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RESEARCH

Trajectories of fear of progression in nasopharyngeal carcinoma patients receiving proton and heavy ion therapy

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Abstract

Objective The study examined the growth trajectory of fear of progression(FOP) in nasopharyngeal carcinoma (NPC) patients. In addition, sociodemographic and clinical variables of each trajectory class were analyzed.

Method Two hundred sixteen NPC patients undergoing proton and heavy ion therapy were measured beginning (T0) and end of a 4-week proton and heavy ion therapy (T1), 3 months (T2) and 6 months (T3) after discharge. And data from the final 197 NPC patients were analyzed. NPC patients' FOP was investigated by the Fear of Progression Questionnaire-Short Form (FOP-Q-SF) form T0 to T3. SPSS and Mplus were used for statistical analysis. The LGMM was used to analyze the trajectory of FOP followed up over 6 months after proton and heavy ion therapy. The logistic regression was utilized to compare the differences in sociodemographic and clinical characteristics of patients in different trajectory groups of FOP.

Results One hundred ninety-seven NPC patients were analyzed. LGMM analysis showed that three-group trajectory solution was the best fitting (low-fear decline FOP (14.21%), the moderate-fear stable FOP(43.15%), and high-fear rising FOP (42.64%). Significant positive associations were found between age < 30 years ($\beta = 3.399$, $p = 0.023$), with or without children ($\beta = 3.1$, $p = 0.002$), primary/recurrence ($\beta = -6.196$, $p < 0.001$), diagnosis < 3 months ($\beta = 4.435$, $p = 0.031$), high school education ($\beta = 2.98$, $p = 0.048$), and high fear rising FOP. Patients who had moderate financial stress ($\beta = 2.51$, $p = 0.041$), with or without children ($\beta = 1.564$, $p = 0.003$), primary/recurrence ($\beta = -2.578$, $p = 0.005$), less than 30 radiotherapy times ($\beta = 0.979$, $p = 0.046$) tended to report significant moderate-fear stable FOP over time.

Conclusion 42.64% of the NPC patients showed high-fear rising FOP over the 6 months after treatment. Age 18–30 years, with or without children, relapsed, diagnosis < 3 months, and high school education and reporting being a pessimist predicts higher FOP scores. Early identification of age 18–30 years, with or without children, relapsed, diagnosis < 3 months, and high school education might help to identify populations experiencing long-term FOP. Clinical teams responsible to develop the target interventions for management of FCR in clinical practice.

Keywords Nasopharyngeal carcinoma · Fear of progression · Trajectory · Proton and heavy ion therapy · Multi-measurement

Background

Approximately 133,000 new cases of nasopharyngeal carcinoma are diagnosed worldwide each year, with a year-on-year increasing trend [1, 2]. China accounts for 46.9% and 43.0% new cases and deaths of nasopharyngeal cancer worldwide [3], with a high incidence rate in southern regions in particular [4, 5]. Because of its unique anatomical location and sensitivity to radiotherapy, radiotherapy is the primary treatment for NPC. As the most advanced radiotherapy recognized in the world, proton and heavy ion therapy can centrally blast tumor target areas, with moderate side effects and a high local control rate [6]. Despite

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advancements in medical technology, the rate of recurrence and distant metastases to local or cervical lymph nodes in the nasopharynx is 20–30%, with 65–85% of patients recurring within 3 years [7–9]. A Hong Kong study investigating 3328 patients with non-metastatic NPC found that the local control rate of NPC in stage IV was only 55–88%, with a median time to local recurrence of approximately 30 months [10]. When cancer recurs or metastasizes, the difficulty of re-diagnosis and re-radiation toxicity considerably worsens the retreatment and the risk of major consequences such as deafness, radiation encephalopathy and fatal haemorrhage, greatly reducing the survival rate and quality of life of patients [11–13].

