Outcomes of induction chemotherapy for head and neck cancer patients

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Purpose or Objective: To present the present role of induction chemotherapy that has remained a subject of controversy. In this study, we directly compared the survival of patients receiving induction chemotherapy using docetaxel or platinum given before concomitant chemoradiotherapy (CCRT) with upfront chemoradiotherapy alone.

Material and Methods: The National Health Insurance claims database and cancer registry databases from The Collaboration Center of Health Information Application in Taiwan were linked for the analysis. Head and neck cancer patients from January 1, 2002 to December 31, 2011 were included in the study. The follow-up duration was from the index day to December 31, 2013. The inclusion criteria were having a head and neck cancer (identified according to the International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 140.0-148.9), being aged > 20 years, being at American Joint Committee on Cancer (AJCC) clinical cancer stage III or IV, and having undergone induction chemotherapy or platinum-based CCRT. Exclusion criteria were having been diagnosed with cancer before the head and neck cancer was confirmed, having distant metastasis, being at AJCC clinical cancer stages I or II, having platinum and docetaxel combined use before radiotherapy (RT), being younger than 20 years, one's gender being unknown, and having docetaxel use during or after RT, induction chemotherapy beyond 8 weeks before RT, only one course of induction chemotherapy before RT, ceturiximab use, adjuvant chemotherapy within 90 days after completion of RT, <7000 cGy dose of RT, curative head and neck cancer surgery before RT, nasopharyngeal cancer, carcinoma in situ, a sarcoma, and head and neck cancer recurrence. The total number of enrolled head and neck cancer patients was 30,990 persons.

Results: In total, 10,721 stage III or IV head and neck cancer patients without distant metastasis were included in the study, and the median follow-up duration was 4.18 (interquartile range, 1.52-2.75) years. The TNM stages were I: 215 (34%), II: 161 (25%), III: 129 (20%), and IV 130 (20%). Gross LNs were present in 131 (21%) patients. LWNK-LNs were present in 55/213 (26%) cases, all of which also had overt LNs in the upper neck (levels 2 +/- 3). Median GTV-RT was 4 cc (range: 0.1-17.3), and GTV-N was 8 cc (range: 0.9-178.0). Systemic agents were used in 81 (13%) patients. Larger GTV-RT (>4 cc vs <=4 cc) or GTV-N (>8 cc vs <=8 cc), or presence of LWNK-LN inferior 3-year OS (GTV- T: 65% vs 89%; GTV-N: 37% vs 75%; LWNK-LN: 41% vs 65%, all p<0.001) and DC (GTV-RT: 87% vs 97%; GTV-N: 71% vs 87%; LWNK-LN: 72% vs 84%, all p<0.001). MVA (adjusted for treatment) confirmed that TNM stage was the strongest PF for OS [III/IV vs I/II: HR 2.52 (1.78-3.56), p<0.001] and DM [HR 6.24 (2.67-14.57), p<0.001], DC (GTV-RT: per 10 cc increment) was also a PF for OS [HR 1.15 (1.07-1.23), p<0.001] and DM [HR 1.18 (1.03-1.36), p<0.015]. GTV-N was a PF for OS [HR 1.13 (1.07-1.20), p<0.001] but not for DM (p=0.22). LWNK-LN was not a PF for OS (p=0.18) nor for DM (p=0.67) although it became significant for OS [HR 1.97 (1.32-2.93), p<0.001] when GTV-RT and GTV-N were excluded from the MVA model.

Conclusion: The TNM classification remains the strongest PF for OS and DM. GTV-RT is also a PF for OS and DM in addition to TNM. GTV-N is a PF for OS but not for DM. Presence of LWNK-LN is always associated with upper neck LN involvement (likely a surrogate for lymph node burden), and seems to lack independent impact on DM and OS if controlling for GTV-RT and GTV-N.

PO-0632
A multivariate model predicting grade ≥ 2 neck fibrosis at 6 months after radio(chemo)therapy

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Purpose or Objective: Evidence suggests that gross tumor volume (GTV) is a prognostic factor (PF) for laryngeal cancer beyond TNM staging. Lower neck lymph nodes (LWNK-LNs) have been linked to increased risk of distant metastasis (DM) although are generally evident when upper neck disease also exists. We hypothesized that primary GTV (GTV-T) and total lymph node (LN) GTV (GTV-N) may differentially impact overall survival (OS) and DM, and that LWNK-LN may lack independent effect.

Material and Methods: All newly diagnosed laryngeal cancers treated with definitive intensity modulated radiotherapy (IMRT) +/- chemotherapy in 2005-2012 were included. GTV-T and GTV-N were delineated for IMRT treatment (confirmed with staging CT/MRI) and peer-reviewed at quality assurance meetings. Levels IV or Vb LNs were considered LWNK-LNs. GTV-N was the summed LN volume receiving full-prescribed dose (lower doses were occasionally used to spare brachial plexus). OS and distant control (DC) were compared between larger/smaller GTV-T, GTV-N (both dichotomized at median value), and presence/absence of LWNK-LN. Multivariate analysis (MVA) identified PFs for OS and DM.

Results: A total of 635 cases [456 (72%) glottic, 164 (26%) supra- and 15 (2%) sub-glottic cancers] were included. TNM stages were I: 215 (34%), II: 161 (25%), III: 129 (20%), and IV 130 (20%). Gross LNs were present in 131 (21%) patients. LWNK-LNs were present in 55/131 (42%) cases, all of which also had overt LNs in the upper neck (levels 2 +/- 3). Median GTV-RT was 4 cc (range: 0.1-17.3), and GTV-N was 8 cc (range: 0.9-178.0). Systemic agents were used in 81 (13%) patients. Larger GTV-RT (>4 cc vs <=4 cc) or GTV-N (>8 cc vs <=8 cc), or presence of LWNK-LN inferior 3-year OS (GTV- T: 65% vs 89%; GTV-N: 37% vs 75%; LWNK-LN: 41% vs 65%, all p<0.001) and DC (GTV-RT: 87% vs 97%; GTV-N: 71% vs 87%; LWNK-LN: 72% vs 84%, all p<0.001). MVA (adjusted for treatment) confirmed that TNM stage was the strongest PF for OS [III/IV vs I/II: HR 2.52 (1.78-3.56), p<0.001] and DM [HR 6.24 (2.67-14.57), p<0.001], DC (GTV-RT: per 10 cc increment) was also a PF for OS [HR 1.15 (1.07-1.23), p<0.001] and DM [HR 1.18 (1.03-1.36), p<0.015]. GTV-N was a PF for OS [HR 1.13 (1.07-1.20), p<0.001] but not for DM (p=0.22). LWNK-LN was not a PF for OS (p=0.18) nor for DM (p=0.67) although it became significant for OS [HR 1.97 (1.32-2.93), p<0.001] when GTV-RT and GTV-N were excluded from the MVA model.

Conclusion: The TNM classification remains the strongest PF for OS and DM. GTV-RT is also a PF for OS and DM in addition to TNM. GTV-N is a PF for OS but not for DM. Presence of LWNK-LN is always associated with upper neck LN involvement (likely a surrogate for lymph node burden), and seems to lack independent impact on DM and OS if controlling for GTV-RT and GTV-N.