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ORIGINAL ARTICLE

Treatment effect of concurrent chemoradiotherapy after surgery and its effect on postoperative swallowing function of patients with locally advanced hypopharyngeal carcinoma

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Summary

Purpose: *To study the treatment effect of concurrent chemoradiotherapy (CCRT) after surgery and its effect on postoperative swallowing function of patients with locally advanced hypopharyngeal carcinoma.*

Methods: *The clinical data of 84 patients with advanced hypopharyngeal carcinoma treated in our hospital were retrospectively analyzed. The patients were randomly divided into experimental group and control group, with 42 cases in each group. After both groups of patients were treated with radical neck dissection, the control group received adjuvant radiotherapy while the experimental group received CCRT.*

Results: *The Burke score in the experimental group after treatment was significantly lower than that in the control group (p<0.001). The objective remission rate in the experimental group was significantly higher than that in the control group (p<0.05). The jitter and shimmer in the experimental group after treatment were significantly lower than those in the control group (p<0.05). The quality of life scores of patients in the two groups after treatment were significantly higher than those before treatment (p<0.001), and the quality of life score in the experimental group was significantly higher than that in the control group (p<0.001). And the incidence of gastrointestinal reactions and neutropenia in the experimental group after treatment was significantly lower than that in the control group (p<0.05). The 3-year cumulative survival rate after surgery in the experimental group was significantly higher than in the control group (p<0.05).*

Conclusions: *CCRT after surgery can effectively improve the swallowing function of patients with locally advanced hypopharyngeal carcinoma, which is worthy of promotion and application.*

Key words: *advanced hypopharyngeal cancer, surgery, concurrent chemoradiotherapy, treatment effect, swallowing*

Introduction

Hypopharyngeal carcinoma is a malignant tumor involving the ears, nose and throat, accounting for 0.3-0.5% of the all malignant tumors [1,2]. Related medical studies have shown that hypopharyngeal carcinoma is more likely to occur in middle-aged and elderly men aged 50-70. Drinking, smoking, ionizing radiation and reflux esophagitis are independent risk factors for hypopharyngeal carcinoma. Since its early clinical features are not obvious and lesion locations are hidden, most patients have entered middle and advanced stages when diagnosed, easily leading to cervical lymph node metastasis, esophageal cancer and poor clinical prognosis. Especially in advanced hypopharyngeal carcinoma, the 5-year survival rate is only 35-45% regardless of whether the patients receive surgical or non-surgical treatment[3-5]. In addition, progressive dysphagia, loss of language function and head pain will seriously affect the quality of life of patients with advanced hypopharyngeal car-

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cinoma which is prone to deterioration. With the advancement of medical research and radiotherapy technology, concurrent chemoradiotherapy (CCRT) has become the preferred treatment for patients with locally advanced hypopharyngeal carcinoma [6,7]. This treatment can directly act on the patients' primary lesions, control or eliminate latent metastatic lesions, prevent further expansion of cancer cells and improve prognosis. Although surgery can effectively remove the lesions, it is often not accepted by patients because the wide range of resection will affect their laryngeal function to some extent [8]. Based on this, in order to further confirm the treatment effect of CCRT after surgery and its effect on postoperative swallowing function of patients with locally advanced hypopharyngeal carcinoma, the clinical data of 84 patients with advanced hypopharyngeal carcinoma treated in our hospital from April 2015 to April 2017 were retrospectively analyzed.

Methods

General information

The clinical data of 84 patients with advanced hypopharyngeal carcinoma treated in our hospital from April 2015 to April 2017 were retrospectively analyzed. The patients were randomly divided into the experimental group and control group, with 42 cases in each group.

Inclusion criteria

(1) The diagnostic criteria of hypopharyngeal carcinoma, and the tumor stages were III-IV; (2) Before treatment, the liver, kidney and electrocardiogram of patients were normal; (3) The study was approved by the hospitalethics committee, and the patients and their families knew the purpose and the process of the experimental study, and signed the informed consent form.

