World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Check for updates

Radiotherapy in the Management of Nasopharyngeal Carcinoma: A Retrospective Analysis of Long-Term Outcomes and Toxicity in 459 Patients

Abdelkarim Uakkas *, Zenab Alami, Jihane Bouziane, Samia Khalfi, Kaoutar Soussy, Wissal Hassani, Fatima Zahraa Farhane and Touria Bouhafa

Department of Radiation Oncology, Hassan II University Hospital, Fez, Morocco.

World Journal of Advanced Research and Reviews, 2025, 27(03), 1489-1499

Publication history: Received on 05 August 2025; revised on 20 September 2025; accepted on 23 September 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.27.3.3289

Abstract

Background: Nasopharyngeal carcinoma (NPC) represents a therapeutic challenge due to its unique pathological behavior, complex anatomical location, and high incidence in endemic regions such as the Maghreb. Advances in radiotherapy techniques, particularly intensity-modulated radiotherapy (IMRT), combined with chemotherapy have improved tumor control and reduced toxicity.

Methods: We conducted a retrospective study of 459 patients with NPC treated at the Radiotherapy–brachytherapy Department of CHU Hassan II, Fès, Morocco, between January 2014 and December 2022. All patients underwent biopsy with histopathological confirmation and staging investigations. Treatment protocols included induction chemotherapy followed by concomitant chemoradiotherapy (68%), exclusive concomitant chemoradiotherapy (30%), or radiotherapy alone (2.2%). IMRT was used in all cases. Survival outcomes were estimated with the Kaplan–Meier method, and toxicities graded according to CTCAE v5.

Results: The mean age was 48.3 years, with a male/female ratio of 1.94. Undifferentiated carcinoma of nasopharyngeal type (UCNT) was predominant (94.8%). Most patients presented at advanced stages (III–IV: 72.4%). Acute toxicities included mucositis (61.7%, grade ≥3 in 11%), radiodermatitis (40.8%, grade ≥3 in 2%), and hematologic toxicity (32.3%). Late toxicities included xerostomia (68%), hearing loss (29.8%), trismus (10.7%), and cervical fibrosis (4.5%). At a median follow-up of 5 years, overall survival was 81% at 5 years and 71% at 8 years, while metastasis-free survival was 77% and 73%, respectively. Nodal stage significantly impacted prognosis, with 5-year OS ranging from 91.1% (N0) to 43.2% (N3, $p<0.001$).

Conclusion: Our findings confirm that IMRT-based concurrent chemoradiotherapy, with or without induction chemotherapy, achieves high rates of tumor control and survival in an endemic population, with manageable toxicity. Nodal involvement remains the strongest prognostic factor. These results support the need for multidisciplinary, personalized strategies and ongoing refinement of therapeutic protocols for NPC in the Maghreb region.

Keywords: Nasopharyngeal carcinoma; Intensity-Modulated Radiation Therapy; Chemoradiotherapy; Undifferentiated carcinoma of nasopharyngeal type

1. Introduction

Nasopharyngeal carcinoma (NPC) represents a major therapeutic challenge in oncology due to its unique pathological behavior, complex anatomical location, and its sensitivity to multimodal treatment approaches. It therefore constitutes a public health problem given its therapeutic and evolutionary impact. At the Radiotherapy Department of CHU Fès in

* Corresponding author: Abdelkarim Uakkas

Morocco, NPC management is based on a multidisciplinary strategy in which radiotherapy plays a central role. The use of conformationnal radiotherapy techniques such as IMRT has made it possible to optimise tumour control while minimising exposure of healthy structures, thereby improving the local control/toxicity ratio for our patients.

In an epidemiological context where NPC has a significant incidence in the Maghreb region, our retrospective study aims to describe the clinical and therapeutic outcomes achieved at our center, with a particular focus on locoregional control, survival, and treatment tolerance. Our objective is to identify predictive factors of success and potential areas for further optimization of therapeutic protocols.

2. Materials and methods

This work is a retrospective study involving 459 patients with nasopharyngeal carcinoma treated with concurrent radio-chemotherapy, either preceded by induction chemotherapy or not, within the Radiotherapy-brachytherapy Department at the University Hospital Hassan II of Fès over a 9-year period from January 1, 2014, to December 30, 2022.

All patients underwent cavoscopy with tumour biopsy and pathological study. Assessment of local extension included a complete ENT examination, cervico-facial computed tomography (CT) and/or magnetic resonance imaging (MRI) of the cavum. Long-distance evaluation included a thoraco-abdomino-pelvic CT scan (or chest X-ray and abdominal ultrasound) with bone scintigraphy. Treatment protocols were established at multidisciplinary consultation meetings and varied according to the tumour stage, age and condition of the patient (induction chemotherapy followed by concomitant chemo-radiotherapy, concomitant chemo-radiotherapy or exclusive radiotherapy). At the end of treatment, patients were followed up at our outpatient clinic every 3 months for 2 years, then every 6 months for 3 years. After 5 years, patients were monitored annually.

Patients were identified using data from the Hosixnet hospital network database as well as TPS ARIA. Survival curves were generated using the Kaplan-Meier method, and toxicities were graded according to version 5 of the Common Terminology Criteria for Adverse Events (CTCAE).

3. Results and statistical analysis

The mean age in our series was 48.3 years, with an M/F sex ratio of 1.94.

The most frequent reason for consultation was lymph node syndrome, which was present in 67.8% of cases in our series, while rhinological and otological signs occurred in 56.6% and 50.3% of patients respectively. Neurological symptoms were present in 27% of cases.

