The Feasibility of Selective High-Risk Area Irradiation for Supraglottic Laryngeal Carcinoma With Positive Lymph Nodes Only in Areas II and IIIThe Feasibility of Selective High-Risk Area Irradiation for Supraglottic Laryngeal Carcinoma With Positive Lymph Nodes Only in Areas II and III

jianfeng zhou
Jilin University Second Hospital https://orcid.org/0000-0002-4208-9854
hongyong Wang
Jilin University Second Hospital
li Bian
Jilin University Second Hospital
tiejun Wang (drwangtiejun@yeah.net)
Jilin University Second Hospital

Research

Keywords: laryngeal malignant tumour, positive lymph nodes in areas II and III after operation, selective high-risk area irradiation

Posted Date: December 9th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-122173/v1

Abstract

Objective

To study the prognosis of patients with positive lymph nodes in area II and III after supraglottic laryngocarcinoma surgery and to evaluate the feasibility of selective irradiation of a high-risk area.

Methods

From February 2010 to March 2015, the complete clinical data for 181 patients treated for supraglottic laryngeal cancer at the Radiotherapy Department of the Second Hospital of Jilin University were analysed retrospectively. Among them, 100 patients were treated with whole neck prophylactic irradiation and 81 patients were treated with selective high-risk irradiation; i.e., lymph drainage of areas II and III.

Results

The median follow-up time was 38.5 months; the 5-year OS, PFS, and NFS were 67.9%,58.1%,64.6% respectively. Among them, there were 6 cases of lymph node recurrence, 4 cases of local recurrence, 8 cases of distant metastasis and 58 deaths. However, there was no significant difference in recurrence between the selective high-risk radiation group and the total neck prophylactic radiation group. The OS, PFS and NFS of the two groups were 67.9% vs. 68%, 58.02% and 58%, and 62.9% and 66%, respectively, and the P values were 0.9161, 0.8916 and 0.7333,respectively. For late toxicity resulting from radiotherapy, the incidence of cervical fibrosis (2.47% vs. 10%, $P = 0.043$) and the incidence of throat mucosa injury (6.17% vs. 24%, $P = 0.001$) in patients in the selective high-risk area irradiation group were reduced.

Conclusion

The preliminary data show that selective high-risk area irradiation is safe and feasible for patients with supraglottic laryngeal cancer accompanied by positive lymph nodes only in areas II and III, and the treatment can reduce the long-term adverse reactions and improve the quality of life. However, more evidence is needed.

Purpose And Background

Laryngeal squamous cell carcinoma (LSCC) is one of the most expansive subgroups of head and neck squamous cell carcinoma (HNSCC) and one of the most common malignant tumours in the United States[1]. The incidence of LSCC has increased by 23.1% in the past 10 years[2]. The incidence rate of supraglottic laryngeal carcinoma is second only to laryngeal cancer[3]. The treatment strategy for supraglottic carcinoma lacks unity and the prognosis is relatively poor, so further research is needed. With the improvement in living standards and the progress of medical technology, early diagnosis and treatment will be helpful to improve the prognosis of malignant tumours. However, according to recent American data, the 5-year survival rate of systemic cancer treatment in the United States is on the rise, while the survival rate for laryngeal cancer is on the decline. Therefore, it is necessary to explore the standard treatment of laryngeal cancer.

The supraglottic region is rich in the lymph network[4], and lymph node metastasis shows an orderly pattern, where jumping metastasis is rare. According to the literature, the cervical lymph node metastasis of supraglottic carcinoma is mainly along the jugular vein chain, mainly in zone II, followed by zone III, while rarely involving zone I and zone IV. The incidence of cervical lymph node metastasis in zone II and zone III of supraglottic carcinoma is 79.6% and 7.58%, respectively, but it is only 1% in zone I[5]. Therefore, whether selective neck irradiation is suitable for postoperative lymph node positive irradiation deserves further study.