Exclusion criteria

(1) The expected survival time of the patients was no more than 3 months; (2) The patients were complicated with other malignant tumors; (3) The patients had severe cardiovascular disease.

Methods

Both groups of patients underwent radical neck dissection. After surgery, the control group received adjuvant radiotherapy with platinum alone (20mg/m^2, d1-d5), and was simultaneously injected with Shuganning injection (SFDA approval number: Z20025660; manufacturer: Guizhou Ruihe Pharmaceutical Co., Ltd.; specification: 2ml/vial) by intravenous drip after the injection was diluted with 500mg of dextrose injection (10%). The patients were treated with glucocorticoids in order to stabilize the condition and orally took dexamethasone acetate tablets (SFDA approval number: H41021038; manufacturer: Suicheng Pharmaceutical Co., Ltd.; specification: 0.75mg*100s)[9].

The patients in the experimental group received CCRT after surgery. The patients were treated with anti-epidermal growth factor receptor (EGFR) monoclonal antibody targeted therapy with treatment regimens including TP regimen (cisplatin+docetaxel), single cisplatin and PE regimen (cisplatin+5-fluorouracil), which were repeated every 21 days. The targeted drugs were nimotuzumab (SFDA approval number: S20080001; manufacturer: Biotech Pharmaceutical Co., Ltd.; specification: 50mg/bottle) and cetuximab (registration number: S20050095; manufacturer: Merck KGaA; specification: 100mg/50ml), which were administered according to the instructions.

Observation indexes

Burke scale [10] was used to evaluate the swallowing function of patients in the two groups before and after treatment. The scale had 6 items, a total score of 42 points and each item of 7 points. The higher the score, the more serious the dysphagia of patients.

The efficacy of the two groups after treatment was evaluated according to Response Evaluation Criteria In Solid Tumors from WHO [11]. (1) Complete remission: All lesions disappeared, and the maintenance time was no less than 4 weeks; (2) Partial remission: Tumor volume decreased by more than 30% and the maintenance time was no less than 4 weeks; (3) Stability: Tumor volume decreased by no more than 30% or increased by no more than 20%; (4) Progression: Tumor volume increased by more than 20% or new lesions appeared. Objective remission rate = complete remission + partial remission.

Multidimensional voice analysis software was used to evaluate the vocal function of patients in the two groups before and after treatment. The examination was carried out in a quiet environment, with the ambient noise less than 40 dB, the distance between the mouth and the microphone 30cm, and continuous pronunciation of the of vowel /a/ over 3s. The shimmer and jitter values were recorded.

The Chinese version of the European Organization for Research and Treatment of Cancer (EORTC) head and neck cancer module (QLQ-H&N35) [12] was used to evaluate the quality of life of the two groups before and after treatment. The scale had 15 scoring items, with a total score of 100 points. The higher the score, the higher the patient quality of life.

The incidence of adverse reactions in the two groups after treatment was counted and compared.

The survival time was determined according to the follow-up results. The 1-year and 3-year cumulative survival rates were compared between the two groups.

Statistics

The experimental data were statistically analyzed and processed by SPSS21.0 software. GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to draw figures of the data. The count data were tested by x^2, expressed by n (%), and the measurement data were measured by t-test, expressed by mean±SD. The difference was statistically significant when $p<0.05$.

Results

Comparison of clinical data between the two groups

There were no significant differences in gender, age, BMI, smoking history, drinking history, marital status, tumor types, tumor staging, pathological types and residence between the two groups (p>0.05), indicating comparability, as shown in Table 1.

Comparison of Burke scores between the two groups before and after treatment

The Burke scores of patients in the two groups after treatment were significantly lower than those before treatment (p<0.05), and the Burke score in the experimental group after treatment was significantly lower than that in the control group (p<0.05), as shown in Figure 1.