Existing difficulties in retreatment and high risk of recurrence instills fear of progression.Fear of progression (FOP) was defined as fear, worry, or concern about disease progression or cancer recurrence [14]. NPC patients have an incidence of FOP as high as 67%, with a relatively severe degree and long duration [5, 6]. Studies showed that the higher the FOP, the worse the quality of life [15, 16]. FOP triggers uncontrollable obsessive thoughts [17], causes distress such as pain, fatigue, and sleep disturbance [18], leads to excessive medical examinations, increases family financial stress [19, 20]. FOP increases the risk of psychological problems such as anxiety, depression and uncertainty [11, 21], triggers concerns about side effects of drugs, and reduces adherence to treatment [22]. Lots of surveys have shown that the level of FOP dynamically over time and varies among patients with different cancer types [11, 12]. The occasion of investigation is critical in identifying the trajectory of FOP. Studies have shown that before and at the end of proton and heavy ion therapy, 3 months and 6 months after treament are important points for FOP trajectory [23, 24]. The level of FOP was significantly and positively correlated with symptom severity ($r = 0.29$, $p = 0.02$) [25]. At the end of proton and heavy ion therapy, NPC patients suffer the deepest side effects such as oral mucositis, dry mouth, facial numbness, diplopia, and tinnitus [26]. The severity of somatic symptoms worsens as the level of FOP rise. Thus, at the end of treatment, FOP may worse. Study reveals levels of FOP increased as the time of screening approached [24]. Patients who are reexamined 3 and 6 months following proton and heavy ion therapy may have an elevated FOP. However, 3 months after the end of treatment, inflammatory responses such as oral mucositis and skin reactions have largely subsided, somatic symptoms have got better [27]. The level of FOP may also decrease. Thus, the course of FOP at 3 months post-treatment is uncertain and warrants further exploration. At 6 months after the end of treatment, long-term reactions and injuries from radiotherapy, such as hearing loss, difficulty opening the mouth, radiation temporal lobe necrosis, and cranial nerve damage, become apparent or worsen, the level of FOP may rise [28, 29]. In summary, the options of the longitudinal survey of FOP in this study was chosen beginning and end of proton and heavy ion therapy, 3 months and 6 months after treatment.

Furthermore, socio-demographic and clinical characteristics were compared between classes of the trajectory of FOP by the logistic regression. The aim of this research is to provide a favorable basis for healthcare practitioners to identify high-FOP calss and implement psychological interventions to alleviate patients' level of FOP.

Methods

Participants and procedures

The study has been approved by Shanghai Proton and Heavy on Center Institutional Review Board(ethical approval reference number:2202-53-02), and was performed in accordance with the ethical stands as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Patients provided written informed consent were recruited from Proton and Heavy Ion Center in Shanghai, China. Two hundred sixteen patients with confirmed NPC receving proton and heavy ion therapy recruited from April 2022 to December 2022. Inclusion criteria were cases with age $\geq$ 18 years; good reading and communication skills in Chinese;a clinicopathological histological or cytological diagnosis NPC; volunteer for this study. Exclusion criteri were sudden exacerbation of cancer;receiving psychotherapy during the study. Patients completed a self-report survey assessing variables at four time points: beginning (T0) and end of a 4-week proton and heavy ion therapy (T1), 3 months (T2) and 6 months (T3) after discharge. Research approved by the hospital ethics committees, the researcher accesses the participant's information system and distributes the questionnaire. The researcher informed the study objective, its significance and the precautions to be followed and notifies that patients are free to withdraw from the investigation at any moment.Data dropped out or lost to follow-up will not be included in the analysis. Figure 1 shows the sampling and attritions.Of 216 eligible NPC patients, 197 completed the four assessments.And 19 cases were lost to follow-up, with a loss rate of 8.8%.

Measures

FCR was assessed using the Fear of Progression Questionnaire-Short Form(FOP-Q-SF). The scale, for measuring

