

BMJ Open Geographical disparities in the prognosis of patients with nasopharyngeal carcinoma treated with intensity-modulated radiation therapy: a large institution-based cohort study from an endemic area

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To cite: Lin S-T, Meng D-F, Yang Q, *et al.* Geographical disparities in the prognosis of patients with nasopharyngeal carcinoma treated with intensity-modulated radiation therapy: a large institution-based cohort study from an endemic area. *BMJ Open* 2020;**10**:e037150. doi:10.1136/bmjopen-2020-037150

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-037150>).

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Received 22 January 2020
Revised 28 July 2020
Accepted 16 September 2020



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ABSTRACT

Objectives Geographical disparities have been identified as a specific barrier to cancer screening and a cause of worse outcomes for patients with cancer. In the present study, our aim was to assess the influence of geographical disparities on the survival outcomes of patients with nasopharyngeal carcinoma (NPC) treated with intensity-modulated radiation therapy (IMRT).

Design Cohort study.

Setting Guangzhou, China.

Participants A total of 1002 adult patients with NPC (724 males and 278 females) who were classified by area of residence (rural or urban) received IMRT from 1 January 2010 to 31 December 2014, at Sun Yat-sen University Cancer Center. Following propensity score matching (PSM), 812 patients remained in the analysis.

Main outcome measures We used PSM to reduce the bias of variables associated with treatment effects and outcome prediction. Survival outcomes were estimated using the Kaplan-Meier method and compared by the log-rank test. Multivariate Cox regression was used to identify independent prognostic factors.

Results In the matched cohort, 812 patients remained in the analysis. Kaplan-Meier survival analysis revealed that the rural group was significantly associated with worse overall survival (OS, $p<0.001$), disease-free survival (DFS, $p<0.001$), locoregional relapse-free survival (LRRFS, $p=0.003$) and distant metastasis-free survival (DMFS, $p<0.001$). Multivariate Cox regression showed worse OS (HR=3.126; 95% CI 1.902 to 5.138; $p<0.001$), DFS (HR=2.579; 95% CI 1.815 to 3.665; $p<0.001$), LRRFS (HR=2.742; 95% CI 1.359 to 5.533; $p=0.005$) and DMFS (HR=2.461; 95% CI 1.574 to 3.850; $p<0.001$) for patients residing in rural areas.

Conclusions The survival outcomes of patients with NPC who received the same standardised treatment were significantly better in urban regions than in rural regions. By analysing the geographic disparities in outcomes for NPC, we can guide the formulation of healthcare policies.

Strengths and limitations of this study

- The study was based on 1002 adult patients with nasopharyngeal carcinoma (NPC) in an endemic area who were followed for 8 years.
- We defined residential areas by China's household registration system, as done in previous literature.
- Geographical disparities, as one of the socioeconomic factors, have been identified as a specific barrier to cancer screening and a cause of worse outcomes for patients with NPC.
- The differences in outcomes for residency status were due to some socioeconomic factors rather than guideline-concordant cancer treatment.
- The main limitation of this analysis is its retrospective, single-institute nature, and prospective studies are needed to validate our results.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a common type of head and neck cancer that originates from the nasopharyngeal epithelium and has highly aggressive characteristics and metastatic potential.¹ NPC is an endemic cancer with a higher incidence in certain regions of southern China, Southeast Asia and Africa than elsewhere.² In southern regions of China, particularly in Guangdong Province, it occurs in approximately 25–30 cases per 100 000 persons, which is 25 times higher than the incidence in other areas.² Radiotherapy (RT) is the main treatment for NPC because NPC cells are more sensitive to radiation.³ The US National Comprehensive Cancer Network clinical practice guidelines recommend induction chemotherapy (IC)

followed by platinum-based concurrent chemoradiotherapy (CCRT) as the first-line treatment for advanced NPC cases.^{4–6} The survival outcomes have dramatically improved over the past three decades because of progress in the management of NPC, including more accurate staging, the development of RT technology and the extensive application of chemotherapy.^{7,8}