Table 1. Comparison of clinical data between the two groups

Items	*Experimental group (n=42) n (%)*	*Control group (n=42) n (%)*	x^2/t	*p*
Gender			0.048	0.827
Male	23 (54.76)	22 (52.38)		
Female	19 (45.24)	20 (47.62)		
Average age (years old)	56.85±2.38	56.87±2.41	0.038	0.970
BMI (kg/m^2)	21.32±1.76	21.34±1.79	0.052	0.959
Smoking history			0.474	0.491
No	16 (38.10)	13 (30.95)		
Yes	26 (61.90)	29 (69.05)		
Drinking history			0.295	0.587
No	15 (35.71)	13 (30.95)		
Yes	27 (64.29)	29 (69.05)		
Marital status			0.213	0.645
Unmarried	3 (7.14)	2 (4.76)		
Married	39 (92.86)	40 (95.24)		
Tumor types				
Pyriform sinus carcinoma	13 (30.95)	14 (33.33)	0.055	0.815
Posterior pharyngeal wall carcinoma	11 (26.19)	13 (30.95)	0.233	0.629
Postcricoid area cancer	18 (42.86)	15 (35.71)	0.449	0.503
Tumor staging			0.192	0.661
III	24 (57.14)	22 (52.38)		
IV	18 (42.86)	20 (47.62)		
Pathological types			0.105	0.746
Squamous cell carcinoma	36 (85.71)	37 (88.10)		
Other	6 (14.29)	5 (11.90)		
Residence			0.191	0.662
Urban area	19 (45.24)	21 (50.00)		
Rural area	23 (54.76)	21 (50.00)		

Table 2. Comparison of clinical treatment effect between the two groups

Group	*n*	*Complete remission n (%)*	*Partial remission n (%)*	*Stability n (%)*	*Progression n (%)*	*Objective remission rate*
Experimental group	42	14 (33.33)	16 (38.10)	8 (19.05)	4 (9.52)	71.43% (30/42)
Control group	42	8 (19.05)	13 (30.95)	13 (30.95)	8 (19.05)	50.00% (21/42)
x^2						4.043
p						0.044

Comparison of clinical treatment effect between the two groups

The objective remission rate in the experimental group was significantly higher than that in the control group (p<0.05), as shown in Table 2.

Comparison of vocal function between the two groups before and after treatment

The jitter and shimmer of patients in the two groups after treatment were significantly lower than those before treatment (p<0.05), and the jitter and shimmer in the experimental group after treatment were significantly lower than those in the control group (p<0.05), as shown in Table 3.

Comparison of quality of life scores between the two groups before and after treatment

The quality of life scores of patients in the two groups after treatment were significantly higher than those before treatment (p<0.05), and the quality of life score in the experimental group after treatment was significantly higher than that in the control group (p<0.05), as shown in Figure 2.

Comparison of the incidence of adverse reactions between the two groups

There was no significant difference in the incidence of skin reaction, pharyngeal fistula and infection, while flap necrosis between the two groups

Table 3. Comparison of vocal function between the two groups before and after treatment ($\bar{x}$±s)

Group	*n*	*Time*	*Shimmer (%)*	*Jitter (×10⁹L)*
Experimental group	42	Before treatment	4.83±0.59	1.44±0.19
		After treatment	2.72±0.24	1.12±0.23
Control group	42	Before treatment	4.85±0.61	1.43±0.21
		After treatment	4.08±0.22*	1.23±0.21*

The vocal function of both groups after treatment was significantly lower than that before treatment.* indicates the comparison of vocal function between the experimental group and the control group after treatment (p<0.05).

