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Original article

A comparative study of locoregionally advanced nasopharyngeal carcinoma treated with intensity modulated irradiation and platinum-based chemotherapy

Étude comparative de carcinomes du nasopharynx évolués pris en charge par radiothérapie avec modulation d'intensité et chimiothérapie à base de platine

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ABSTRACT

Purpose. – To investigate the prognosis of three subgroups of locoregionally advanced nasopharyngeal carcinoma treated with intensity-modulated radiotherapy and platinum-based chemotherapy.
Patients and methods. – Hundred and eighty-one consecutive patients with locoregionally advanced untreated nasopharyngeal carcinoma were retrospectively divided into three subgroups: locally advanced group (T3-4N0-1M0), regionally advanced group (T1-2N2-3M0) and the mixed group (T3-4N2-3M0). They were all treated with definitive intensity-modulated radiotherapy and platinum-based chemotherapy. Their prognosis were investigated and compared. Multivariate analysis was applied to identify the independent risk factors of study endpoints.
Results. – The 3-year locoregional control rates for locally advanced group, regionally advanced group, and the mixed group were 91.5%, 90.6% and 84.3% respectively, no significant difference was observed ($P = 0.656$, $P = 0.429$). The 3-year distant metastasis-free survival rates were 89.6%, 75.7% and 76.3%, respectively. The distant metastasis-free survival rate of the locally advanced group was significantly higher than the other two subgroups ($P = 0.028$, $P = 0.028$). The 3-year progression-free survival rates were 85.5%, 67.9% and 67.1% respectively with significance also favoring the locally advanced group ($P = 0.043$, $P = 0.023$). Nodal stage and the performance status were the independent risk factors of distant metastasis in the observed period.
Conclusions. – In the context of intensity-modulated radiotherapy and platinum-based chemotherapy, the locally advanced group had a better prognosis compared with the regionally advanced group and the mixed group. Treatment stratification may be based on nodal stage.

Mots clés :
Carcinome localement évolué du nasopharynx
Radiothérapie conformationnelle avec modulation d'intensité
Chimiothérapie

RÉSUMÉ

Objectif. – Étudier le pronostic de trois sous-groupes de carcinome du nasopharynx localement évolués dont la prise en charge a consisté en une radiothérapie conformationnelle avec modulation d'intensité et une chimiothérapie à base de platine.
Patients et méthodes. – Un total de 181 patients consécutifs atteints d'un carcinome du nasopharynx localement évolué non prélablement traité ont été rétrospectivement divisés en trois sous-groupes : tumeur localement évoluée (T3-4N0-1M0), tumeur régionalement évoluée (T1-2N2-3M0) et tumeur localement et régionalement évoluée (T3-4N2-3M0). Tous les traitements étaient à visée curative. Leurs facteurs pronostiques et d'échec ont été étudiés et comparés. Une analyse multifactorielle a été réalisée pour identifier les facteurs de risque indépendants.

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Résultats. – Les taux de contrôle locorégional à trois ans étaient respectivement dans les trois groupes de 91,5 %, 90,6 % et 84,3 %, sans différence significative ($p = 0{,}656$, $p = 0{,}429$). Les taux de survies sans métastase à trois ans étaient respectivement de 89,6 %, 75,7 % et 76,3 % ; ils étaient significativement plus élevés dans le premier groupes que dans les deux autres ($p = 0{,}028$, $p = 0{,}028$). Les taux de survies sans progression à trois ans étaient respectivement de 85,5 %, 67,9 % et 67,1 %, en faveur du groupe des patients atteints de tumeur localement évoluée ($p = 0{,}043$, $p = 0{,}023$). L'extension ganglionnaire et l'indice de performance étaient des facteurs de risque indépendants de dissémination métastatique à distance durant la période considérée.

Conclusions. – Le pronostic s'est avéré plus favorable en l'absence d'extension ganglionnaire. Le traitement pourrait être stratifié sur la base de la classification ganglionnaire.