All our patients underwent nasofibroscopy with biopsy. The most frequent histological type was undifferenciated Carcinoma of Nasopharyngeal Type (UCNT), observed in 97.4% of cases, while only 2.6%—that is, 12 patients in our series—had squamous cell carcinoma (SCC). For locoregional assessment, a cervicofacial CT scan was performed in 94.8% of patients, and an MRI was conducted in only 5.2% of cases. The extension workup consisted of a thoraco-abdomino-pelvic CT scan and bone scintigraphy in almost 90% of cases.

The classification adopted was the 8th edition of the 2017 TNM classification for nasopharyngeal cancer, with stage II in 27.6% of cases, stage III in 42.9%, stage IVA in 23.9% and stage IVB in 5.6% of cases.

Table 1 Patient characteristics

Parameters	**N(%)**
SEX	
Male	303 (66%)
Female	156 (34%)
Mean age	48.3
Clinical presentation	
Lymph node syndrom	311 (67.8%)

Rhinological signs	260 (56.6%)
Otological signs	231 (50.3%)
Neurogical signs	124 (27%)
Histological type	
UCNT	446 (94.8%)
Squamous cell carcinoma	12 (5.2%)
T Classification	
T1	58 (12.6%)
T2	183 (39.9%)
T3	115 (25.5%)
T4	101 (22%)
N Classification	
N0	76 (16.6%)
N1	144 (31.4%)
N2	197 (42.9%)
N3	42 (9.2%)
Classification M	
M0	432 (94.1%)
M1	27 (5.9%)

Treatment consisted of induction chemotherapy followed by concomitant radio-chemotherapy in 68% of patients. The most commonly used induction chemotherapy protocols (nearly 90%) in our series were cisplatin-Gemcitabine and cisplatin-doxorubicin. Concomitant radio-chemotherapy without induction CMT was used in 30% of cases while radiotherapy alone without concomitant chemotherapy was performed in 2.2% of patients. The irradiation technique used was IMRT, with a total dose of 70gy in 35 fractions of 2Gy per fraction concurrently with cisplatin-based chemotherapy. The median overall treatment time was 55 days.

With regard to acute toxicities induced by treatment, the following were observed:

- -Radiodermatitis, mainly grade I and II in 38.8% of patients (grade 3 in 2% of cases)
    - Radiomucositis, mainly grade I and II in 61.7% of patients (grade 3 in 11% of cases resulting in swallowing difficulties and impaired nutrition)
    - Grade I-II dysphagia was reported in 31.2% of patients
    - Haematological toxicity, dominated by neutropenia, was found in 32.3% of patients
    - Chemotherapy-related digestive toxicity was observed in 17.2% of cases, while impaired renal function was observed in only 3% of patients.

During our follow-up, the main late toxicities observed were: - Grade I and II xerostomia in 68% of cases, trismus in 10.7% of patients, hypoacusis in 29.8% of patients, dysgeusia in 5.8% of patients, ocular disorders in 5% and cervical fibrosis in 4.5% of cases.

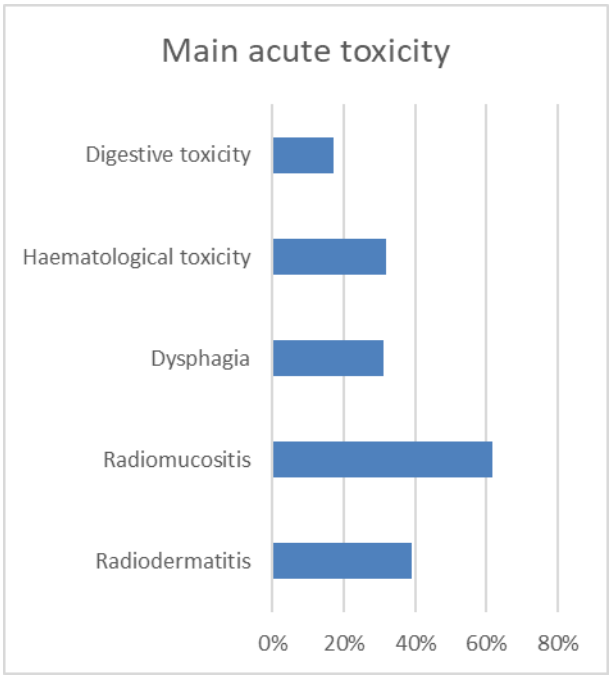

Figure 1 Main Acute toxicities

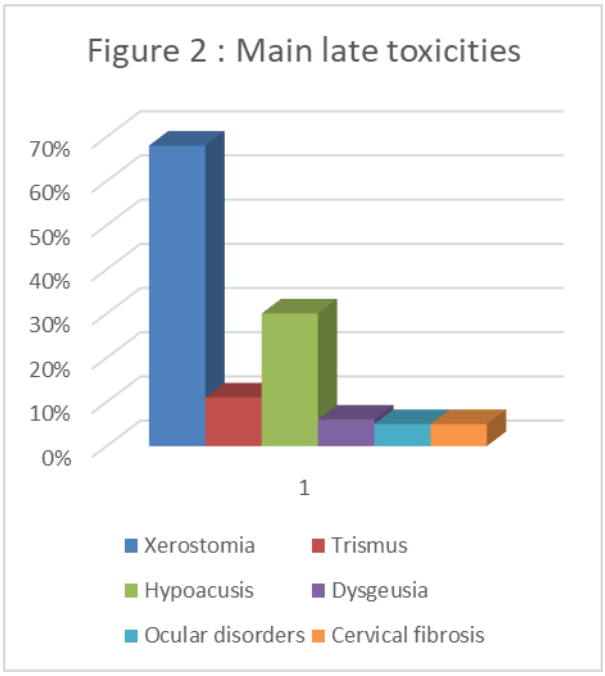

Figure 2 main late toxicities

In our series, 12% of patients had locoregional recurrence.