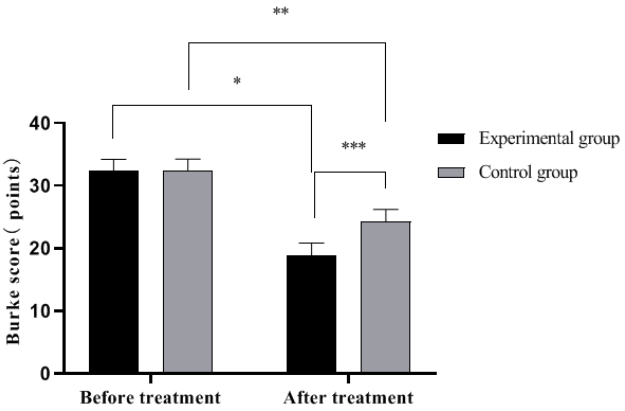

Figure 1. Comparison of Burke scores between the two groups before and after treatment ($\bar{x}$±s). The abscissa represents before treatment and after treatment, and the ordinate represents Burke score (points). The Burke scores of the experimental group before and after treatment were 31.26±2.45 and 17.53±2.76, respectively, while those of the control group were 31.29±2.47 and 23.03±2.64, respectively.
*indicates that there was a significant difference in the Burke scores in the experimental group before and after treatment (t=24.110, p=0.000). **indicates that there was a significant difference in the Burke scores in the control group before and after treatment (t=14.807, p=0.000). ***indicates that there was a significant difference in the Burke scores between the two groups after treatment (t=9.333, p=0.000).

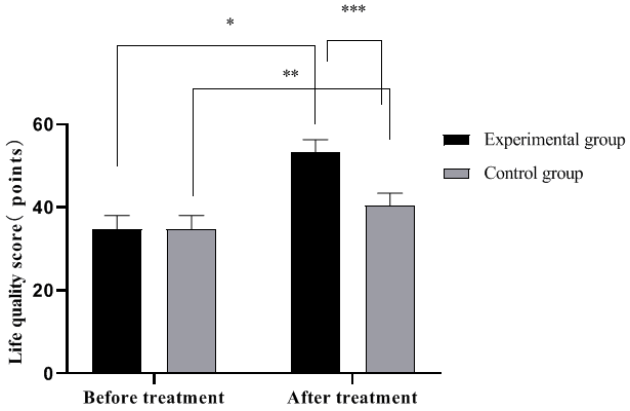

Figure 2. Comparison of quality of life scores between the two groups before and after treatment ($\bar{x}$±s). The abscissa represents before treatment and after treatment, and the ordinate represents quality of life score (points). The quality of life scores of the experimental group before and after treatment were 32.57±4.53 and 51.03±4.37, respectively, while those of the control group were 32.54±4.57 and 38.26±4.29, respectively.
*indicates that there was a significant difference in the quality of life scores in the experimental group before and after treatment (t=19.007, p=0.000); **indicates that there was a significant difference in the quality of life scores in the control group before and after treatment (t=5.914, p=0.000). ***indicates that there was a significant difference in the quality of life scores between the two groups after treatment (t=13.514, p=0.000).

Table 4. Comparison of the incidence of adverse reactions between the two groups

Group	*n*	*Gastrointestinal reactions*	*Skin reactions*	*Neutropenia*	*Pharyngeal fistula and infection*	*Flap necrosis*
Experimental group, n (%)	42	14 (33.33)	17 (40.48)	8 (19.05)	6 (14.29)	7 (16.67)
Control group, n (%)	42	23 (54.76)	15 (35.71)	19 (45.24)	13 (30.95)	13 (30.95)
x^2		3.913	0.202	6.604	3.333	2.363
p		0.048	0.653	0.010	0.068	0.124

Table 5. Comparison of 1-year and 3-year cumulative survival rates after surgery between the two groups

Group	*n*	*1-year cumulative survival rate*	*3-year cumulative survival rate*
Experimental group	42	100% (42/42)	100% (42/42)
Control group	42	95.24% (40/42)	88.10% (37/42)
x^2		2.049	5.317
p		0.152	0.021

after treatment (p>0.05), and the incidence of gastrointestinal reactions and neutropenia in the experimental group after treatment was significantly lower than that in the control group (p<0.05), as shown in Table 4.