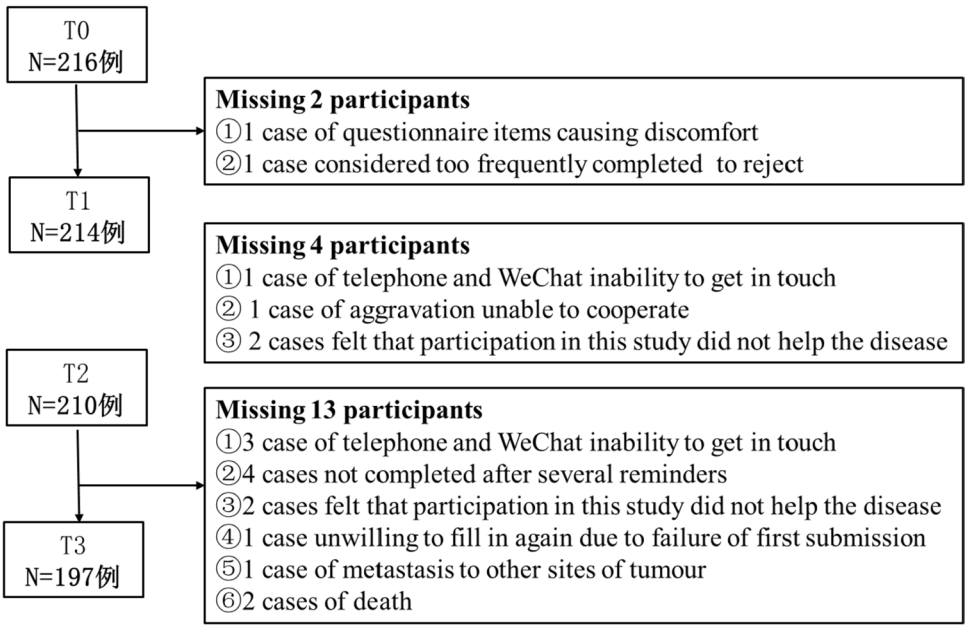

Fig. 1 Inclusion and loss of follow-up chart

the level of FOP in cancer survivors, was developed and validated by the German scholar Mehnert et al. [30]. The 12-item FOP-Q-SF examines the existence, frequency, and intensity of FCR, with item scores ranging from 1 to 5 (never to very often). The total score ranges from 0 to 60, and the cutoff score of ≥ 34 is indicative of clinical FOP [30]. FOP-Q-SF has two dimensions: physical health (items 1,2,3,5,9,10) and social family (items4,6,7,8,11,12),and Cronbach's α was 0.88 [31, 32].

Statistical methods

Data were analyzed performed using SPSS 24.0 and MPlus 8.0. A significance level of 0.05 was applied for analyses. The LGMM, a type of growth mixture model that classifies groups based on the trajectory of study variables over time, was used to identify class membership according to the FOP trajectory over 6 months after radiotherapy. Bayesian information criterion (BIC), sample size-adjusted BIC(aBIC), Akaike Information Criterion(AIC), Lo-Mendell-Rubin Likelihood Ratio test (LMR), and BootstraP-based Likelihood Ratio test (BLRT) were used to determine optimal class solution [33]. Furthermore, EntroPy indicate accuracy of the model. In general, an index > 0.8 indicates good classification quality and its accuracy rate is over 90% [34]. Lower values in AIC, BIC, and SABIC indicates a better model fit.A significant *p*-value in LMR-LRT and BLRT indicates that the class addition improved the fit. Socio-demographic and clinical characteristics were compared between classes of the trajectory of FOP by logistic regression.

Results

Participant sociodemographic and clinical characteristics

Nineteen (8.8%) cases were lost to follow-up. Two cases were lost at T1, 4 cases were lost at T2, and 13 were lost at T3. Finally, 197 NPC patients were included. The specific number of patients lost at each follow-up stage and the reasons are shown in Fig. 1. The logistic regression was used to compare the social demographic and clinical data of the 197 patients included in the study and the 19 patients who were lost to follow-up. Table 1 showed that there were no significant differences between the two groups in terms of socio-demographic and clinical characteristics factors. The majority were men ($n = 122$, 61.9%), 30–45 years old ($n = 98$, 49.7%), married ($n = 141$, 71.6%), with children ($n = 152$, 77.2%), university ($n = 101$, 51.3%), employed ($n = 118$, 59.9%), moderate financia stress ($n = 93$, 47.2%), mostly with initial onset ($n = 160$, 81.2%), stage II ($n = 58$, 29.4%) and stage III ($n = 71$, 36%), diagnosed within 6 months ($n = 130$,66%), and other socio-demographic characteristics are presented in Table 1.