The purpose of this study is to conduct selective high-risk area irradiation under the premise of considering the characteristics of lymph drainage of supraglottic laryngeal carcinoma in order to ensure that the total survival rate (OS), progression free survival period (PFS), recurrence free survival rate (NFS) and recurrence rate remain unchanged, while at the same time reducing the side effects of radiotherapy and improving the quality of life of patients.

Materials And Methods

Patient and pretreatment assessment:

From February 2010 to March 2015, 181 patients were identified for inclusion in the study. The inclusion criteria were as follows: (1) laryngeal squamous cell carcinoma was confirmed by biopsy; (2) total laryngectomy and lymph node dissection had been performed; (3) postoperative pathology showed that lymph node biopsy was positive, and the positive lymph nodes were only in areas II and III while the rest of the lymph nodes were not metastatic; and (4) preoperative MRI scans of the larynx had been performed.

The pretreatment evaluation included medical history, physical examination, laryngoscope, whole blood cell count, liver and kidney function, chest CT, abdominal ultrasound, neck ultrasound and laryngeal MRI scans. PET-CT and bone scan were performed in symptomatic patients.

Radiotherapy:

Total neck prophylactic irradiation group:

The patient was fixed in the supine position with a thermoplastic mask, and a simulated CT location was performed with 3 mm thickness. The upper boundary of the location was the cranial crest, and the lower boundary was 3 cm below the sternoclavicular joint. PTVtb includes the primary tumour bed area with the prescription dose DT: 60 Gy/30 F; PTV is the whole neck prevention area with the prescription dose DT: 50 gy/25 F. The patients were treated once a day, five times a week.

Selective high-risk area irradiation group:

As shown in Fig. 1, PTVtb includes the primary tumour bed area with the prescription dose DT: 60 Gy/30 F; PTV is a selective high-risk area, i.e., areas II and III, with the prescription dose DT: 50 gy/25 F. Patients were treated once a day, five times a week. The other conditions were the same as the whole neck prophylactic irradiation group.

The difference between the two groups was mainly due to the difference of PTV range. Compared with the whole neck radiation group, the selective high-risk area irradiation group only included areas II and III with higher cervical lymph node metastasis rate of supraglottic laryngeal cancer.

From February 2010 to March 2015, 181 patients were identified for inclusion in the study.Among them, 100 patients received whole neck prophylactic irradiation and 81 patients received selective high-risk area irradiation.

Chemotherapy:

After the treatment, the two groups were given 4-6 cycles of TP sequential chemotherapy of paclitaxel 135 mg/m2, D1 and loplatin 30 mg/m2, D2.

Follow up:

In the first year, patients were rechecked every 1-3 months, and in the second year they were rechecked every 2-6 months.

Patients were rechecked every 4-8 months in years 3-5 and every 12 months in years >5. The examination items included chest X-ray or CT, abdominal ultrasound, neck ultrasound, laryngoscopy, laryngoscope, and routine blood work. If necessary, PET-CT and bone scans were performed.

The OS, PFS, NFS, recurrence rate, injury degree of normal tissue and incidence of late toxicity were counted. Recurrent cases diagnosed by imaging were completed by radiotherapists and radiologists. All endpoints were defined as the time interval from the beginning of treatment to failure or final follow-up. All the data were analysed by SPSS 24.0 statistical software after audit, and the counting data were analysed by chi square tests and t-tests, where significance was established at p = 0.05.

We designed and observed the following indexes of normal tissue injury.

1) Radiation-induced oral mucositis (ROM) is a common complication of radiotherapy for head and neck tumours[6]. Oral mucositis usually occurs 7 to 14 days after the start of chemotherapy or radiotherapy, presenting as erythema, ulcer, bleeding, edoema and pain[7]. These complications may cause oral discomfort in patients, thus delaying the treatment and failing to achieve good therapeutic effect. In addition, the loss of mucosal integrity also increases the chance of infection and endangers the life of patients[8]. With the increase in irradiation dose, there will be corresponding changes in the oral cavity. When the dose of irradiation is 20 Gy, the viscosity of saliva increases; when the dose is 30 Gy, erythema and ulcers occur in the oral mucosa, and the taste is abnormal, which can cause secondary infection and

bleeding; when the dose is 40 Gy, saliva secretion stops; when the dose is 50 Gy, oral mucositis is aggravated, which affects eating; and when the dose is 60-70 Gy, it is difficult to speak and swallow.