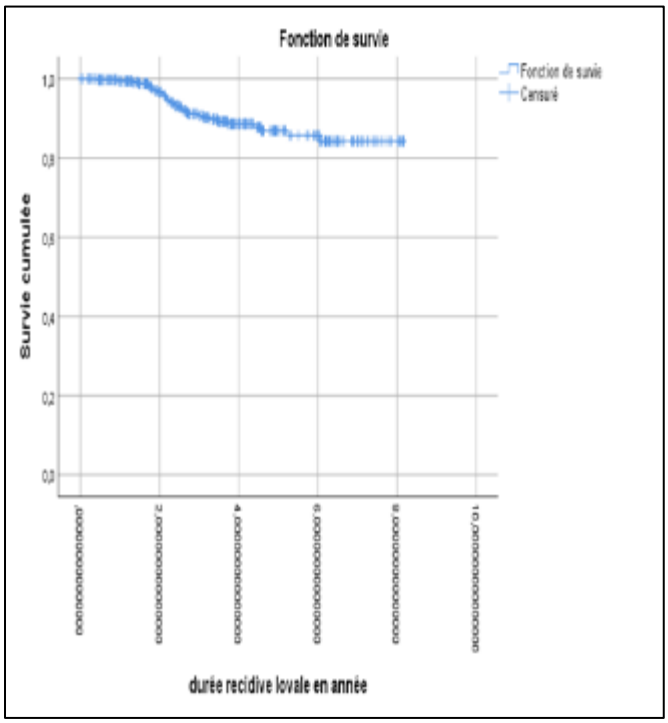

Figure 3 Local recurrence-free survival curve

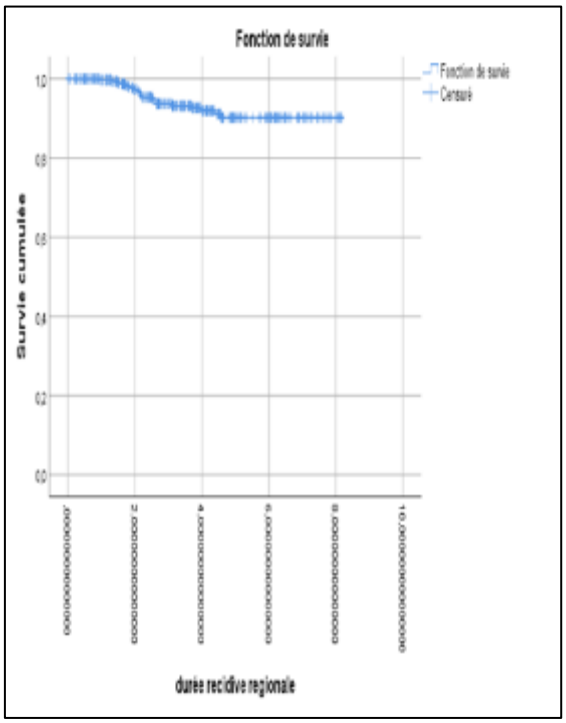

Figure 4 Regional recurrence-free survival curve (KAPLAN MEIER)

Survival free of distant metastases was 77% at 5 years and 73% at 8 years. The most frequent metastatic sites were bone, lung and non-regional lymph nodes in 13.9, 13.1 and 12.2% of cases respectively, while liver and brain metastases accounted for less than 10% of metastatic recurrences. Analysis of metastasis-free survival according to N stage showed a borderline significant difference for lymph node involvement, with five-year DFS rates of 87.8%, 80.9%, 76.2% and 64.6% respectively for tumours classified as N0, N1, N2 and N3 (p = 0.059).

