Nasopharyngeal carcinoma: past, present and future directions

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AKADEMISK AVHANDLING

Som för avläggande av medicine doctorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i Jubileumsklinikens Aula, Gula stråket 2B, Sahlgrenska universitetssjukhuset, Göteborg, fredagen den 2 november 2007, kl 9:00

Zahra Taheri-Kadkhoda, leg. Läkare

Fakultetsopponent:

Professor Cai Grau
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Danmark

Avhandlingen baseras på följande delarbeten:

I Taheri-Kadkhoda Z, Björk-Eriksson T, Johansson K-A, and Mercke C. Long- term treatment results for nasopharyngeal carcinoma: The Sahlgrenska University Hospital experience. *Acta Oncol. 2007;46(6):817-827.*

II Taheri-Kadkhoda Z, Pettersson N, Björk-Eriksson T, and Johansson K-A. Superiority of intensity-modulated radiotherapy over three-dimensional conformal radiotherapy combined with brachytherapy in nasopharyngeal carcinoma: a planning study. *Accepted by The British Journal of Radiology on August 14th,2007.*

III Taheri-Kadkhoda Z, Björk-Eriksson T, Nill S, Wilkens JJ, Oelfke U, Johansson K-A, Huber PE, and Műnter MW. Intensity-modulated radiotherapy of nasopharyngeal carcinoma: a comparative treatment planning study of photons and protons. *Submitted.*

IV Taheri-Kadkhoda Z, Magnusson B, Svensson M, Mercke C, and Björk-Eriksson T. Expression modes and clinical manifestations of LMP1, ki-67, cyclin-B1, and epidermal growth factor receptor in non-endemic nasopharyngeal carcinoma. *In manuscript.*

ABSTRACT

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Nasopharyngeal carcinoma (NPC) is a rare disease in Sweden. The purpose of this thesis was to investigate the clinicopathological manifestations of the disease and its treatment outcomes in a cohort of Swedish NPC patients to identify key features for future improvements in patient care.

From 1991 to 2002, 50 NPC patients were treated with radical three-dimensional conformal radiotherapy (3DCRT) +/- intracavitary brachytherapy (IBT) +/- chemotherapy at Jubileumskliniken, Sahlgrenska University Hospital. Retrospective analysis of the data showed 5-year local, regional, and distant relapse-free survival rates of 70%, 92%, and 77% for 49 nondisseminated patients. Patients with locoregionally advanced disease fared worse with respect to local and distant tumor control rates. Furthermore, the long-term side effects of irradiation were adverse and frequent in the whole cohort of patients.

A comparative treatment planning study between intensity-modulated radiotherapy (IMRT) and 3DCRT + IBT was performed for eight NPC patients. The prescription physical dose for planning target volume of the primary tumor was 72.6 Gy in IMRT and 72 Gy in the combined plans. The comparison of the plans using quantitative parameters revealed that IMRT plans provided more conformal plans with possibility of dose escalation in primary tumor and simultaneous sparing of several normal structures. These were translated into improved tumor control probability of the primary tumor and reduction of normal tissue complication probability for several organs. However IMRT plans resulted in significant increase of the mean volumes of low to intermediate isodoses (0.66 Gy to 19.8 Gy) by 30% to 44%.

A comparative treatment planning study between IMRT and intensity-modulated proton therapy (IMPT) with equivalent dose prescriptions for primary tumour (72.6 Gy_E) in the same cohort of patients showed that conformity of treatment plans and tumor coverage especially for locally advanced tumors were improved further by IMPT plans. Moreover, the integral dose (mean dose) was significantly reduced by a factor of 2 to 3 in several organs. The mean volume of low to intermediate isodoses (0.66 Gy to 19.8 Gy) were 2 to 2.7-fold larger in IMRT plans than in IMPT plans.

Expression of EBV-encoded LMP1, Ki-67, cyclin-B1, and EGFR were analyzed by immunohistochemical assays for 44 (45 for LMP1) NPC patients. LMP1 was expressed in 33% of the patients and its presence was significantly correlated with advanced nodal and tumour stage. Statistically, expression of Ki-67 and cyclin-B1 showed no significant clinical relevance. Strong EGFR staining intensity was significantly correlated with worse 5-year local and locoregional tumor control probabilities as well as poorer disease-free and overall survival rates.

Key words: Nasopharyngeal carcinoma, radiotherapy, side effects, 3DCRT, Intracavitary brachytherapy, IMRT, IMPT, LMP1, EGFR.
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