Geographical disparities, a socioeconomic factor that has been defined as the physical distance to a service supply in rural/urban areas, have been identified as a specific barrier to cancer screening and a cause of worse outcomes for patients with cancer.^{9–10} Geographical disparities are one of the main challenges for public health in the world.¹¹ In the USA, 19% of patients with cancer are from rural regions.¹² Patients with cancer from rural areas have been shown to have a poorer prognosis than their urban counterparts, with vast disparities observed for colorectal, breast, lung, cervical and prostate cancers.^{13–15} In China, according to World Bank statistics, approximately 41% (576.61 million) of the Chinese population lived in rural regions in 2017. The *Cancer Statistics in China, 2015*, indicated that for all cancers combined, rural residents had a notably higher age-standardised (Segi population) mortality rate than urban residents (149.0 per 100 000 vs 109.5 per 100 000 for mortality).¹⁶ Chen *et al* also found substantial variation in the 5-year survival outcome estimate: rural patients with cancer have a much lower survival rate than their city counterparts (30.3% vs 42.8%).¹⁶ The geographical disparities appeared to be far more important than biological differences.¹⁷ These geographical disparities, at least in part, could be explained by the limited access to and utilisation of health services, the financial burden of cancer treatment, the lower levels of healthcare and the larger proportion of patients with late-stage cancer in rural and undeveloped regions in China.^{18–19}

Unfortunately, the survival differences between patients with NPC living in rural and urban areas have not been clearly demonstrated with a large institution-based cohort study in an endemic area. Therefore, whether rural and urban patients with NPC received the same standardised treatment and had different prognoses needs further exploration. In this study, our aim was to estimate the influence of geographical disparities on the survival outcomes of patients with NPC treated with intensity-modulated radiation therapy (IMRT).

MATERIALS AND METHODS

Data collection

In this retrospective cohort study, we used data from the Unionnet Digital Medical Record System (UDMRS) of Sun Yat-sen University Cancer Center (SYSUCC) from 1 January 2010 to 31 December 2014. The UDMRS records each patient's name, medical record number, residency status, sex, age, smoking status, diagnosis, pathological classification, Epstein-Barr virus (EBV) DNA copy number, clinical staging, Karnofsky Performance Score

(KPS), treatment modality and follow-up and clinical endpoints, as well as the name of the doctor. We used only the UDMRS to set up a retrospective cohort to investigate outcomes, and we did not ask the patients new questions.

The eligibility criteria of our study were as follows: (1) histologically confirmed NPC by biopsy of the nasopharynx; (2) no distant metastasis; (3) WHO pathology II/III; (4) nontherapeutic intervention; (5) no other tumour types or serious noncancerous illnesses; and (6) received radical IMRT during comprehensive treatment. A total of 1002 histologically confirmed patients with non-metastatic NPC were included in this criteria.

Our study was approved by the Clinical Research Ethics Committee of SYSUCC, and informed consent was obtained from all patients before treatment. All the methods were conducted according to approved guidelines in the present study.

Diagnosis and treatment

The routine diagnostic and staging workup included a complete medical history, physical examination, flexible fibreoptic nasopharyngoscopy, MRI of the nasopharyngeal and whole neck areas, chest radiography, abdominal sonography and whole-body bone scan, as well as positron emission tomography/computed tomography, if necessary. Molecular biomarkers of EBV-associated NPC were quantified, including the EBV DNA copy number, immunoglobulin A antibodies to EBV viral capsid antigen and EBV early antigen. All patients were restaged according to the seventh edition of the American Joint Committee on Cancer/Union for International Cancer Control staging system.²⁰

All patients were treated according to the principle of treatment for NPC at SYSUCC. The treatment modalities included RT alone, RT following IC (IC + RT), CCRT and CCRT following IC (IC + CCRT). All 1002 patients received radical IMRT at SYSUCC. The prescribed radiation doses were 66–72 Gy at 2.12–2.43 Gy/fraction to the planning target volume (PTVnx) of the primary gross tumour volume (GTVnx), 64–70 Gy to the PTVnd of the involved lymph nodes (GTVnd), 60–63 Gy to PTV1 of the high-risk clinical target volume (CTV1), and 50–56 Gy to PTV2 of the low-risk clinical target volume (CTV2). IC primarily consisted of cisplatin-based regimens: fluorouracil and cisplatin (PF), docetaxel and cisplatin (TP), gemcitabine plus cisplatin (GP) or docetaxel plus cisplatin and fluorouracil (TPF) every 3 weeks for 2–4 cycles. Concurrent chemotherapy was a weekly or 3-weekly cisplatin regimen.

Follow-up and clinical endpoints

Tumours were assessed with the use of flexible fibreoptic nasopharyngoscopy and MRI of the nasopharyngeal and whole neck areas at 1 week after the end of RT alone or CCRT. In the first 3 years of follow-up, all patients were evaluated every 3 months and thereafter every 6 months until death. All endpoints were assessed or confirmed by the attending physician. For suspected lesions, fine-needle aspiration or biopsy was necessary to confirm locoregional or distant disease progression.