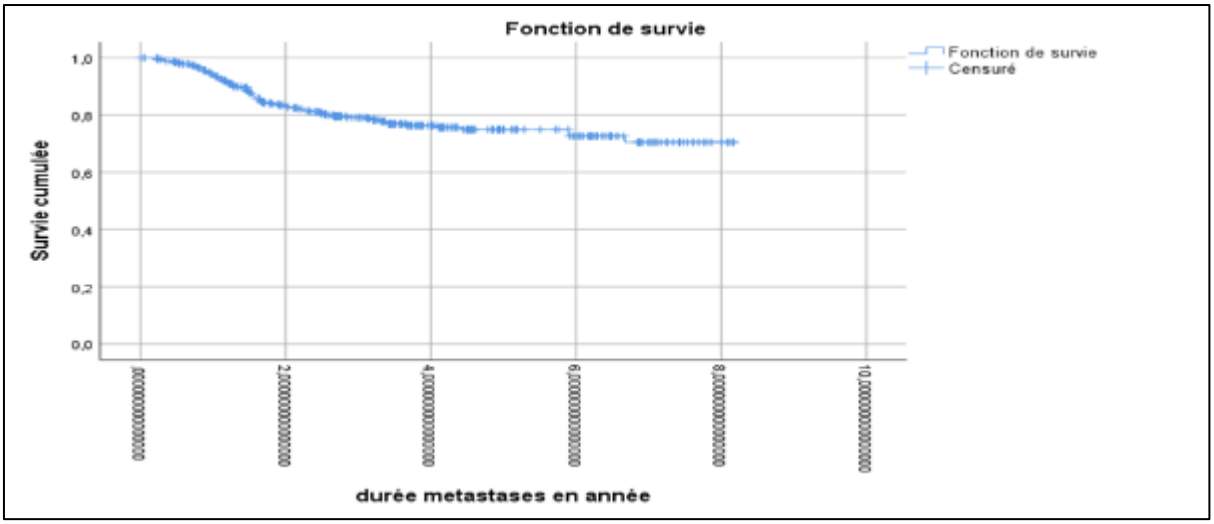

Figure 5 Metastatic recurrence-free survival curve (KAPLAN MEIER**)**

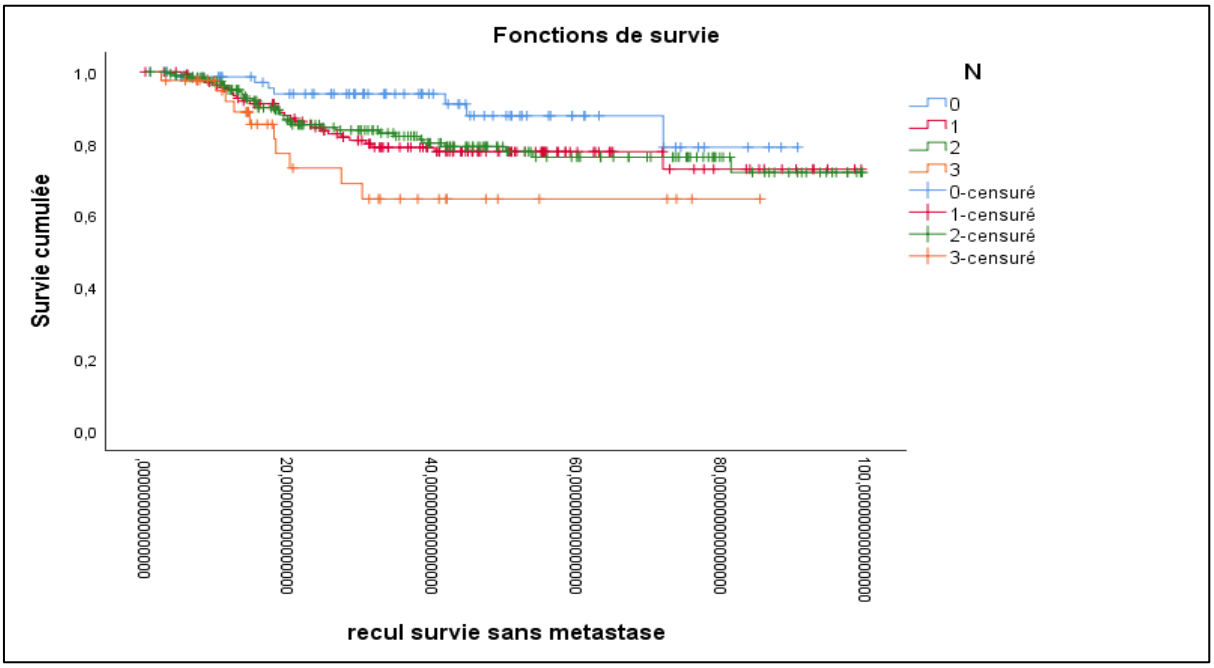

Figure 6 Metastatic free survival curve according to lymph node involvement

Overall survival was 81% at 5 years and 71% at 8 years. Analysis of overall survival according to N stage showed a highly significant difference for lymph node involvement, with five-year OS rates of 91.1%, 80.2%, 83.8% and 43.2% respectively for tumours classified as N0, N1, N2 and N3 ($p<0.001$).

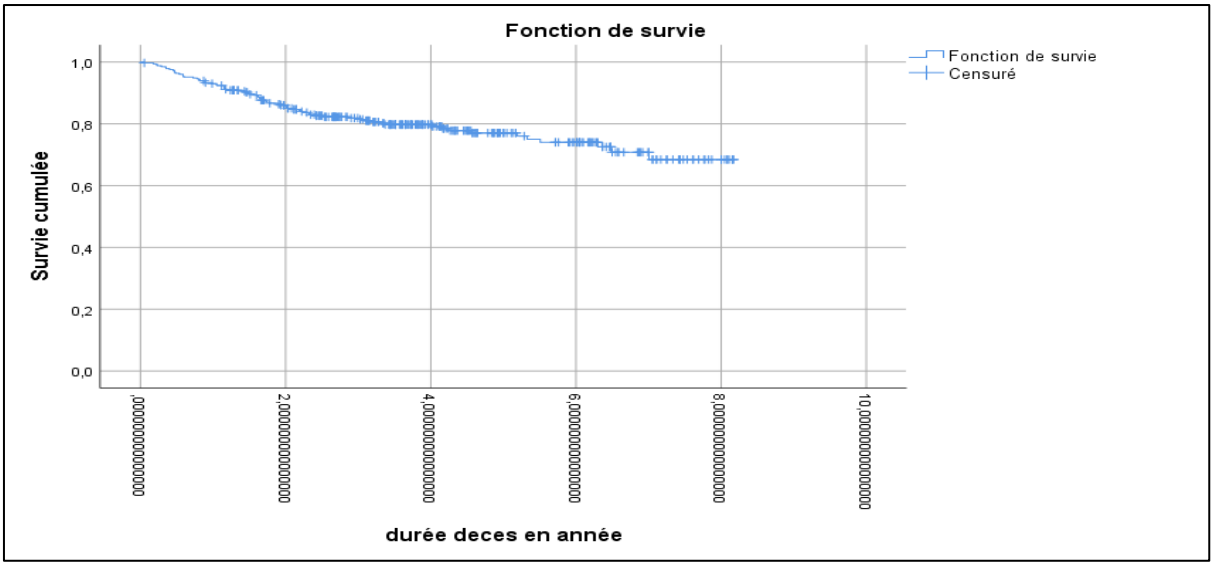

Figure 7 Overall survival curve (KAPLAN MEIER)