Growth trajectories of FCR

The results showed that the FOP in nasopharyngeal carcinoma patients was at a moderate level. The score of FOP was (32.49 ± 8.407points) before treatment, (29.83 ± 7.561 points) at the end of treatment, (29.04 ± 8.704 points) at 3 months after treatment and (28.29 ± 11.959points) at

Table 1 Characteristics of patients included and lost

Variables		Inclusion cases	%	Lost cases	%	X^2	*P*
Gender	Female	75	38.1	7	63.2	0.011	0.916
	Male	122	61.9	12	36.8		
Age at radiotherapy	< 30	21	10.7	2	10.5	0.226	0.995*
	30–45	98	49.7	10	52.6		
	45–60	57	28.9	5	26.3		
	> 60	21	10.7	2	10.5		
Marital status	Unmarried	56	28.4	5	26.3	0.038	0.845
	Married	141	71.6	14	73.7		
Children	Yes	152	77.2	18	94.7		0.084*
	No	45	22.8	1	5.3		
Education	Primary and below	12	6.1	1	5.3	0.874	0.889*
	High School	63	32.0	5	26.3		
	University	101	51.3	12	63.2		
	Postgraduate and above	21	10.7	1	5.3		
Employment	Working	118	59.9	10	52.6	2.334	0.682*
	Unemployed	32	16.2	3	15.8		
	Retired	34	17.3	3	15.8		
	Other	13	6.6	3	15.8		
Financial	Mild	67	34.0	4	21.1	4.430	0.204*
	Moderate	93	47.2	8	42.1		
	Severe	27	13.7	6	31.6		
	Extremely severe	10	5.1	1	5.3		
Religion	Yes	41	20.8	2	10.5		0.378*
	No	156	79.2	17	89.5		
Primary/recurrence	Primary	160	81.2	15	78.9		0.764*
	Recurrence	37	18.8	4	21.1		
Stage	I	28	14.2	4	21.1	2.754	0.433*
	II	58	29.4	8	42.1		
	III	71	36.0	5	26.3		
	IV	40	20.3	2	10.5		
Diagnosis time	0-3 months	68	34.5	7	36.8	2.715	0.436*
	3-6 months	62	31.5	9	47.4		
	6-12 months	21	10.7	1	5.3		
	> 12 months	46	23.4	2	10.5		
Chemotherapy history	Yes	100	50.8	7	36.8	1.343	0.337
	No	97	49.2	12	63.2		
Treatment programme	Proton/heavy ion	74	37.6	10	52.6	1.656	0.223
	Others	123	62.4	9	47.4		
Number of radiotherapy	≥ 31	110	55.8	9	47.4	0.502	0.630
	< 31	87	44.2	10	52.6		
Adjuvant chemotherapy	Yes	77	39.1	9	47.4	0.496	0.625
	No	120	60.9	10	52.6		

Fisher's exact probability tests;Employment other: students;Treatment programme other: Proton and heavy ion therapy

6 months after treatment.The total FOP score in four points (T0,T1,T2,T3) was significantly different according to Single sample Repeated-measures ANOVA ($P < 0.05$). Figure 2 showed the trend of FOP of 197 NPC patients from T0 to T3. The trajectory of the FOP in 197 patients with nasopharyngeal carcinoma showed significant individual heterogeneity, and an in-depth analysis of LGMM were needed. Table 2 shows fit indices of six class solutions. When the number of class increased from 2 to 3, AIC, BIC and aBIC all became smaller, and the *P*-values of LMR

Table 2 Fit indices for the class solutions ($N=197$)

#of classes	K	AIC	BIC	aBIC	EntroPy	*P*	
						LMR	BLRT
1	10	5258.922	5291.754	5260.074	–	–	–
2	14	5347.130	5393.095	5348.743	0.961	0.000	0.000
3	18	5285.837	5344.935	5287.912	0.813	0.0041	0.0000
4	22	5270.635	5342.865	5273.170	0.800	0.000	0.0788
5	26	5258.244	5343.607	5261.240	0.826	0.1652	0.000
6	30	5258.032	5356.528	5261.489	0.856	0.4347	0.2353

