Approaching a cure for nasopharyngeal carcinoma: how close are we from there?

Victor Ho-Fun Lee[a,b,*]

[a]Department of Clinical Oncology, School of Clinical Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China
[b]Clinical Oncology Medical Center, The University of Hong Kong-Shenzhen Hospital, Shenzhen, China

The Lancet Regional Health - Western Pacific 2024;50: 101186
Published Online xxx
https://doi.org/10.1016/j.lanwpc.2024.101186

Nasopharyngeal carcinoma (NPC) is endemic in southern China and southeast Asia. Undifferentiated carcinoma of the nasopharynx, highly associated with Epstein–Barr virus (EBV), is the commonest histological type in endemic regions which is highly sensitive to radiation therapy and chemotherapy.[1] As a result, radiation therapy is the current mainstay of treatment for early-stage diseases while radical concurrent chemoradiation is indicated for locoregionally advanced diseases. With the advent of contemporary radiation techniques including intensity-modulated radiation therapy and helical tomotherapy together with more precise imaging scans and use of adjunct chemotherapy (induction or adjuvant), the survival rates of patients with NPC have dramatically improved over the past few decades, reaching about 80% at 5 years.[2]

In a recent issue of *The Lancet Regional Health—Western Pacific*, Liu and colleagues applied mixture and nonmixture cure models to estimate the cure probabilities and cure times by incorporating the background mortality for the general population, matching by gender, age, and year of diagnosis of 6315 patients with NPC, and compared them with the expected survival of the general population in China.[3] They reported that, with death as the uncured event, the cure model indicated that the likelihood of patients with NPC achieving a life expectancy at par with the general population was 78%. In corollary, to achieve a 95% probability of being cured (with death as the uncured event), the required survival time for a patient was 7.1 years. Similarly, with progression as the uncured event, the likelihood of patients attaining a life expectancy without progression equivalent to that of the general population dropped to 72%. In simple phrases, the required survival time to achieve a 95% probability of cure was 4.7 years.

Based on these results, one may infer that an NPC patient could achieve a "cure" if he or she can survive for 5 years or longer after diagnosis. However, one must also know how this patient could survive without progression or death and attain such a "cure". It is most likely a tribute to the contemporary imaging scans with positron-emission tomography and magnetic resonance imaging, molecular diagnostics with plasma EBV DNA, multimodality radical treatment, dedicated surveillance programmes, and novel effective therapeutics for recurrent diseases. Unfortunately, these substantial advancements of diagnostic and therapeutic strategies are yet to be generalisable to every part of the world, regardless of its geographical endemicity. Most of them are still fairly costly to afford since they are not essential cancer care constituents for NPC. It was reported that the treatment outcomes of NPC in low-and-middle income countries (LMICs) were still grave,[4] which strongly correlated with the paucity of radiation facilities, let alone modern linear accelerators. Moreover, an exponential increase in health expenditure per capita is necessitated for a better treatment outcome.[5] A tremendous amount of health expenses has to be spent in order to obtain a higher cancer site-standardised proxy relative survival. The recently published phase III randomised-controlled trials on immune checkpoint inhibitors in combination with chemotherapy and radiation therapy have further provided a paradigm shift in treating recurrent or metastatic and locoregionally advanced NPC, respectively.[6–9] Most of them have been approved and licensed by China National Medical Products Administration but not in the rest of the world. Even if they are approved outside China, they would still be prohibitively unaffordable in LMICs unless reimbursed or heavily subsidised. Otherwise, this may cause long-lasting financial burden to patients who wish to contain their disease.