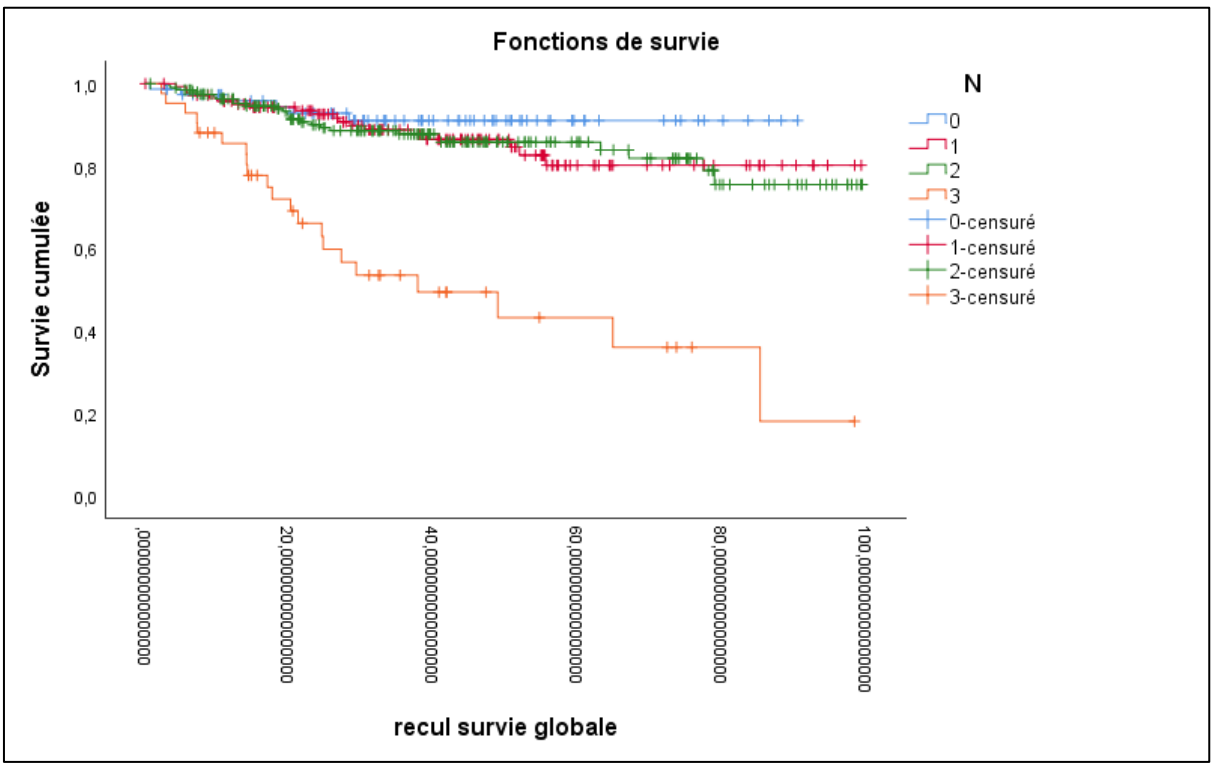

Figure 8 Overall survival curve according to lymph node involvement

4. Discussion

Worldwide, there are three risk areas for nasopharyngeal cancer: a very high frequency area with Southern China, where the incidence is 30 to 80/100,000/year. An intermediate frequency zone (8 to 12/100,000/year) with Taiwan, Vietnam, Thailand, Malaysia, the Philippines, the Caribbean, the Mediterranean basin (Maghreb and Middle East), Alaska and Greenland, and finally a low frequency zone in Europe and the United States (0.5 to 2/100,000/year). This type of cancer is more frequently observed in people over the age of 50. The sex ratio is two to three men to one woman. The results of our retrospective study on 459 NPC patients treated with concurrent radio-chemotherapy with or without

prior induction chemotherapy provide important insights into the effectiveness and tolerability of this multimodal approach at our center. The patient population, characterized by a mean age of 48.3 years and a male-to-female ratio of 1.94, reflects the demographic profile typically observed in regions with a high incidence of NPC, particularly in the Maghreb.

The clinical presentation, dominated by nodal syndrome (67.8%), and complemented by rhinologic, otologic, and neurological symptoms, underscores the often delayed and heterogeneous manifestation of NPC. The TNM classification (8th edition) revealed a predominance of advanced stages (stage III in 42.9% and combined stages IVA/IVB in 29.5%), highlighting the diagnostic challenges and the need for intensive management. Significant lymph node involvement (N2 or N3) was often associated with these cancers, reflecting their lymphophilic nature. The rate of lymph node involvement varies between 33.3% and 69% according to the literature (1,2). In our series, 52.1% of lymph node involvement was classified as N2/N3.