Comparison of 1-year and 3-year cumulative survival rates after surgery between the two groups

There was no significant difference in the 1-year cumulative survival rate after surgery between the two groups (p>0.05), and the 3-year cumulative survival rate after surgery in the experimental group was significantly higher in the control group (p<0.05), as shown in Table 5.

Discussion

Studies have shown that squamous cell carcinoma is the main pathological type of hypopharyngeal carcinoma, and its common lesion location is the pyriform sinus, followed by postcricoid area [13-15]. Although the incidence of this tumor is not high, its clinical prognosis is poor. In addition to the indistinct early symptoms and difficulty in diagnosis, its poor prognosis is related to the complex anatomical structure of human hypopharynx and the poor therapeutic effect. Many researchers at home and abroad believe that the conservative non-surgical treatment is the best treatment to retain organ function and improve quality of life [16-18]. With the continuous progress of medical and physics technology, radiotherapy has certain advantages. But for patients with locally advanced hypopharyngeal carcinoma, radiotherapy alone is difficult to achieve an ideal therapeutic effect, so it is necessary to perform CCRT which has the following clinical advantages: (1) Chemotherapy can be used as a sensitizer of radiotherapy to improve the sensitivity of tumor cells to radiotherapy, thus enhancing clinical efficacy ; (2) CCRT can enhance the therapeutic effect of locally advanced hypopharyngeal carcinoma and reduce the incidence of lesion metastasis; (3) Chemotherapeutic drugs make the lesions basically controlled while radiotherapy plays a further consolidation and strengthening role; (4) CCRT can effectively shorten the treatment time and increase the tolerance of patients [19-21].

In this study, the two groups of patients were given adjuvant radiotherapy and CCRT after surgery, respectively. The Burke score of patients in the experimental group after treatment was significantly lower than tat in the control group (p<0.05), indicating that CCRT can significantly improve the swallowing function of patients with locally advanced hypopharyngeal carcinoma, reduce the damage to their laryngeal function and improve their quality of life. Dysphagia can affect food intake and nutrient absorption, and increase the incidence of aspiration pneumonia, adding to the difficulty of treatment [22-24]. This is because the wide resection range due to the large number of pharyngeal lesions affects the swallowing function of patients to a certain extent. In addition, this study confirmed that the objective remission rate and 3-year cumulative survival rate of CCRT after surgery were significantly higher than those of adjuvant radiotherapy after surgery in the treatment of locally advanced hypopharyngeal carcinoma (p<0.05), which was consistent with the results of Linz et al [25] who pointed out in their paper that the objective remission rate of CCRT after surgery (72.36%) was significantly higher than that

of adjuvant radiotherapy after surgery (52.31%) in patients with locally advanced hypopharyngeal carcinoma, fully demonstrating that CCRT can benefit patients in clinical efficacy and survival rate. Surgery, radiotherapy or chemotherapy not only have positive significance in improving head and neck cancer, but also are accompanied by many treatment risks. With the continuous exploration of the pathology and treatment of hypopharyngeal carcinoma, more and more authors consider how to reduce postoperative complications while improving the therapeutic effect of patients [26,27]. There was no significant difference in the incidence of skin reaction, pharyngeal fistula and infection, and flap necrosis between the two groups after treatment ($p>0.05$), while the incidence of gastrointestinal reactions and neutropenia in the experimental group after treatment was significantly lower than in the control group ($p<0.05$), indicating that CCRT can reduce the complications of patients after treatment, with high safety.

In conclusion, CCRT after surgery can significantly improve the swallowing function and vocal function of patients with locally advanced hypopharyngeal carcinoma, with significant efficacy, which is worthy of promotion and application.

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Conflict of interests

The authors declare no conflict of interests.

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