The primary endpoint was overall survival (OS), which was the time from diagnosis to death from any cause. The secondary endpoints included disease-free survival (DFS), which was the time from diagnosis to disease progression or death from any cause; locoregional relapse-free survival (LRRFS), which was the time from diagnosis to local or regional recurrence; and distant metastasis-free survival (DMFS), which was the time from diagnosis to the first distant metastasis. Patients who failed to be followed up were censored at the date of the last follow-up. Of 1002 patients with NPC, 130 were lost to follow-up.

Explanatory variables

Based on the distribution of the population, China's Registration Household (Hukou) System classifies individuals as having an agricultural (rural) or a non-agricultural (urban) residency status.^{21 22} In our study, we categorised residential areas into two groups: rural areas (regions that are located outside of towns and cities, including countryside areas, villages and hamlets) and urban areas (areas with a high population density and an infrastructure of built environments, including cities, towns and suburban areas).

Statistical analysis

We used propensity score matching (PSM) to reduce the bias of variables associated with treatment effects and outcome prediction. Variables based on clinical practice were identified by logistic regression and introduced to generate a propensity score. A one-to-one nearest neighbour matching algorithm with a calliper of 0.2 and without replacement was used. We tested the differences between the rural group and urban group according to covariates by using the χ^2 test. Survival outcomes were estimated by using the Kaplan-Meier method and compared by the log-rank test. The multivariate Cox proportional hazards model was used to estimate HRs, 95% CIs and independent prognostic factors. We further carried out an interaction analysis to explore whether the prognostic value of residency status varied in the subgroups defined according to T classification, N classification, EBV DNA and treatment modality. The interaction analysis was conducted by means of a test of treatment-by-covariate interaction on the basis of the Cox proportional hazards model. All statistical tests were two sided, and $p < 0.05$ was considered significant. All analyses were conducted using Statistical Package for Social Sciences V.22 (SPSS Inc, Chicago, Illinois, USA).

Patient and public involvement

The patients or the public were not involved in the design, conduct, reporting or dissemination of this specific study.

RESULTS

Patient baseline characteristics

Initially, 1002 adult patients with NPC (724 males and 278 females) who were classified by area of residence received IMRT from 1 January 2010 to 31 December, 2014, at SYSUCC. Following PSM, 812 patients remained in the analysis. In the matched cohort, the median age for the

whole cohort was 45 years, and the male-to-female ratio was 2.46:1. There were 114 (14.04%) patients with stage I–II NPC and 698 (85.96%) patients with stage III–IVB NPC. Among 812 patients with NPC, 96 (11.82%) patients received RT alone, 57 (7.02%) patients received IC + RT, 319 (39.29%) patients received CCRT and 340 (41.87%) patients received IC + CCRT. The two groups had similar treatment modalities ($p < 0.678$). The host-related and tumour-related factors (sex, age, smoking, histology, T classification, N classification, clinical stage, EBV DNA, treatment modality and KPS) were well balanced between the rural and urban groups. The baseline characteristics are summarised in [table 1](#).

Long-term outcome analysis

The median follow-up time for the whole cohort was 58.0 months (range 1.0–98.0). During the follow-up period, 103 (25.37%) of 406 patients in the rural group and 45 (11.08%) of 406 patients in the urban group experienced disease progression. Eighty-three of 812 patients died: 62 (15.27%) patients in the rural group and 21 (5.17%) patients in the urban group. Patients with rural versus urban residences had 5-year OS, DFS, LRRFS and DMFS rates of 84.73% versus 94.83% (344 of 406 vs 385 of 406, $p < 0.001$), 74.63% versus 88.92% (303 of 406 vs 361 of 406, $p < 0.001$), 93.35% versus 97.78% (379 of 406 vs 397 of 406, $p = 0.002$) and 84.73% versus 93.1% (344 of 406 vs 378 of 406, $p < 0.001$), respectively. Kaplan-Meier survival analysis revealed that the rural group was significantly associated with worse OS ($p < 0.001$), DFS ($p < 0.001$), LRRFS ($p = 0.003$) and DMFS ($p < 0.001$, [figure 1](#)).