The complex anatomy of the nasopharynx makes surgical access particularly difficult. Since the 1950s, the first-line surgical approach has been abandoned in favour of less invasive treatments, and the majority of current protocols are based on concomitant radio-chemotherapy (3). Several studies have shown that radiotherapy alone can achieve 10-year survival rates of 34%, 37% and 43% (4,5), although it is only reserved for stage I NPC. Concomitant radio-chemotherapy (CRT) is the standard treatment for locally advanced nasopharyngeal cancers of stage T2 and above, or N1 and above. The 0099 intergroup trial (6) was the 1st randomised trial (RT) to demonstrate a gain in progression-free survival (PFS) and overall survival (OS) in favour of CCT compared with HBRT alone in locally advanced cavum cancer (T3-T4,N2-N3). Six other ERs followed, all of which showed the superiority of CCR in terms of PFS, CL and OS. Then the MAC-NPC meta-analysis (7) published in 2006 analysed the updated individual data from 8 randomised trials and confirmed the 5-year OS benefit of 6% in favour of CCR with a reduced risk of locoregional and distant relapse for chemotherapy regardless of its modalities.Its update presented at the ASCO in 2014, including 19 trials and 4,798 patients with a follow-up of 7.1 years: absolute benefit in OS of 6.4% with benefit in the case of CCR with or without adjuvant CMT (regardless of age, sex or tumour stage (8).

Induction chemotherapy (ITC) is indicated for stages III (especially in the case of N2 or multiple or large adenopathies) and IV: a French phase III trial (GORTEC TRIAL) compared CCR vs 3 courses of induction chemotherapy (TPF regimen) for T2-T4 regardless of N showed an improvement in progression-free survival and overall survival in favour of the induction chemotherapy + CCR arm. The Chinese phase III trial (9) published in the NEJM in 2019 compared gemcitabine CDDP in induction before RCC vs RCC alone for stage III-IV patients with N+ with an improvement in PFS and OS in favour of CTI.Finally, the MAC NPC update in 2020 included 28 trials with more than 8,000 patients comparing CCR vs CCR+adjuvant chemotherapy vs ITC+CCR vs RTH alone + induction or RTH alone + adjuvant chemotherapy, with the conclusion that the addition of induction or adjuvant chemotherapy to CCR is superior to to CCR alone not only in terms of OS but also in terms of PFS, CLR, cancer-related death and metastatic control (10).

Overall survival at 5 years, reported by several randomised studies, varies between 49.7% and 78.4% (11,12,13,14). In our series, which was carried out in a population considered to be endemic, the survival results are consistent with those reported in the literature, in particular the series from the Maghreb (15) and the Middle East, with an overall 5-year survival of 81% and a metastasis-free survival of 77%, with N3 lymph node involvement being a major factor in poor prognosis.According to the series by Chen et al (14), the 5-year overall survival for tumours classified as N2 and N3 was 74% versus 29.4% respectively, with a significant difference ($p=0.0009$), which is consistent with our series where the overall survival for N2 and N3 was 83.8% versus 43.2% respectively, with a significant difference ($p<0.001$).

The rate of locoregional recurrence and the occurrence of distant metastases, with a predominance of bone, lung and lymph node sites, illustrate the efficacy of treatment in controlling tumour, while indicating the need for multimodal approaches to reduce the risk of dissemination.

The last few decades have seen impressive advances in the radiotherapeutic management of nasopharyngeal carcinoma.

The intensive use of IMRT, magnetic resonance imaging and combined chemoradiotherapy has led to encouraging therapeutic results (16,17,18,19,20),

The results of our retrospective study highlight a notable frequency of acute toxicities in patients treated for nasopharyngeal carcinoma.

Radiodermatitis occurs in approximately 80% of patients (21). It is responsible for a deterioration in quality of life likely to lead to temporary or even permanent interruption of treatment (22). This toxicity is dose-dependent and appears

around the third week of treatment (23). In our series, radiodermatitis was found in more than 40% of cases. Acute radiodermatitis is constant, usually mild to moderate (grade I or II), but 11% of patients will suffer grade III toxicity with conventional fractionation according to Calais G et al (24). For our patients, mild to moderate toxicity (grade I to II) predominated, with grade III occurring in 2% of cases.

Mucositis is observed in the vast majority of patients treated by radiotherapy with concomitant chemotherapy, representing more than 60% (25,26), which is comparable with the results of our series. Radiomucositis generally appears within 2 to 3 weeks of the start of irradiation(27).

According to the literature, 20% of patients present with grade II dysphagia (28). Dysphagia was recorded in approximately 30% of our patients and was grade I to II in the majority of cases.

These side effects disappear between one and four weeks after the end of radiotherapy, but complete healing may take one to three months. These complications, by altering patients' quality of life and nutritional status, underline the importance of personalised and optimised management during treatment.

Medium and long-term follow-up identified several late complications. Among these, xerostomia remains the most common, affecting approximately 60 to 70% of patients at 12 months. This complication, linked to irradiation of the salivary glands, results in an alteration in oral comfort, an increased risk of dental caries and difficulty swallowing.

The degree of xerostomia depends largely on the dose/volume ratio of the salivary gland in the irradiation field. IMRT can limit the dose delivered to these glands without compromising tumour coverage. Numerous clinical studies have shown a lower degree of xerostomia after IMRT compared with the 2D and 3D techniques. Pow et al (29) showed that IMRT was significantly better than conventional RT in terms of parotid sparing and improved quality of life in early NPC.

Lee et al (30) also showed that only 14% of patients had grade 2 xerostomia one year after the start of IMRT and that 35% of patients had no complaints of xerostomia at all. The results of the present study are in close agreement with those of Lee.

Miah et al (31) analysed the effect of concomitant chemotherapy on parotid gland function after intensive head and neck radiotherapy, concluding that concomitant platinum chemotherapy had no significant negative effect on subjective xerostomia symptoms and saliva flow rates at one year after the end of radiotherapy.

A sizeable proportion of patients (around 30%) experienced progressive ototoxicity, manifested by hearing loss, which had an impact on communication and social integration. The study reported by Lee et al (30) showed that age, concomitant chemotherapy and the median dose received by the cochlea were significant factors in the development of auditory toxicities.

