Abstract

Significance of volumetric staging and molecular profiles in radiotherapy for H&N cancer

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BACKGROUND
TNM staging and clinicopathological features are commonly used to assess the prognosis and to optimize treatment for squamous cell cancer of the head and neck (H&NC). An improvement in prognostic and predictive tools is, however, required to further increase cure rates.

HYPOTHESIS
Volumetric staging (Tv) may be a valuable supplement of TNM system in planning of the optimal dose fractionation in H&NC. Moreover, molecular predictors may enhance our ability to select the optimal fractionation schedule.

METHODS
The value of volumetric staging as a supplement of TNM staging was assessed in a group of 225 patients with T2 laryngeal cancer treated with radiotherapy; 3 yr local tumor control rates were used as the endpoint. Also, 279 cases of H&N cancer with high clinical risk of the postoperative failure were recruited to the III phase trial on conventional vs. accelerated postoperative RT. The predictive value of gene expression profile (HPV, EGFR, nm-23, p-53, Ki-67, CyclinD) relative to the effect of shortening of the overall treatment time was prospectively assessed.

RESULTS
Strong correlation between the initial tumor volume of T2N0M0 laryngeal cancer and 3 yr local control (LC) was noted with a decrease in LC from about 90% for 0.5 cm^3 tumors to about 23% for 20cm^3 tumors. To keep the LC constant and high, tumors with the highest volume within T2 stage need at least 7 Gy dose increment, compared to the smallest tumors within the same TNM category. When locoregional control for postoperative radiotherapy for H&N tumors with high clinical risk of local failure was analyzed, no difference in treatment outcome after conventional fractionation (pCF) and accelerated 7 days/week irradiation (pCAIR) was noted. Patients who had tumors with low Ki-67, low p-53, high EGFR expression levels and oral cavity/oropharyngeal primary cancer sites tended to benefit from p-CAIR. A joint score for the gain in LRC from p-CAIR based of these features was used to separate the patients into two groups: those who benefited significantly from p-CAIR with respect to LRC and those who did not benefit from p-CAIR. For patients with 0-2 of the above features no difference between pCF and pCAIR was observed, but for cases with 3-4 features significant difference in 5 yrs LC in favor of pCAIR was found (78% for pCAIR vs. 38% for pCFx). In conclusion, the analysis of the data on T2 laryngeal cancer demonstrate that routine estimation of tumor volume may be essential in selection of optimal radiation dose for patients in this clinical stage. The assessment of molecular signatures of H&N tumors with high clinical risk of postoperative local failure may help in individual selection of optimal fractionation schedule