Prognostic factors for patients with NPC with rural/urban residences

Multivariate analysis was performed to adjust for potential prognostic factors, including sex, smoking, N category, EBV DNA, KPS, area of residence and treatment modality. The results of the multivariate analysis using the standard Cox proportional hazards model are shown in [table 2](#). The multivariate Cox regression results showed worse OS (HR=3.126; 95% CI 1.902 to 5.138; $p < 0.001$), DFS (HR=2.579; 95% CI 1.815 to 3.665; $p < 0.001$), LRRFS (HR=2.742; 95% CI 1.359 to 5.533; $p = 0.005$) and DMFS (HR=2.461; 95% CI 1.574 to 3.850; $p < 0.001$) for patients residing in rural areas. In addition, EBV DNA was an independent prognostic factor for OS (HR=3.031; 95% CI 1.945 to 4.723; $p < 0.001$), DFS (HR=2.733; 95% CI 1.955 to 3.818; $p < 0.001$) and DMFS (HR=3.657; 95% CI 2.339 to 5.718; $p < 0.001$). These results indicated that residency status represented a valuable independent prognostic factor for patients with NPC.

Subgroup analysis

To further assess the prognostic value of residency status, the patients with NPC were stratified into subgroups based on T classification (categorised as T1–2 or T3–4), N classification (categorised as N0–1 or N2–3), clinical stage (categorised as stage I–II or III–IVB), EBV DNA

Table 1 Baseline patient characteristics according to the area of residence

Characteristics	Unmatched (n=1002)			Matched (n=812)		
	Area of residence			Area of residence		
	Rural No (%) (n=421)	Urban No (%) (n=581)	P value*	Rural No (%) (n=406)	Urban No (%) (n=406)	P value*
Sex			0.549			0.588
Male	300 (71.26)	424 (72.98)		292 (71.92)	285 (70.20)	
Female	121 (28.74)	157 (27.02)		114 (28.08)	121 (29.80)	
Age (years)			0.11			0.706
Median	45	46		45	45	
Range	18–69	19–70		18–69	19–70	
Smoking status			0.064			0.714
No	267 (63.42)	401 (69.02)		259 (63.79)	264 (65.02)	
Yes	154 (36.58)	180 (30.98)		147 (36.21)	142 (34.98)	
Histology			0.646			0.483
WHO type						
II	15 (3.56)	24 (4.13)		15 (3.69)	19 (4.68)	
III	406 (96.44)	557 (95.87)		391 (96.31)	387 (95.32)	
T classification†			0.006			0.068
T1	40 (9.50)	52 (8.95)		40 (9.85)	30 (7.39)	
T2	52 (12.35)	105 (18.07)		51 (12.56)	77 (18.97)	
T3	210 (49.88)	307 (52.84)		204 (50.25)	193 (47.54)	
T4	119 (28.27)	117 (20.14)		111 (27.34)	106 (26.11)	
N classification†			0.072			0.804
N0	44 (10.45)	80 (13.77)		43 (10.59)	52 (12.81)	
N1	170 (40.38)	240 (41.31)		168 (41.38)	162 (39.90)	
N2	158 (37.53)	218 (37.52)		154 (37.93)	152 (37.44)	
N3	49 (11.64)	43 (7.40)		41 (10.10)	40 (9.85)	
Clinical stage			0.005			0.718
I	11 (2.61)	20 (3.44)		11 (2.71)	10 (2.46)	
II	40 (9.50)	74 (12.74)		40 (9.85)	53 (13.05)	
III	214 (50.83)	335 (57.66)		211 (51.97)	206 (50.74)	
IVA	106 (25.18)	109 (18.76)		102 (25.12)	97 (23.89)	
IVB	50 (11.88)	43 (7.40)		42 (10.34)	40 (9.85)	
EBV DNA (copies/mL)			<0.001			0.715
<3000						
≥3000	258 (61.28)	417 (71.77)		257 (63.30)	262 (64.53)	
	163 (38.72)	164 (28.23)		149 (36.70)	144 (35.47)	
Characteristic	Unmatched (n=1002)			Matched (n=812)		
	Area of residence			Area of residence		
	Rural No.(%) (n=421)	Urban No.(%) (n=581)	P value*	Rural No.(%) (n=406)	Urban No.(%) (n=406)	
Treatment modality			0.367			0.678
RT alone						
IC + RT	44 (10.45)	75 (12.91)		43 (10.59)	53 (13.05)	
CCRT	31 (7.36)	31 (5.34)		31 (7.64)	26 (6.40)	
IC + CCRT	166 (39.43)	237 (40.79)		161 (39.66)	158 (38.92)	
	180 (42.76)	238 (40.96)		171 (42.12)	169 (41.63)	

Continued

Table 1 Continued

Characteristics	Unmatched (n=1002)			Matched (n=812)		
	Area of residence		P value*	Area of residence		P value*
	Rural No (%) (n=421)	Urban No (%) (n=581)		Rural No (%) (n=406)	Urban No (%) (n=406)	
KPS			0.849			1
<90	3 (0.71)	6 (1.03)		3 (0.74)	3 (0.74)	
≥90	418 (99.29)	575 (98.97)		403 (99.26)	403 (99.26)	

*P values were calculated using the χ^2 test for categorical variables and the Mann-Whitney test for continuous variables.