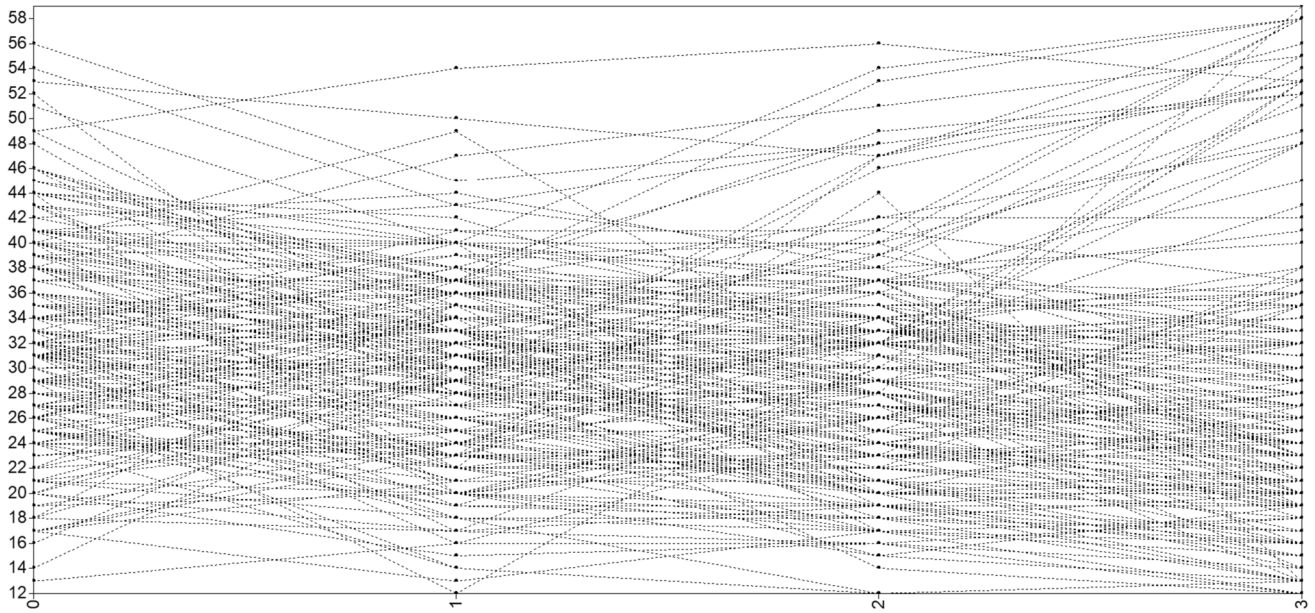

Fig. 2 Trend of FOP in 197 NPC patients

and BLRT were significant ($P<0.05$) indicating that the fit of 3 categories was better than 2 categories, and Entropy reached 0.813 with higher classification accuracy. When the number of potential categories increased to 4 and 5, although the AIC and BIC and Entropy increased, but the *P*-values for LMR and BLRT were gradually insignificant ($P>0.05$), indicating that the results for 4 and 5 classes were not better than those for 3 classes, and the fitted model for 3 classes was recommended. In summary, the 3-category model was selected as the best-fitting model.

Figure 3 and Table 3 depict the three classes based on the FCR trajectory: the class 1 (14.21%, low-fear decline FOP), the class 2 (43.15%, moderate-fear stable FOP), and the class 3 (42.64%, high-fear rising FOP). Eighty-four patients (42.64%) were in the low fear descending class. The score of FOP at T0 was (28.14 ± 6.462). The score of FOP was 25.77 ± 6.235 at T1, 23.07 ± 5.931 at T2, and 19.15 ± 4.438 at T3. The mean intercept and slope of low-fear decline class were 28.217 ($P=0.000$) and -4.552 ($P=0.000$), indicating that patients showed a

Table 3 Socers of FOP in three classes from T0 to T3($N=197$)

Of classes	Cases	%	M ± SE			
			T0	T1	T2	T3
Class1(high fear rising FOP)	28	14.21%	43.64 ± 6.093	36.07 ± 7.702	41.36 ± 8.341	52.07 ± 5.643
Class2(moderate-fear stable FOP)	85	43.15%	33.11 ± 7.140	31.78 ± 6.531	30.88 ± 5.480	29.49 ± 5.528
Class3(low-fear decline FOP)	84	42.64%	28.14 ± 6.462	25.77 ± 6.235	23.07 ± 5.931	19.15 ± 4.438

Table 4 Sociodemographic and clinical characteristics among classes($N=197$)

