Original Article
The end-of-treatment telephone response and prognosis of post-radiotherapy nasopharyngeal carcinoma patients in southern China

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Abstract: Nasopharyngeal Carcinoma (NPC) patients' end-of-treatment survival status has drawn more attention in recent years. Telephone follow-up, as a most operative approach among all the clinical follow-ups, is an effective means to extend medical service to patients' home and is thus widely used in clinical practice. This study aimed to analyze the post-radiotherapy NPC patients' phone response rate and its factors, and to discuss the independent prognostic factors of NPC patients' radiotherapy. We prospectively designed a nurses-led telephone follow-up to include 2520 NPC patients who received simple radical radiotherapy between Jan. 2007 and Jun. 2012 at Sun Yat-sen University Cancer Center. The patients' response rate and its factors were calculated. Survival analysis was used to estimate the patients' survival and the influencing factors. The overall response rate was 90.5%; Patients with reserved contact type of mobile + landlinephone or landline phone had higher follow-up response rate than patients with mobile contact only; patients with 2 or more reserved contacts, and family cancer history had higher response rate than patients with only 1 number and those without family history. Patients' cumulative survival rate of 1, 3 and 5 years were 98.9%, 75.3%, 50.3%, respectively. T-staging, N-staging, higher clinical staging, with basicranial invasion were the influencing factors of the patients' poor prognosis. The telephone follow-up response was affected by reserved contact type, number of contacts and family medical history; T-staging, N-staging, higher clinical staging, with basicranial invasion were the influencing factors of the patients' poor prognosis. This study provides a scientific basis for increasing the NPC patients' end-of-treatment response and promoting the individualized clinical treatment.

Keywords: Nasopharyngeal carcinoma, telephone follow-up, radiotherapy, prognosis

Introduction

Nasopharyngeal Carcinoma (NPC) is one of the most common malignant squamous cell carcinoma in China [1], especially in southern China area. Radiotherapy is the primary cure to it [2] and with the continuous development of medical technology, the survival and recovery rates are increasing. Meanwhile patients' end-of-treatment survival state and life quality have drawn more attention [3, 4]. And it is essential for clinical researchers to conduct follow-ups to the post-radiotherapy patients so as to know their treatment prognosis. Telephone follow-up, as a most operative approach among all the clinical follow-ups, was an effective means to extend medical service to patients' home and was hence widely used in clinical practice [5].

Nevertheless, the response rate varied a lot in different studies, which is regarded as an important indicator of the efficiency of the follow-ups. Therefore, it is necessary to explore the potential influencing factors of response rate among post-radiotherapy nasopharyngeal carcinoma patients. This study designed a nurses-led telephone follow-up with 2520 cases of NPC patients who received single radical radiotherapy at the Sun Yat-sen University Cancer Center (SYSUCC) in Guangzhou between Jan. 2007 and Jun. 2012. In this study the patients' response rate was calculated, and it's determinates were estimated. Moreover, a prognostic analysis on single radical radiotherapy patients was carried out to build the prognostic index for NPC's post-radiotherapy. Thus it can provide a scientific basis for increasing the

Table 1. The NPC patients' telephone follow-up response during 2007-2012

Variable	Year					
	2007	2008	2009	2010	2011	2012
Total cases	408	427	434	456	502	293
Response cases	322	368	383	432	485	291
Response rate (%)	78.9	86.2	88.2	94.7	96.6	99.3

NPC radiotherapy patients' end-of-treatment response and the individualized clinical treatment for this disease.

Materials and method

General data

The data of 2520 cases of NPC patients who received single radical radiotherapy at the Sun Yat-sen University Cancer Center (SYSUCC) in Guangzhou between Jan. 2007 and Jun. 2012 were collected and they were included in the telephone follow-up. With the telephone numbers left by patients before the end of their treatments, the follow-up was completed between Jan. And Jun. 2014. The inclusion criteria were as follows: all patients who were diagnosed as NPC without distant metastasis; with CT or MRI; and received radical radiotherapy for the first time without chemotherapy or other comprehensive treatment, and had completed the radical radiotherapy within the required time.