Other late toxicities, such as trismus and cervical fibrosis, were reported in around 15% of patients. These observations are consistent with the literature, which emphasises that the incidence and severity of late toxicities are closely linked to the total radiation dose, the volume irradiated and the association with concomitant and induction chemotherapy. Elderly patients and those with co-morbidities appear to be particularly vulnerable to these complications.

Late toxicities can be life-threatening or can considerably erode the patient's quality of life (QoL) and functional status, hence the importance of regular follow-up and personalised care during post-treatment monitoring consultations.

5. Conclusion

This study provides a regional perspective on the management of NPC and underscores the importance of tailoring therapeutic strategies to local specificities. Our findings offer a robust basis for further refining therapeutic protocols at our center and contributing to the evolution of radiotherapy-oncology standards in NPC management. Ultimately, our experience illustrates the relevance of a personalized, multidisciplinary approach to addressing the therapeutic challenges posed by nasopharyngeal carcinoma in the Maghreb context.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Boussen H, Noureddine Bouaouina, Olfa Daldoul, Farouk Benna, Said Gritli, Abdrrahman Ladgham. Actualités des traitements médicaux des cancers du nasopharynx. Bulletin du cancer. 2010;97(4):417–426. doi: 10.1684/bdc.2010.1091

[2] Rouge ME, Brisse H, Helfre S, Teissier N, Freneaux P, Orbach D. Le carcinome indifférencié du nasopharynx de l´enfant et de l´adolescent. Bulletin du cancer. 2011;98(3):337–345. doi: 10.1684/bdc.2011.1329

[3] Wu F, Wang R, Lu H, Wei B, Feng G, Li G, et al. Concurrent chemoradiotherapy in locoregionally advanced nasopharyngeal carcinoma: treatment outcomes of a prospective, multicentric clinical study. Radiotherapy and Oncology. 2014;112(1):106–111. doi: 10.1016/j.radonc.2014.05.005

[4] Sanguineti G, Geara FB, Garden AS, et al. Carcinoma of the nasopharynx treated by radiotherapy alone: determinants of local and regional control. Int J Radiat Oncol Biol Phys. 1997;37(5):985–96. doi: 10.1016/s0360-3016(97)00104-1.

[5] Lee AW, Poon YF, Foo W, et al. Retrospective analysis of 5,037 patients with naso- pharyngeal carcinoma treated during 1976-1985: overall survival and patterns of failure. Int J Radiat Oncol Biol Phys. 1992;23(2):261–70. doi: 10.1016/0360-3016(92)90740-9.

[6] Al-Sarraf M, LeBlanc M, Giri PG, et al. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized intergroup study 0099. J Clin Oncol. 1998;16(4):1310–7. doi: 10.1200/JCO.1998.16.4.1310.

[7] Baujat B, Audry H, Bourhis J, Chan AT, Onat H, Chua DT, Kwong DL, Al-Sarraf M, Chi KH, Hareyama M, Leung SF, Thephamongkhol K, Pignon JP; MAC-NPC Collaborative Group. Chemotherapy as an adjunct to radiotherapy in locally advanced nasopharyngeal carcinoma. Cochrane Database Syst Rev. 2006 Oct 18;2006(4):CD004329

[8] Meta-analysis of chemotherapy in nasopharyngeal carcinoma (MAC-NPC): An update on 4,798 patients. Pierre Blanchard, Anne W. M. Lee, Julie Leclercq, Sophie Marguet, Wai Tong Ng, Jun Ma, Anthony T. C. Chan, Peiyu Huang, Guopei Zhu, Daniel TT Chua, Hai Qiang Mai, Joseph Wee, Dora LW Kwong, James Moon, Kwan Hwa Chi, George Fountzilas, Masuto Hareyama, Li Zhang, Jean Bourhis, Jean-Pierre Pignon Journal of Clinical Oncology 2014 32:15_suppl, 6022-6022

[9] Y. Zhang et al. Gemcitabine and Cisplatin Induction Chemotherapy in Nasopharyngeal Carcinoma N Engl J Med Med 2019;381:1124-11352019

[10] Network-meta-analysis of chemotherapy in nasopharyngeal carcinoma (MAC-NPC): An update on 8,221 patients. Claire Petit, Anne WM Lee, Alexandra Carmel, Wai Tong Ng, Jun Ma, Anthony TC Chan, Ruey-Long Hong, Ming-Yuan Chen, Lei Chen, Guopei Zhu, Wen-Fei Li, Sharon Poh, Roger Ngan, Hai-Qiang Mai, Pei-Yu Huang, Li Zhang, George Fountzilas, Jean Bourhis, Jean-Pierre Pignon, Pierre Blanchard Journal of Clinical Oncology 2020 38:15_suppl, 6523-6523

[11] Shyh-An Yeh, Yeh Tang, Chun-Chung Lui, Yu-Jie Huang, Eng-Yen Huang. Treatment outcomes and late complications of 849 patients with nasopharyngeal carcinoma treated with radiotherapy alone. Int J Radiation Oncology. 2005;62(3):672–679. doi: 10.1016/j.ijrobp.2004.11.002

[12] Arman J, Strojan P. Nasopharyngeal carcinoma in Slovenia: 1990-2003 (results of treatment with conventional two-dimensional radiotherapy) Reports of practical oncology and radiotherapy. 2012;17(2):71–78. doi: 10.1016/j.rpor.2012.01.002

[13] Wu F, Wang R, Lu H, Wei B, Feng G, Li G, et al. Concurrent chemoradiotherapy in locoregionally advanced nasopharyngeal carcinoma: treatment outcomes of a prospective, multicentric clinical study. Radiotherapy and Oncology. 2014;112(1):106–111. doi: 10.1016/j.radonc.2014.05.005