†According to the seventh edition of the AJCC/UICC staging system.

AJCC/UICC, American Joint Committee on Cancer/Union for International Cancer Control; CCRT, chemoradiotherapy; EBV, Epstein-Barr virus; IC, induction chemotherapy; IC + CCRT, chemoradiotherapy following induction chemotherapy; IC + RT, radiotherapy following induction chemotherapy; KPS, Karnofsky Performance Score.

(categorised as <3000 or ≥3000) and treatment modality (categorised as patients with or without IC). Subgroup analysis also revealed that the patients residing in rural areas had worse OS, DFS and DMFS than their urban counterparts (figure 2). However, no significant difference in LRRFS was observed in the T1–2 subgroup ($p=0.470$), N0–1 subgroup ($p=0.167$), stage I–II subgroup ($p=0.348$), low EBV DNA levels subgroup ($p=0.093$), and treatment without IC subgroup ($p=0.166$). The stratification analysis demonstrated that the mortality risk was

more pronounced in patients with advanced NPC who lived in rural areas, had higher EBV DNA copy numbers and were treated without IC.

DISCUSSION

Numerous previous studies have reported that rural patients with cancer have worse outcomes than their urban counterparts.^{23 24} However, no prior studies have systematically compared the geographical distribution

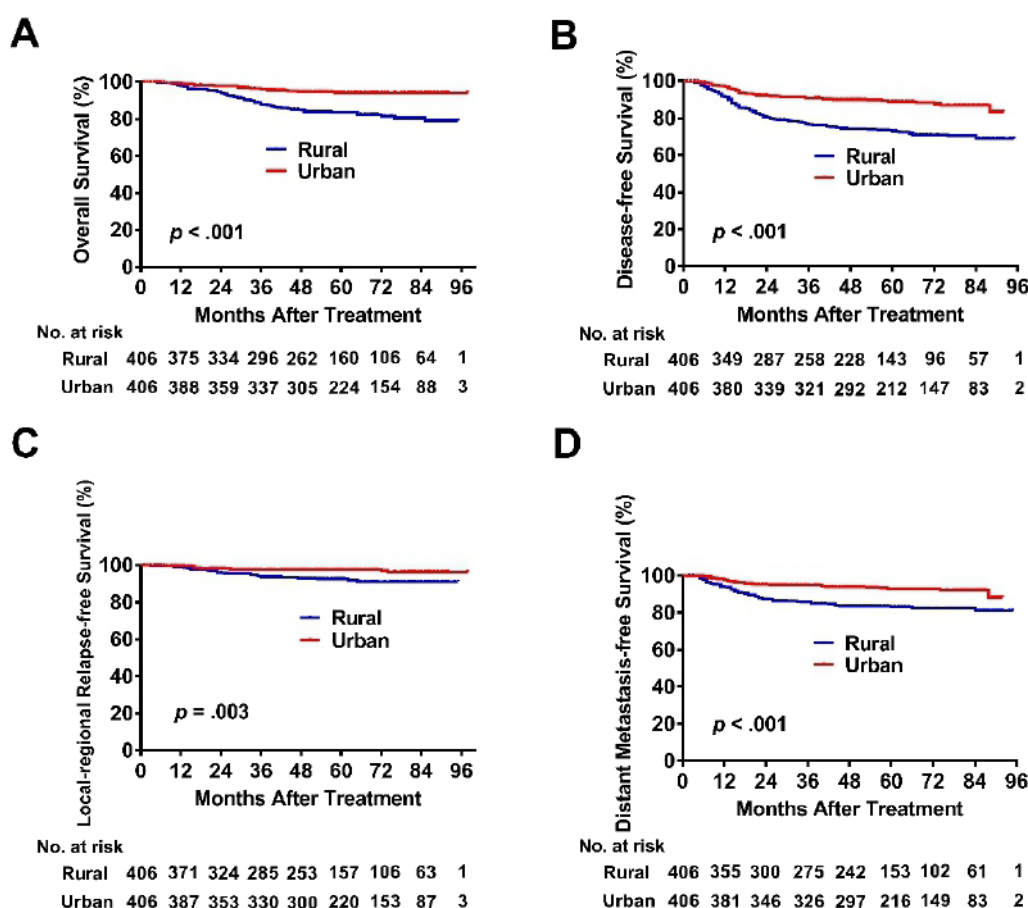


Figure 1 Kaplan-Meier OS (A), DFS (B), LRRFS (C) and DMFS (D) curves for patients with NPC stratified as the area of residence. DFS, disease-free survival; DMFS, distant metastasis-free survival; LRRFS, locoregional relapse-free survival; NPC, nasopharyngeal carcinoma; OS, overall survival