Follow-up method

The researchers carried out the telephone follow-up according to a structured form table, which was mainly led by nurses. The dialing time was 19:30-20:30 p.m which was supposed to be the dinner break. If there were a busy line or unanswered call, the dialing would be made again in a few minutes. If the numbers were incorrect, powered off or out of service, it would be recorded and the follow-up would be continued the next day. If all the reserved numbers left by one patient (including the patient's own or his/her relatives numbers) were not available for 3 times, it would be treated as a withdraw case.

Follow-up contents

The main purpose of follow-up is to access the patients' survival times and results, majorly including survival state (alive or dead, date of death, cause of death), recurrence or metastasis (whether recurred or transferred, date and position of recurrence or metastasis), recheck (whether rechecked, date of recheck, rechecked items, results) and/or other relevant information. Through the hospitals' clinical information system we further accessed the patients' previous medical history to collect and complete the patients' basic information, clinical staging, pathological types, radiotherapy dose and/or other relevant data.

Statistical analysis

The patients' complete information were entered into EpiData 3.10 (The EpiData Association, Odense, Denmark) database and the statistically analysis was processed with the SPSS 17.0 (SPSS Inc., Chicago, Illinois, USA) software. The differences among patients' follow-up response rate was calculated by χ^2 test. Influencing factors of their end-of-treatment response was estimated by *Multifactor Logistic Regression Analysis*; the *Kaplan-Meier Method* was adopted to calculate the patients' survival rate; the *Log-rank Method* was applied to compare the correlations between the NPC patients' different factor level and the prognosis; the *Multifactor Cox Regression Analysis* was applied to estimate the independent risk factors of NPC patients' prognosis. Two-sided *P*-values <0.05 were considered to be statistically significant.

Results

Demographic and telephone follow-up results

Among all the 2520 patients, there were 1874 males and 646 females (2.9:1), with an average of 47.77 ± 16.27 (range: 16-79). Among the 2520 patients who have left their contact numbers, there were 134 patients who left invalid number or numbers used by another person, 62 patients who refused to be followed-up, and another 43 patients who were uncooperative during the follow-up, or provided incomplete information and thus their survival could not be accessed. The overall response rate was 90.5% (2281/2520). The patients' response rate showed a yearly increase from 2007 to 2012 (**Table 1**).

Table 2. Correlation of response rate with patients' basicinformation and clinical characteristics

Variable	Total	Response	No response	χ^2	P
Sex				0.125	0.724
Male	1874	1694	180		
Female	646	587	59		
Age				29.811	<0.001
<40	368	353	15		
40~	720	670	50		
50~	619	544	75		
60~	813	714	99		
Residence				28.829	<0.001
Rural	1511	1329	182		
Urban	1009	952	57		
Education				2.238	0.525
Primary school	1016	915	101		
Junior high school	750	677	73		
High school	435	393	42		
College graduateor above	319	296	23		
Occupation				2.217	0.529
Farmers	809	729	80		
Management agencies and institutions	378	343	35		
Teachers/staff/employees	408	377	31		
Retirement/unemployed	925	832	93		
Reserved phone number type				58.909	<0.001
Mobile phone	1588	1384	204		
Landline	284	267	17		
Mobile Phone + Landline	648	630	18		
Number of contacts left				25.180	<0.001
1	1213	1064	149		
2	1006	928	78		
≥3	301	289	12		
Family history of cancer				6.102	0.014
No	2268	2042	226		
Yes	252	239	13		

Influencing factors of response rate

Univariate analysis: we used χ^2 test to compare the differences between or among various demographic factors (Including: gender, age, residence, education, occupation), different disease factors (including T-staging, N-staging, clinical staging and family medical history), other factors (including: reserved phone number type, number of contacts left) and the patients' response rate during the telephone follow-up. The results showed that factors correlated with the patients' end-of-treatment response rate were: age (χ^2=29.811, P<0.001), residence (χ^2=28.829, P<0.001), reserved phone number type (χ^2=58.909, P<0.001), number of contacts (χ^2=25.180, P<0.001), and family medical history of tumors (χ^2=6.102, P=0.014), (**Table 2**).

