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Abstract #4853

TP53 mutations and S-Phase fraction are independent prognostic indicators in locally advanced laryngeal squamous cell carcinoma

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Larynx tumor is a rare neoplasia that represent only the 2% of all human tumor. In particular, the 90% of tumor that occur in this organ correspond to the laryngeal squamous cell carcinoma (LSCC). From the biomolecular point of view, it was shown that the **TP53** gene mutations are the most common events observed in the early phases of LSCC carcinogenesis. However, them prognostic significance remains controversial. Besides, the prognostic significance of DNA ploidy has been well established for other solid tumors, but its role in LSCC is still controversial. The aim of this study was, therefore, to prospectively evaluate the prognostic significance of **TP53** mutations, DNA-ploidy and S-phase fraction (SPF) in LSCC patients. Prospective analysis of 81 patients who underwent resective surgery for primary operable locally advanced LSCC patients (stages III and IV) was performed. Tumor DNA was screened for **TP53** mutations by PCR/SSCP and sequencing; DNA flow cytometry was performed on mechanically disaggregated sample of frozen tumor tissue. The median follow-up time in our study group was 71 months (range 11-137 months). Fourthy-four percent of patients (36/81) have, at least, a mutation in the **TP53** gene. Of them, 22% (8/36) have double mutations and 6% (2/36) have triple mutations. In total, 47 **TP53** mutations were observed. The majority (42%) of these occur in exon 5 (20/47), while the mutations in exons 6, 7 and 8 are represented in 14, 7 and 6 patients respectively (30%, 15% and 13%). The flow cytometry analysis showed that sixty-three percent of the cases (51/81) were DNA aneuploidy and 14% of these (7/51) were multiclonal. LSCC patients were divided into two groups using median SPF level as cut-off point: low SPF 15.1 % and high SPF >15.1 %, Even though it seems that **TP53** mutations promotes the LSCC carcinogenesis in young people ($p < 0.05$), there was not any association between this variable and the clinicopathological or the other biomolecular variables. At univariate analysis, the Kaplan and Meier text show that DNA aneuploidy, high SPF, any **TP53** mutations and, in particular, the mutations that occur in exons 5 and 8 proved to be significantly related to quicker disease relapse and short OS. At multivariate analysis, the Cox proportional hazards model show that the major significant predictors for both disease relapse and death were high SPF and any **TP53** mutations. In conclusion, any **TP53** mutations, more than specific mutations in exon 5 and 8, are important biological indicators to predict the outcome of patients indicating these mutations have biological relevance in terms of LSCC disease course. Our study has also identify high SPF as independent prognostic factors in locally advanced LSCC patients.