[14] Chen CY, Han F, Zhao C, Lu LX, Sun Y, Liu XF, et al. Treatment results and late complications of 556 patients with locally advanced nasopharyngeal carcinoma treated with radiotherapy alone. The British Journal of Radiology. 2009; 82(978):452–458. doi: 10.1259/bjr/72813246

[15] Korbi AE, Tkhayat SB, Bouatay R, Ferjaoui M, Kolsi N, Harrathi K, Koubaa J. Résultats thérapeutiques des carcinomes nasopharyngés: étude monocentrique à l´hôpital universitaire Fattouma Bourguiba de Monastir en Tunisie [Therapeutic outcomes of nasopharyngeal carcinomas: a single-center study conducted at the Fattouma Bourguiba University Hospital in Monastir, Tunisia]. Pan Afr Med J. 2021 Feb 9;38:143. French. doi: 10.11604/pamj.2021.38.143.15510. PMID: 33912313; PMCID: PMC8052626

[16] Lee N, Xia P, Quivey JM, Sultanem K, Poon I, Akazawa C, Akazawa P, Weinberg V, Fu KK (2002) Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: an update of the UCSF experience. Int J Radiat Oncol Biol Phys 53: 12–22.

[17] Wolden SL, Chen WC, Pfister DG, Kraus DH, Berry SL, Zelefsky MJ (2006) Intensity-modulated radiation therapy (IMRT) for nasopharynx cancer: Update of the Memorial Sloan-Kettering experience. Int J Radiat Oncol Biol Phys 64: 57–62.

[18] Tham IW, Hee SW, Yeo RM, Salleh PB, Lee J, Tan TW, Fong KW, Chua ET, Wee JT (2009) Treatment of nasopharyngeal carcinoma using intensity-modulated radiotherapy- The National Cancer Centre Singapore experience. Int J Radiat Oncol Biol Phys 75: 1481–1486.

[19] Wong FC, Ng AW, Lee VH, Lui CM, Yuen KK, Sze WK, Leung TW, Tung SY (2010) Whole-field simultaneous integrated-boost intensity-modulated radiotherapy for patients with nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys 76: 138–145.

[20] Ng WT, Lee MC, Hung WM, Choi CW, Lee KC, Chan OS, Lee AW (2011) Clinical outcomes and patterns of failure after intensity-modulated radiotherapy for nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys 79: 420–428.

[21] Bernier J, Russi EG, Homey B, Merlano MC, Mesia R, Peyrade F, et al. Management of radiation dermatitis in patients receiving cetuximab and radiotherapy for locally advanced squamous cell carcinoma of the head and neck: proposals for a revised grading system and consensus management guidelines. Ann Oncol2011; 22:2191–200.

[22] Hopewell JW. The skin: its structure and response to ionizing radiation. Int J Radiat Biol 1990; 57:751–73

[23] Bernier J, Russi EG, Homey B, Merlano MC, Mesia R, Peyrade F, et al. Management of radiation dermatitis in patients receiving cetuximab and radiotherapyfor locally advanced squamous cell carcinoma of the head and neck: proposalsfor a revised grading system and consensus management guidelines. Ann Oncol2011 ;22 :2191–200.

[24] Calais G, Alfonsi M, Bardet E, Sire C, Germain T, Bergerot P, et al. Randomized trial of radiation therapy versus concomitant chemotherapy and radiation therapy for advanced-stage oropharynx carcinoma. J Natl Cancer Inst 1999; 91:2081–6.

[25] Smichmidt-Ullrich RK, Johnson C, Wazer DE, et al. Accelerated super fractionated irradiation for advanced carcinoma of head and neck: concomitant boost technique. Int J Radiat Oncol Biol Phys 1991; 21:563–8.

[26] Taylor SG, Murthy AK, Vann Etzel JM, et al. Randomized comparison of neoadjuvant cisplatin and fluorouracil infusion followed by radiation versus concomitant treatment in advanced head and neck cancer. J Clin Oncol 1994; 12:385–95.

[27] Rubenstein EB, Peterson DE, Schubert M, Keefe D, McGuire D, Epstein J, et al. Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. Cancer 2004;100: 2026–46.

[28] Levendag PC, Teguh DN, Voet P, Est H van der, Noever I, de Kruijf WJ, Kolkman-Deurloo IK, Prevost JB, Poll J, Schmitz PI, Heijmen BJ: Dysphagia disorders in patients with cancer of the oropharynx are significantly affected by the radiation therapy dose to the superior and middle constrictor muscle: a dose-effect relationship. Radiother Oncol 2007, 85:64-73

[29] Pow EH, Kwong DL, McMillan AS, Wong MC, Sham JS, Leung LH, Leung WK (2006) Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: Initial report on a randomized controlled clinical trial. Int J Radiat Oncol Biol Phys 66: 981–991.

[30] Lee AW, Ng WT, Hung WM, Choi CW, Tung R, Ling YH, Cheng PT, Yau TK, Chang AT, Leung SK, Lee MC, Bentzen SM (2009) Major late toxicities after conformal radiotherapy for nasopharyngeal carcinoma: patient and treatment-related risk factors. Int J Radiat Oncol Biol Phys 73: 1121–1128.

[31] Miah AB, Gulliford SL, Bhide SA, Zaidi SH, Newbold KL, Harrington KJ, Nutting CM (2013) The effect of concomitant chemotherapy on parotid gland function following head and neck IMRT. Radiother Oncol 106: 346–351.