1. Introduction

Nasopharyngeal carcinoma is the most common head-and-neck malignancy in Southeast Asia people, especially in those with Chinese origin [1]. Because of mild symptoms at an early stage, over 70% patients were diagnosed at a locoregionally advanced stage (III, IVa or IVb, AJCC 7th), which had been demonstrated to be associated with high locoregional recurrences and distant metastasis after treatment [2]. Clinically, the locoregionally advanced nasopharyngeal carcinoma could be divided into three subgroups: locally advanced group (T3-4N0-1M0), regionally advanced group (T1-2N2-3M0) and the mixed group (T3-4N2-3M0). Previous studies investigated locoregionally advanced cases as a whole group, but general statistical results might not clearly reflect the clinical characteristics of each subgroup [3–8]. They may differ in prognosis or failure patterns after similar treatment. Comparison of prognosis among the subgroups may help us develop new treatment strategy of stratification if difference really exists. To the best of our knowledge, no comparative studies were conducted among the subgroups of locoregionally advanced nasopharyngeal carcinoma in the context of intensity modulated radiotherapy (IMRT) and platinum-based chemotherapy.

2. Patients and methods

2.1. Patients

Between June 2009 and October 2010, 223 consecutive patients with newly pathologically confirmed, untreated and non-disseminated nasopharyngeal carcinoma were registered in our center for therapy. All patients had standardized pretreatment examinations, including a complete history, physical examinations, routine blood examinations, blood biochemistry examinations, a chest X-ray, electrocardiogram (ECG), whole-body computed tomography (CT), abdominal sonography, and standardized magnetic resonance imaging (MRI). According to the 7th edition of American Joint Committee on Cancer (AJCC) staging system, 186 patients were diagnosed as locoregionally advanced cases, including T3-4N0-1M0 (locally advanced group) 67 patients, T1-2N2-3M0 (regionally advanced group) 43 patients and T3-4N2-3M0 (mixed group) 76 cases. A total of 181 cases were included for analysis. Five (2.7%) patients were excluded because they could not be followed up regularly after initial therapy. Patient characteristics are presented in Table 1.

2.2. Radiotherapy

All patients received intensity-modulated radiotherapy. Patients were immobilized in the supine position with a thermoplastic mask fixing the head and shoulders. Contrasted CT simulation was performed with a scanning scale from the top of the head to the bottom of the inferior head of the clavicle. Target volume contouring was based on the results of standardized MRI, which consisted of T1-weighted fast spin-echo images in the axial, coronal and sagittal planes, T2-weighted fat-suppressed fast spin-echo MR images in the axial, coronal and sagittal planes, and gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) contrasted T1-weighted fat-suppressed images in axial, coronal, and sagittal planes. Section thickness was 5 mm with a 1-mm interslice gap for the axial plane, coronal and sagittal planes. Skull base involvement, cranial nerve invasion, and lymph node metastasis had to meet their diagnostic criteria [9–11].

The primary tumour with its direct extensions (including metastatic retropharyngeal lymph node, RPN) were defined as gross tumour volume (GTV) 1, and received a median dose of 72.13 Gy/34 fractions (range, 67.6 Gy/31f–78 Gy/35f), Metastatic cervical lymph nodes were defined as GTV2, and received a median dose of 70 Gy/33f (range, 60 Gy/32f–85 Gy/39f). For patients staged T3-4, a boost of 5 to 6 Gy in 2 to 3 fractions was given to the residual lesions if any. Electron beam was used as an alternative boost when a cervical metastatic lymph node received an X-ray dose of more than 75 Gy.The high-risk area was defined as clinical target volume (CTV) 1, which included the entire GTV1, whole nasopharyngeal

Table 1
Locoregionally advanced nasopharyngeal carcinoma clinical characteristics ($n = 181$).
Caractéristiques cliniques.

	Locally advanced ($n = 66$)	Regionally advanced ($n = 42$)	Mixed type ($n = 73$)	P^a
Patient gender				0.282
Male	46	33	59	
Female	20	9	14	
Age				0.487
≤ 50 years	32	17	38	
> 50 years	34	25	35	
ECOG				0.950
≤ 1	56	36	61	
2	10	6	12	
Pathology				0.427
Non-keratinizing	64	42	70	
Undifferentiated	2	0	3	
Radiation dose				0.373
< 70 Gy	3	0	2	
≥ 70 Gy	63	42	71	
With/without radiation boost				
To the residual primary tumor	43/23	9/33	41/32	0.000
To the residual Lymph nodes	15/51	15/27	33/40	0.021

[a] Pearson χ^2 test.