Table 2 Multivariate analysis for prognostic factors in the 812 patients with NPC

Endpoints	HR (95% CI)	P value
OS		
Sex		0.02
Female	Reference	
Male	2.168 (1.164 to 4.039)	
EBV DNA (copies/mL)		<0.001
<3000	Reference	
≥3000	3.031 (1.945 to 4.723)	
KPS		0.017
≥90	Reference	
<90	4.657 (1.425 to 15.222)	
Area of residence		<0.001
Urban	Reference	
Rural	3.126 (1.902 to 5.138)	
DFS		
Smoking		0.015
No	Reference	
Yes	1.495 (1.081 to 2.068)	
N category		0.01
N0–1	Reference	
N2–3	1.555 (1.110 to 2.177)	
EBV DNA (copies/mL)		<0.001
<3000	Reference	
≥3000	2.733 (1.955 to 3.818)	
Area of residence		<0.001
Urban	Reference	
Rural	2.579 (1.815 to 3.665)	
LRRFS		
KPS		0.001
≥90	Reference	
<90	12.552 (3.001 to 52.508)	
Area of residence		0.005
Urban	Reference	
Rural	2.742 (1.359 to 5.533)	
DMFS		
Smoking		0.003
No	Reference	
Yes	1.875 (1.239 to 2.838)	
Endpoints	HR (95% CI)	P value
N category		<0.001
N0–1	Reference	
N2–3	2.543 (1.601 to 4.040)	
EBV DNA (copies/ml)		<0.001
<3000	Reference	
≥3000	3.657 (2.339 to 5.718)	

Continued

Table 2 Continued

Endpoints	HR (95% CI)	P value
Treatment modality		0.001
Patients with IC	Reference	
Patients without IC	2.187 (1.404 to 3.408)	
Area of residence		<0.001
Urban	Reference	
Rural	2.461 (1.574 to 3.850)	

P values were calculated using a Cox proportional hazard regression model with backward elimination.

DFS, disease-free survival; DMFS, distant metastasis-free survival; EBV, Epstein-Barr virus; IC, induction chemotherapy; KPS, Karnofsky Performance Score; LRRFS, locoregional relapse-free survival; OS, overall survival.

and survival outcomes for rural versus urban patients with NPC. Our comprehensive analysis examined 1002 patients with NPC, and 812 eligible patients were uniformly staged, treated and followed up. To our knowledge, this retrospective study was the first to identify that rural and urban patients with NPC who received IMRT have significantly different prognoses and that there was a statistically significant risk of mortality for patients with NPC in rural regions compared with those in urban regions. Therefore, the findings of previous analyses were reinforced by the observation of a significant difference in clinical prognosis between rural and urban patients with NPC in our study.

This finding suggested that previously observed differences in outcomes for residency status were due to some socioeconomic factors rather than clinical characteristics of the disease and treatment. Several theories have been proposed to explain these findings, including geographic distribution, travel distance/time to healthcare services, low socioeconomic status, low income, lower educational level and lack of publicly financed health insurance coverage.^{25 26}

Access to healthcare services could be characterised by geographic factors, such as region, travel distance and time.²⁷ Oncology resources for providers in rural communities are scarce; approximately one-fifth of the US population lives in rural areas, but only 3% of medical oncologists work in rural areas.²⁸ The situation is similar in China, where every 1000 Chinese rural residents have access to 1.59 practising physicians, which is much lower than the number of physicians for every 1000 urban residents, which is 3.92.²⁹ Lin *et al* evaluated the relationship between the density of oncologists and the receipt of adjuvant chemotherapy in patients with stage III colon cancer. They found that patients who lived in rural areas with a lower oncologist density were less likely to receive adjuvant chemotherapy.⁹ Studies have demonstrated that geographic access to care is a potentially modifiable factor that decreases the utilisation of adjuvant chemotherapy.⁹ In cancer diagnosis, a greater availability of oncologists