	Variables	β	SE	Waldχ^2	P	OR	95%CI	
C1 vs C3	Age							
	< 30 years	3.399	1.499	5.140	0.023	29.932	1.585	565.331
	Children(Yes/No)	3.1	0.997	9.676	0.002	22.2	3.148	156.556
	Primary/recurrence	−6.196	1.768	12.283	0.000	0.002	6.371	14.065
	Diagnosis time							
	0-3 months	4.435	1.728	6.592	0.031	84.394	2.856	493.682
	Education							
	High School	2.98	1.509	3.897	0.048	19.680	1.022	379.072
C2 vs C3	Financial stress							
	Moderate	2.51	0.985	6.498	0.041	12.303	1.786	84.730
	Children(Yes/No)	1.564	0.529	8.750	0.003	4.776	1.695	13.458
	Primary/recurrence	−2.578	0.913	7.970	0.005	0.076	0.013	0.455
	Numbe rof radiotherapy							
	< 30 times	0.979	0.490	3.983	0.046	2.661	1.018	6.960
C1 vs C2	Age							
	< 30 years	4.314	6.830	2.947	0.037	17.801	4.318	370.346
	Diagnosis time							
	0-3 months	0.123	0.591	0.043	0.015	1.131	0.355	3.603

C1 high-fear rising FOP; *C2* moderate-fear stable FOP class; *C3* low-fear decline FOP class

significant downward trend during the whole investigation period. The intercept and slope of moderate-fear stable class were 32.685 ($P=0.000$) and -1.225 ($P=0.108$), indicating that the overall change of patients during the whole investigation period was not significant and showed a steady trend. The mean intercept and slope of the trajectory of the high fear rising class were 44.163 ($P=0.000$) and 2.723 ($P=0.001$), demonstrating that throughout the entire investigation period, there was a noticeable increase in the FOP.

The demographic and clinical characteristics of classes of FOP trajectory

This study further comparing demographic and clinical characteristics of the each groups of FOP trajectories by logistic regression found significant difference in age with or without children, primary/recurrence, diagnosistime,education,financial stress,number of radiotherapy. C1 vs. C3, age < 30 years, with or without children,primary/recurrence, diagnosis < 3 months, and high school education were all associated with C1.C2 vs. C3, moderate financial stress, with or without children, primary/recurrence, less than 30 radiotherapy times are more likely to be classed as C2.C1 vs. C2, age < 30 years and duration of illness less than 3 months are categorised as C1 (Table 4).

Discussion

The trend graph of FOP in NPC patients shows class heterogeneity in the trajectory of FOP. The LGMM further differentiated the trajectories into Class1 (high fear rising FOP), Class2 (moderate-fear stable FOP),

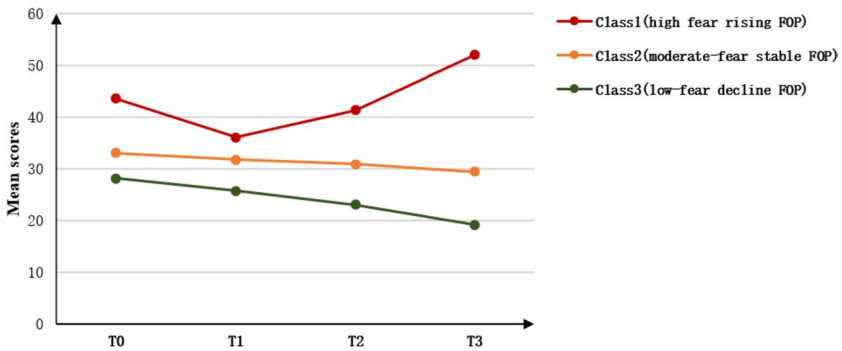

Fig. 3 Three classes of growth trajectory of the FOP

and Class3 (low-fear decline FOP). The results were similar to those of a Korean study that investigated the trajectory of FOP in 167 surgically treated breast cancer patients [35].