Multivariate analysis: Binary logistic regression model was constructed to estimate the determinants of response rate, by taking the patients' response as the dependent variable (*answered: Y=1, unanswered: Y=0*), and the relevant factors selected by the univariate analysis with statistical significance as independent variables. Patients' reserved phone number type, number of contacts and family medical history of tumors are the influencing factors of

Table 3. The NPC patients' post-radiotherapy response rate of the phone follow-up

Factors	B	S.E	Wald χ^2	P	OR	OR 95% CI
Reservation phone type	-	-	10.728	0.001	-	-
Mobile phone	Reference	-	-	-	-	-
Landline	0.418	0.154	7.374	0.007	1.518	1.123~2.052
Mobile phone + Landline	0.956	0.423	8.024	0.003	2.602	1.135~5.967
Reservation phone numbers	-	-	13.527	<0.001	-	-
1	Reference	-	-	-	-	-
2	0.486	0.173	7.882	0.005	1.626	1.158~2.283
≥3	1.254	0.448	9.734	0.002	3.503	1.455~8.439
Family history of cancer	0.988	0.497	5.686	0.016	2.689	1.105~7.101

the patients' end-of-treatment response rate during the phone follow-up (**Table 3**).

The follow-up results

The start time of this research was the time when patients finished the radical radiotherapy within required time. The outcome event was when patients died of tumor. The end time of the follow-up observation was Jun. 30th 2014. We used the overall survival (OS) to present the patients' surviving time. That is, between the starting point of the observation and the outcome event, or the end of observation (for cases of survived patients). The follow-up ended at 30. Jun. 2014. It lasted for 8~90 months, the median being 58 months. During the follow-up, 1207 cases (47.9%) died of recurrence or metastasis of the tumor. The patients' overall survival rate (OS) of 1, 3 and 5 years are respectively 98.9%, 75.3%, 50.3%.

NPC patients' prognosis

Univariate analysis: using the Log-rank method to compare the NPC patients that received single radical radiotherapy of their different demographic characteristics (gender, age, family medical history of tumors), their clinical manifestation (T-staging, N-staging, Clinical stage, radiotherapy dose, performance status, basicranial invasion, cranial nerve invasion) and the prognosis. Results have shown that older, lower radiotherapy dose, higher T-staging, N-staging, Clinical stage, with basicranial invasion and cranial nerve invasion predicts shortermedian survival time (**Table 4**).

Multifactor analysis: Regarding surviving result (died of tumor) and survival time as dependent variables, risk factors screened by single factor

analysis as of significance were brought into the equation and performed with multifactor Cox regression analysis. Screen method: Forward: Conditional, variable inclusion criteria, *α=0.05*, exclusion criteria being *0.1*. The results has revealed that T-staging, N-staging, higher clinical staging, with basicranial invasion would prominently reduce the patients' survival, thus are the influencing factors of the radical radiotherapy NPC patients' poor prognosis (**Table 5**).

Discussion

The morbidity of Nasopharyngeal Carcinoma (NPC) shows an increasing trend as a consequence of the social economic development and the change of lifestyle. Follow-up on the other hand is that the hospital or physicians continue to observe the patients received at their hospitals of the treatment and development of the diseases or to obtain other information through various means. It is of great importance to generalize and/or improve the treatment of tumor patients and to raise the clinical research level. The means of follow-up include phone, clinic, letter, home visit, e-mail, community etc. Among them telephone follow-up as the most operative clinical approach can increase the patients' compliance and reduce complication thus is broadly used in clinical practice [6, 7].

In this research, the patients' telephone response rate during 2007-2012 was between 78.9%~99.3%, with overall rate of 90.5%. The lower response rate was, the longer the patient left the hospital. The analysis on factors that affects NPC patients's response after the radiotherapy showed that Patients with a reserved

Table 4. Univariate analysison patients'clinical characteristicsand prognosis

Variable	Total	Median survival time (months)	Log-rank	P
Sex			0.458	0.744
Male	1694	58.7		
Female	587	61.3		
Age			43.121	<0.001
<40	353	79.8		
40~	670	55.9		
50~	544	43.2		
60~	714	54.3		
Family history of cancer			1.045	0.467
No	2042	60.5		
Yes	239	57.1		
T stage			122.348	<0.001
T_1	312	70.4		
T_2	814	59.3		
T_3	714	58.1		
T_4	441	32.2		
N stage			76.254	<0.001
N_0	712	69.6		
N_1	804	50.8		
N_2	312	51.9		
N_3	453	28.3		
Clinical stage			47.587	<0.001
I	503	75.8		
II	201	69.7		
III	897	63.5		
IV	680	34.5		
Radiotherapy dose			30.741	<0.001
60-70 Gy	1487	53.4		
>70 Gy	794	67.0		
Cranial nerve invasion			104.75	<0.001
No	1784	69.8		
Yes	497	29.6		
Skull-base invasion			114.97	<0.001
No	1577	68.5		
Yes	704	37.9		

