated with radical radiotherapy (RT) was performed to determine the early mortality rate and associated risk factors.

Materials/Methods: All HNSCC patients treated from 1998-2014 in our province with curative intent RT, as indicated on the RT prescription by the radiation oncologist, were included (n = 5658). Data was abstracted from our institution's electronic record that is linked to our provincial vital statistics registry. Early mortality was defined as death within 90 days of the first RT fraction. Logistic regression analysis was used to determine factors associated with early mortality.

Results: The median age at diagnosis was 63 years (Interquartile Range 55-72). Three quarters (76%) were male. Tumour sites included oropharynx (40%), larynx (27%), oral cavity (20%), hypopharynx (6%), nasopharynx (3%), paranasal sinus (3%) and salivary gland (1%). Tumour stages were T0 (0.3%), T1 (28%), T2(35%), T3(18%), T4(12%) and Tx (7%). Nodal stages were N0 (43%), N1 (13%), N2(33%), N3(4%) and Nx (6%). IMRT was used for 40% and 3DCRT for 60%. The majority (95%) of patients received 50 Gy or higher, 29% received concurrent chemotherapy and 25% had initial surgery. The mortality rate at 90 days after starting RT was 3.6%. The cause of death was attributed to HNSCC for 79% of patients. The majority (94%) did not have an autopsy. Multivariate analysis demonstrated that increasing age (years) (HR 1.05, 95% CI 1.03-1.07, p<0.001), not receiving concurrent chemotherapy (HR 1.7, 95% CI 1.1-2.6, p = 0.009), N3 disease (HR 3.3, 95% CI 1.3-8.5, p = 0.012) and T4 disease (HR 2.6, 95% CI 1.1-6.2, p = 0.03) were associated with an increased risk of early mortality. IMRT technique, sex, initial surgery, tumour site and treatment year were not associated with early mortality risk (all p>0.05).

Conclusion: Early mortality after radical RT for HNSCC in our population is 3.6%. The risk did not decrease over the study period and with modern treatment techniques (IMRT). Future analysis will focus on chart review to more accurately determine specific causes of 90-day mortality (treatment related toxicity, cancer progression, intercurrent disease) in our population.

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The First Cut: the Importance of the Initial Specimen Margin for Oral Cavity Cancer

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Purpose/Objective(s): During the resection of an oral cavity squamous cell carcinoma (OCSCC) the pathologist may discover tumor approaching or at the surgical specimen edge(s) that are cleared by the surgeon by performing additional resections. It is not known how patients with margins that are negative after additional excision (NAAE) compare to those with initially negative or positive margins. We sought to determine the impact of NAAE and whether it is an indication for adjuvant radiation.

Materials/Methods: Two pathologists re-reviewed all available pathologic specimens of patients with OCSCC treated with surgical resection at our institution. The distance of tumor to the edge of the main surgical specimen was categorized as positive (tumor < 0.1 cm) or negative (tumor ≥ 0.1 cm). For patients with positive margins of the primary specimen, if additional excisions were taken and found to clear the margins, they were categorized as NAAE margins. The following were considered adverse risk features: perineural invasion (PNI), lymphovascular invasion (LVI), stage T3-4, and stage N2-3. We used the 8th edition of the AJCC staging system, which incorporates tumor depth and extracapsular extension (ECE). Locoregional recurrence (LRR) differences were determined with Gray's test and Fine-Gray models. Differences in Progression Free Survival (PFS) were determined with log-rank tests and Cox regression models. A conditional landmark analysis using 3 months after resection was used.

Results: We identified 416 adult patients with OCSCC treated with surgical resection from 1998-2014 with a median follow up of 39 months. 412 specimens were available for review. 198 patients had NAAE margins, 181