The "high fear rising FOP" comprised approximately 14.21% of all patients. The level of FOP tended to increase significantly over the survey period. The lowest levels were found at T1. The level of FOP increased at T2 and T3. The relatively low number of patients in "high fear rising FOP" class may be related to the traditional cultural background in China. The Chinese believe that old age, sickness, and death are preordained by fate and are natural laws that no one can resist or avoid. Therefore, when faced with life-threatening illnesses such as cancer, the Chinese may tend to let nature take its course.

Patients in the "high fear rising FOP" showed an increased trend. Studies show that patients with higher initial levels of FOP are more likely to have increased levels of FOP at follow-up [36]. A qualitative study in the US found that death-related images and thoughts recur daily and are difficult to control, with fear of death-related thoughts increasing over time as the disease progresses [37]. Six months after discharge 26% of patients still need medical help to alleviate FOP [38]. The results of this study suggest that T2 and T3 are important time points for implementing psychological support to alleviate patients' FOP and help them actively cope with the threat of disease and return to normal life as soon as possible.

The level of FOP tended to decrease over time in the "low-fear decline FOP," with the highest level at T0 and the lowest level at T3, with the fastest rate of decrease. The "moderate-fear stable FOP" class accounted for 43.15% of all patients, with the highest degree of FOP at the start of proton and heavy ion therapy and at a moderate level after proton and heavy ion therapy. FOP levels were stable and weren't changed significantly over time.

On the one hand, just before proton and heavy ion therapy, patients have insufficient knowledge of their illness, and they are concerned about the consequences of proton and heavy ion therapy and harmful side effects. On the other hand, the patients had high expectations for the effect of proton and heavy ion therapy, and they themselves felt unreliable and concerned about not being able to get the best radiation effect due to not good enough co-operation, and the cancer cell was not totally burned by the radiation [39]. Studies have shown that negative emotions such as anxiety, depression and illness uncertainty can increase the level of FOP in cancer patients [33, 40]. Therefore the level of FOP in NPC patients is high at T0. Less side effects and higher local control rate with proton and heavy ion therapy compared to conventional photon radiotherapy (蒋国梁, 2017). There is less damage to the normal tissue surrounding the cancer site, a lesser degree of side effects such as radiation dermatitis and oral mucositis, and a lower symptom burden on the patient at the end of treatment [6], so the level of FOP at the end of proton and heavy ion therapy is lower. Three and six months after discharge, the level of FOP in the "low-fear decline FOP" and the "moderate-fear stable FOP" showed a decreasing trend, which is consistent with the findings of Zhang Yang's study, which found that the level of FOP in 279 lymphoma patients in Henan Province, China, showed decreasing trend at the time of disease progression, 3 and 6 months after progression [41]. During hospitalization, patients receive education about the disease from care professionals and have more objective understanding and experience of the disease and treatment. At the same time, patients are removed from the hospital environment and are mostly at home, receiving more support from family, relatives and friends.

Considering the differences in the severity and trends of FOP among three classes, it is necessary to compare the essential characteristics of NPC patients in each class, so as to provide foundation for clinical staff to screen the high-risk class of FOP at the optimal time and implement effective interventions.

The socio-demographic and clinical characteristics of the "moderate-fear stable FOP" group were dominated by patients with moderate financial stress, with or without children, primary/recurrence, less than 30 radiotherapy times. With or without children and primary/recurrence have higher probability of attribution to "high-fear rising FOP" class. Financial status determines the patient's choice of treatment options. The cost of proton and heavy ion therapy is more expensive than conventional photoradiotherapy, increasing the financial burden of the family. Patients and their families, who have spent more time and money, are extremely keen to get the best possible results and are particularly fearful of a recurrence of the disease. The less the number of radiotherapy sessions, the smaller the total radiation dose and the more restricted symptom burden. The more limited side effects of radiotherapy, NPC patients suffer the lower FOP. The findings suggest that healthcare professionals should focus on following up the FOP in patients with moderate financial stress, with or without children, primary/recurrence, less than 30 radiotherapy times and help to increase their confidence and hopeby guiding patients to alleviate their distant symptoms and psychological support.