contact type of mobile + landline phone and fixed phone have respectively a higher response than patients leaving mobile contact only; patients with 3 or more reserved numbers and 2 numbers is higher in response rate than that of patients leaving only 1 number. The main reason is that fixed-line telephones are usually home phone and they are not easily changed, while mobile phones are portable and conve-nient to change. As a result some of the patients' phone number in question became invalid or wrong number and thus impossible to be reached. Yet patients who have left more numbers usually include him or her self's, family members' and other relative's. In that way they could be connected with through multiple means, providing a higher chance of success [8]. Meanwhile patients with a family medical history of neoplasm have prominently higher response than patients without such a medical history. This is possibly because such patients and/of their relatives are more conscious about cancer. They tend to care more about the health issue, and they have a greater need for relevant knowledge [9]. This research has conducted a multifactor analysis on the single radical radiotherapy NPC patients' prognosis, to compare the correlations between different factor level and the prognosis, alongside their phone response and its influencing factors. Results have shown that T-staging, N-staging, higher clinical staging, with basicranial invasion are the influencing factors of the single radiotherapy patients' poor prognosis. To be more specific, NPC patients of T_3, T_4 in T-staging face a death risk respectively 1.951 and 3.498 times of that of T_1 patients; Patients of N_2, N_3 in N-staging has a risk of 1.586 and 1.741 times of N_0 patients; that of Clinical Stage III and IV patients are 1.536 and 1.918 times of Clinical Stage I; Patients with basicranial invasion has death risk 3.781 times of patients without basicranial invasion. Relevant literature also shows that, T-staging, N-staging, higher clinical staging, with basicranial invasion would prominently reduce the patients' survival, thus are the influ-

Table 5. Multifactor Cox regression analysis on radical radio-therapy NPC patients' prognosis

Factor	RR (95% CI)	B	χ^2	P
T stage				
T_1	1			
T_2	1.551 (0.131~7.434)	0.413	0.109	0.741
T_3	1.951 (1.366~2.787)	0.668	13.484	<0.001
T_4	3.498 (1.999~6.119)	1.252	19.247	<0.001
N stage				
N_0	1			
N_1	1.317 (0.280~6.196)	0.275	0.031	0.861
N_2	1.586 (1.069~2.352)	0.461	5.259	0.022
N_3	1.741 (1.182~2.564)	0.554	7.867	0.005
Clinical stage				
I	1			
II	1.421 (0.907~6.226)	0.351	0.099	0.754
III	1.536 (1.292~3.146)	0.429	12.291	<0.001
IV	1.918 (1.319~2.789)	0.651	14.617	<0.001
Skull-base invasion				
No	1			
Yes	3.781 (2.071~6.982)	1.333	8.262	0.004

encing factors of the radical radiotherapy NPC patients' poor prognosis [10, 11].

In conclusion, the response rate of post-radiotherapy NPC patients still needs to be increased, especially patients who have been discharged longer before. It is a long-term and hard work to increase the tumor patients' response rate and the follow-up quality. It requires the medical workers to continuously study in their professional knowledge and to come up with reasonable follow-up methods. While the patients and their family and relative's understanding and cooperation is also necessary. It is worth noting that the data collected in this study is solely from only one hospital, it needs to be further testified by multi-central, larger-scaled samples and longer follow-up duration.

Conclusion

The telephone follow-up response is affected by reserved contact type, number of contacts and family medical history; T-staging, N-staging, higher clinical staging, with basicranial invasion are the influencing factors of the patients' poor prognosis.

Relevance to clinical practice

It can provide a scientific basis for increasing the NPC patients' end-of-treatment response and promoting the individualized clinical treatment.

Disclosure of conflict of interest

None.

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