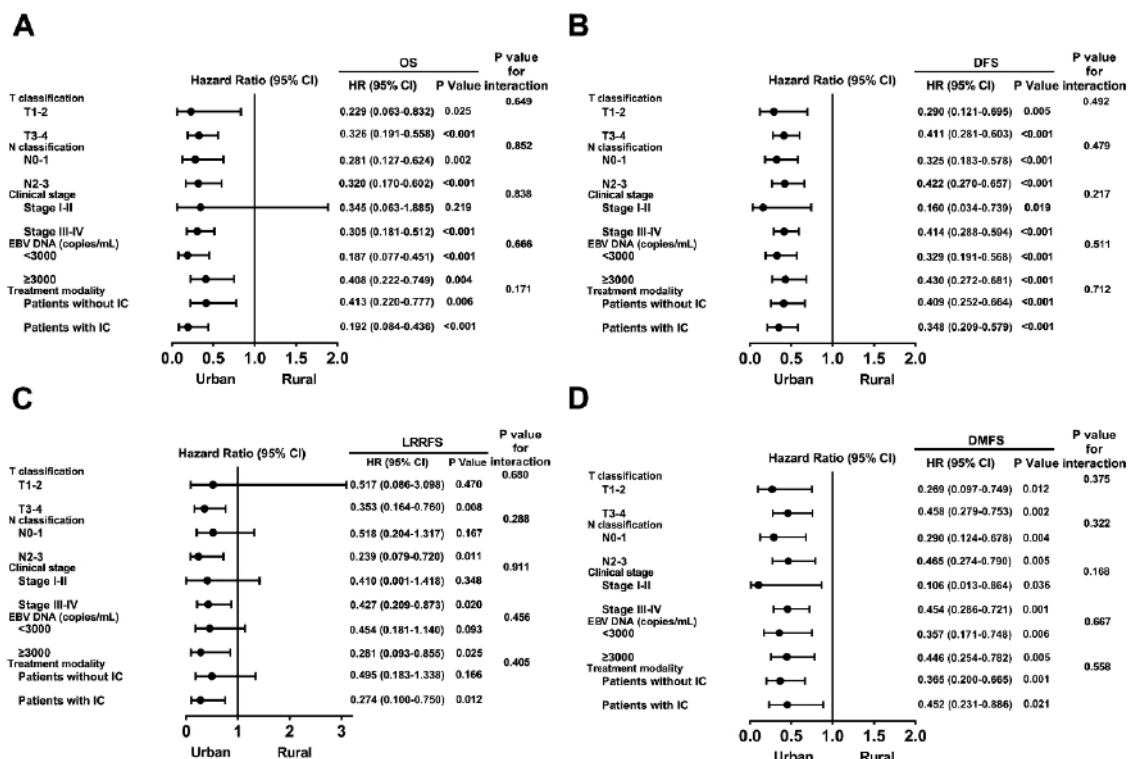


Figure 2 Subgroup analysis for OS, DFS, LRRFS and DMFS according to the area of residence with T classification, N classification, clinical stage, EBV DNA copy number and treatment modality. DFS, disease-free survival; DMFS, distant metastasis-free survival; EBV, Epstein-Barr virus; IC, induction chemotherapy; LRRFS, locoregional relapse-free survival; OS, overall survival.

seems to be related to early diagnosis and better prognosis.³⁰ However, rural residents often seek treatment for NPC that is considered to lack access to cancer screening, diagnosis and therapy.¹ Effective population screening can improve treatment outcomes by identifying early stages of the disease. Plasma EBV DNA detection and fiberoptic nasopharyngoscopy are useful for NPC screening.² Unlike plasma EBV DNA testing, however, fiberoptic nasopharyngoscopy requires the expertise of oncologists. Rural residency is associated with a smaller number of NPC specialists, medical oncologists and radiation therapists. Even the patients with NPC who resided in rural regions and received IMRT also had unmet supportive care needs compared with urban residents. Therefore, the significantly fewer providers of screening and adjuvant therapy for NPC in rural regions may affect the availability of their services, which leads to worse prognosis for patients with advanced NPC who seek treatment.³¹

For physician workforces that are not widely geographically distributed, access to care may be limited, which can be measured by the travel distance and travel time. Rural residents with cancer are affected by increased travel distances to receive treatment, adding considerable time and economic burdens to treatment.⁹ Laura-Mae found that fewer than 50% of rural patients with colorectal cancer had a medical or radiation oncologist within 30 miles. The increased transportation barriers to healthcare can result in low levels of standard care.³² Other studies have analysed the complicated relationship between

travel distance and nursing care among patients with cervical cancer. In rural areas, patients with cancer who lived ≥ 15 miles from the nearest facility were less likely to receive primary surgery compared with the national average.³³ A retrospective cohort study identified that patients diagnosed with stage III colon cancer who travelled 50 to 250 miles had a significantly decreased likelihood of receiving adjuvant chemotherapy, regardless of insurance status.⁹