The socio-demographic characteristics of patients in the "high-fear rising FOP" class are age 18–30 years, with or without children,primary/recurrence, diagnosis < 3 months, and high school education. In terms of age, 18–30 years are the prime years of life, when patients are full of expectations and hopes for the future, and the psychological impact of a cancer diagnosis on younger patients is greater. At the same time treatment complications such as jaw stiffness,

altered taste and memory loss lead to negative emotions such as low self-esteem. Patients' anxieties are made worse by their fears of being rejected by coworkers at work, losing their employment, and losing their existing social status. Patients with recurrence are concerned about whether they can still receive proton and heavy ion therapy, the world's most advanced oncology radiotherapy technology, if they have recurrence or metastasis. The incidence of late adverse reactions to recurrent nasopharyngeal carcinoma is higher than in patients with initial disease, and the incidence of carotid artery rupture haemorrhage is over 40%, which seriously affects the quality of survival and prognosis of patients [42], who believe that the disease is incurable and therefore worry excessively about their families and children, and have a higher level of FOP. The impact of the event of developing cancer is higher within 0–3 months of diagnosis. The stress and anxiety of coping with treatment and prognosis adds to the psychological burden of the patient as less is known about the disease in a short period of time. Studies have shown that within 3 months of cancer, patients' attitudes towards death are dominated by avoidance and the tendency to accept death is lowest [43]. Patients with lower levels of education have limited access to resources, are less rational about their illness and can make objective judgements about the effectiveness of treatment and survival prognosis. The patients obtained their knowledge about the disease primarily through such as TikTok, Baidu, and other people's experience sharing, so they did not have enough professional knowledge about the proton and heavy ion therapy and were more inclined to doubts about the treatment effect. The results of the study prompted clinical practitioners to focus on high-FOP risk groups of 18–30 years old, recurrence, and 0–3 months after diagnosis with follow-up 6 months after the end of proton and heavy ion therapy, to assess changes in patients' levels of FOP and to remotely guide patients to recognize the difference between side effects of radiotherapy and signs of recurrence, so that they remain alert to cancer recurrence or metastasis and avoid excessive worry.

Clinical implications

This study provided new evidence regarding the trajectory of FOP in NPC patients treated with proton and heavy ion therapy.FOP of "high-fear rising FOP" class continues to rise over time.While NPC patients diagnosed with age 18–30 years, with or without children,relapsed, diagnosis < 3 months, and high school education reported higer FOP to the cancer recurrence. This study improves our understanding of survivor's psychological responses about their FOP. Clinicians should identify the high-risk patients of "high-fear rising FOP" class based on socio-demographic and clinical characteristics, accurately predict the time point of develop FOP, and considered in clinical practice and intervention development.

Study limitations

This study only explored the trajectory of FOP in NPC patients over 6 months after the end of proton and heavy ion therapy. However, the trajectory of FOP has not yet reached a plateau and further follow-up is needed. A US study investigating the levels of FOP in 2337 cancer patients at 1.3, 2.2, and 8.8 years after diagnosis showed that the low fear level group decreased and then increased; the medium fear level group continued to decrease; and the high fear level group had a more pronounced initial decrease, which slowed down at 2.2 and 8.8 years [44]. The differing results from the present study necessitated an extension of the observation period of the study.The study population was recruited from only one proton heavy ion hospital, with limited representation of the included sample.

Future studies were recommended be conducted in multiple proton and heavy ion hospitals with large samples and longer follow-up times. Longitudinal qualitative studies should also be added to identify resources and challenges for patients coping with FOP.

Conclusions

"High fear rising FOP" appear to persist and even increase over time.Early identification of high-risk groups and early psychological support measures are essential to alleviate the level of FOP in NPC patients and to shorten the period of fear of disease progression. Patients in the "high fear of progression group" were prone than the other two groups to be age 18–30 years, with or without children, relapsed, diagnosis < 3 months, and high school education.

Author contribution Mimi Zheng:Conceptualization; data curation; formal analysis; inves-tigation; methodology; project administration; software; validation;writing–original draft; writing–review and editing.

Shuman wang:Conceptualization; data curation; formal analysis; inves-tigation; methodology; writing–original draft.

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Data availability The datasets generated during and/or analyzed during the current stud yare available from the corresponding author upon reasonable request.

Declarations

Competing interests The authors declare no competing interests.

Ethics statement The study has been approved by Shanghai Proton and Heavy on Center Institutional Review Board(ethical approval reference number:2202-53-02).

Conflict of interest The authors declare no competing interests.

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