The peak age of onset of NPC is typically between 30 and 40 years, when these patients are most productive. It may take years for them to recover from the treatment-related toxicities and regain full working capacities after radical treatment. High disability-adjusted life years are therefore anticipated during their treatment and recovery process. Even if they can survive for more than a decade, they may start to fear about the development of second primary cancers (SPCs),[10] which may be even more intractable and difficult to treat owing to its poor responsiveness to conventional treatment. Sadly, the absolute excess risk of developing SPCs reaches the top when these NPC survivors approach

DOI of original article: https://doi.org/10.1016/j.lanwpc.2024.101147
*Corresponding author. Department of Clinical Oncology, School of Clinical Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.
E-mail address: vhflee@hku.hk.

retirement. SPCs after prior treatment for NPC can occur in many sites including oral cavity, oropharynx, paranasal sinuses, salivary glands, thyroid, skin, lung, bones and muscles, which can drastically compromise their physiological organ functions and quality of life. They accounted for 9% of all deaths among NPC survivors. The 10-year SPC-specific mortality was only 3% despite salvage treatment.

We are still away from curing NPC unless widespread access to the indispensable diagnostic and treatment facilities as well as novel therapeutics can be made available and affordable to all in need. A statistical cure for malignant diseases can then be hopefully achievable worldwide without geographical and economic constraints. Concerted global efforts are urgently warranted to devise a comprehensive and financially sustainable cancer plan and enhance access equity.

Contributors

Dr. Lee wrote the original draft of the manuscript, approved the final version of the manuscript and agreed to be responsible for the work.

Editor note

The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of interests

VH-FL reports personal fees and grants from AstraZeneca and Merck Sharp and Dohme; and personal fees from AQUILAB, Amgen, Boston Scientific, Eli Lilly, Merck Sharp and Dohme, Novartis, Pfizer, and Takeda, all outside this submitted work.

References

1 Zhang Y, Rumgay H, Li M, Cao S, Chen W. Nasopharyngeal cancer incidence and mortality in 185 countries in 2020 and the projected burden in 2040: population-based global epidemiological profiling. *JMIR Public Health Surveill*. 2023;9:e49968.

2 Au KH, Ngan RKC, Ng AWY, et al. Treatment outcomes of nasopharyngeal carcinoma in modern era after intensity modulated radiotherapy (IMRT) in Hong Kong: a report of 3328 patients (HNPCS 1301 study). *Oral Oncol*. 2018;77:16–21.

3 Liu Y, Liu X, Sun S, et al. Evidence of being cured for nasopharyngeal carcinoma: results of a multicenter patient-based study in China. *Lancet Reg Health West Pac*. 2024;49:101147.

4 Lam KO, Lee AWM, Choi CW, et al. Global pattern of nasopharyngeal cancer: correlation of outcome with access to radiation therapy. *Int J Radiat Oncol Biol Phys*. 2016;94(5):1106–1112.

5 Choi KCW, Lam KO, Pang HHM, Tsang SKC, Ngan RKC, Lee AWM. Global comparison of cancer outcomes: standardization and correlation with healthcare expenditures. *BMC Public Health*. 2019;19(1):1065.

6 Yang Y, Qu S, Li J, et al. Camrelizumab versus placebo in combination with gemcitabine and cisplatin as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma (CAPTAIN-1st): a multicenter, randomized, double-blind, phase 3 trial. *Lancet Oncol*. 2021;22(8):1162–1174.

7 Yang Y, Pan J, Wang H, et al. Tislelizumab plus chemotherapy as first-line treatment for recurrent or metastatic nasopharyngeal cancer: a multicenter phase 3 trial (RATIONALE-309). *Cancer Cell*. 2023;41(6):1061–1072.e4.

8 Mai HQ, Chen QY, Chen D, et al. Toripalimab plus chemotherapy for recurrent or metastatic nasopharyngeal carcinoma: the JUPITER-02 randomized clinical trial. *JAMA*. 2023;330(20):1961–1970.

9 Liu X, Zhang Y, Yang KY, et al. Induction-concurrent chemoradiotherapy with or without sintilimab in patients with locoregionally advanced nasopharyngeal carcinoma in China (CONTINUUM): a multicentre, open-label, parallel-group, randomised, controlled, phase 3 trial. *Lancet*. 2024;403(10445):2720–2731.

10 Chow JCH, Tam AHP, Cheung KM, et al. Second primary cancer after intensity-modulated radiotherapy for nasopharyngeal carcinoma: a territory-wide study by HKNPCSG. *Oral Oncol*. 2020;111:105012.