As a principal health risk factor in any geographical location, poverty is more prevalent and consistent in rural regions and is often associated with increased rates of cancer.³⁴ According to United States Census Bureau, approximately 16.4% of the rural population lives in poverty compared to 12.9% of the urban population in 2017. There are wide gaps in cancer death rates among low-income, medium-income and high-income counties.³⁵ A study by O'Connor *et al* assessed the relationship between US county income levels across the USA and cancer death rates. The cancer death rate of low-income residents who lived in rural areas was 229.7 per 100 000 person-years in low-income counties, compared with 204.9 and 185.9 per 100 000 person-years in medium-income and high-income counties, respectively.³⁵ In China, 91.1% of households in rural patients with end-of-life cancer were below the poverty line compared with 84.1% of urban patients.³⁶ Rural patients with cancer continued to suffer long-term financial burden and increased out-of-pocket

expenses.³⁶ Moreover, they are also less likely to meet healthcare needs and less likely to receive preventive and therapeutic healthcare.³⁷

These findings have implications that challenge the current policies of the primary healthcare system in China. There are three main types of publicly financed insurance: the Urban Employee Basic Medical Insurance (UEBMI) for urban employees and retired employees, the Urban Resident Basic Medical Insurance (URBMI) for urban residents (children, students, elderly without employment and unemployed persons) and the New Rural Cooperative Medical Scheme (NRCMS) for rural residents.³⁸ Although China has made remarkable achievements in improving its primary healthcare system, the system still faces some challenges, such as ageing and turnover of village doctors, healthcare inequity between rural and urban regions, inadequate qualifications and education of its workforce in rural areas, difficulty obtaining adequate medical services and quality of care.³⁸ One study illustrated that NRCMS and URBMI participants have worse self-reported health status, physical functions and psychological well-being than their UEBMI counterparts.³⁹ In addition, a study indicated that patients in the poorest areas cannot even afford outpatient care expenses after reimbursement from healthcare insurance.⁴⁰ Rural residents were less likely to buy private health insurance, widening the disparities in access to healthcare and preventive services.⁴⁰ In conclusion, a major challenge to the objective of providing equal healthcare for all is unequal insurance schemes in rural and urban areas. To address geographic disparities, the Chinese government should pay more attention to the equality of the healthcare system while providing more funding for NRCMS to ensure that rural residents in need could benefit from medical service utilisation.

Limitations

We acknowledge that our study has several inherent limitations seen in observational studies. First, the main limitation of this analysis is its retrospective and single-institute nature, and prospective studies are needed to validate our results. Second, although our statistical results explained geographic distribution and clinical prognostic factors, other socioeconomic factors, such as education level and household income, might affect the results. For instance, rural patients who received higher education may also be more likely to have a better understanding of disease and have a greater self-care ability.¹¹ Third, travel distance may result in barriers to cancer treatment and is different between rural and urban patients with NPC. However, the influence of travel distance on patients in choosing medical institutions is uncertain. Moreover, a multi-centre population-based cross-sectional survey is needed to comprehensively evaluate the geographical disparities in survival outcomes for patients with NPC treated with IMRT.

CONCLUSIONS

This study shows that the survival outcomes of patients with NPC who receive the same standardised treatment are significantly better in urban regions than in rural regions. This finding further demonstrates the disparities in access to healthcare for rural and urban residents in China. These disparities adversely affect the outcomes of patients with NPC in rural regions. Overall, rural residency is an important predictor of access to healthcare for the general population of patients with cancer. By analysing the geographic disparities in outcomes for NPC, we can guide the formulation of healthcare policies.

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Funding This work was supported by grants from the National Natural Science Foundation of China (No. 81872384, No. 81 672 872 and No. 81 472 386 to C.Q., No. 81972785, No. 81773162, No. 81572901, No. 31 170 151 to B.H.), the Science and Technology Planning Project of Guangdong Province, China (No. 2013B021800065 to R.S., No. 2014A020209024 to B.H.), and the Provincial Natural Science Foundation of Guangdong, China (No. 2016A030311011 to C.Q., No. 2017A030313866 to B.H.).

Competing interests None declared.

Patient consent for publication Parental/guardian consent obtained.

Ethics approval This study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or similar ethical standards.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The data are not available for public access because of patient privacy concerns but are available from the corresponding author on reasonable request approved by the institutional review boards of Sun Yat-sen University Cancer Center.

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