The World Health Organization (WHO) evaluated radiation-induced oral mucositis. The evaluation of radiation-induced oral mucosal reaction recommended by WHO consists of 0-IV standard grades. Grade 0: no symptoms and signs; grade I: erythema, mild pain; grade II: painful erythema, edoema, or ulcer, but able to eat; grade III: painful erythema, edoema or ulcer, only able to feed with liquid; and grade IV: unable to eat, requiring parenteral or enteral support.

2) Xerostomia also may occur. Saliva in the mouth mainly comes from the secretion of three glands, the parotid gland, the submandibular gland and the sublingual gland. The parotid gland secretes more than half of the saliva and is very sensitive to radiation. Because the parotid gland is located in the path of radiotherapy, radiotherapy will inevitably cause parotid gland injury. Severe xerostomia can even lead to mandibular necrosis, which seriously affects the quality of life of patients[9, 10]. The function of the parotid gland is to secrete saliva, and saliva secretion can decrease when the accumulative radiation dose reaches 10 Gy at the earliest; after the accumulative dose reaches 40 Gy, the production of parotid gland saliva has basically stopped; and 60 Gy will cause irreversible damage to the parotid gland. According to the RTOG/EORTC grading standard of acute radiation injury[11], the evaluation standard of xerostomia in this study was determined as follows: Grade I: no significant change compared to before radiotherapy; grade II: Patients' subjective feeling of xerostomia, when they eat dry food, they do not need liquids; grade III: when they eat, they must take liquids, otherwise they cannot eat dry food; and grade IV: when they need to wake up and drink water or speak for a long time, and the mouth feels dry.

3) Taste change is one of the early reactions to radiotherapy for head and neck tumours. This phenomenon was first reported in 1955. In recent years, a large number of clinical and experimental studies have been carried out on this phenomenon[12-15]. More people think that the direct damage to the taste buds by radiation is the cause of taste change, but it may also damage the salivary glands and nerves, which indirectly leads to damage of taste buds, or they may exist at the same time[13-15].

4) Difficulty in opening the mouth is a common complication of head and neck cancer patients after radiotherapy. The temporomandibular joint and masseter muscle degenerate and fibrose under the action of radiation, resulting in muscle atrophy and joint stiffness. The temporomandibular joint tightens and aches when the mouth is opened, and a severe case can have difficulty in pronunciation and eating. For the evaluation of difficulty in opening the mouth after radiotherapy, we used the subjective and objective treatment analysis standard, which is divided into four levels: Level I, limited opening of the mouth, 2.1-3.0 cm between the teeth; level II, difficulty in eating dry food, 1.1-2.0 cm between the teeth; level III, difficulty in eating soft food, 0.5-1.0 cm between the teeth; and level IV, less than 0.5 cm between the teeth, unable to eat, and requiring nasal feeding. Bhatiaks et al. defined the gap between the teeth ≤ 2.5 cm as opening difficulty[16].

5) Cervical fibrosis: there are many factors affecting the occurrence of cervical fibrosis after radiotherapy for laryngeal malignant tumour. The higher the dose of radiotherapy, the more serious the degree of cervical fibrosis[17]. From 3 months to half a year after radiotherapy, the edoema of the face and neck gradually subside, and fibrosis of the neck begins to appear; from 1 to 2 years, severe fibrosis of the neck (grade III to IV) gradually forms; and from 4 to 5 years, the capillaries gradually expand. The mechanism of cervical fibrosis after radiotherapy is that the skin and muscle of the neck undergo an inflammatory reaction after irradiation, including vascular endothelial injury, endothelial cell necrosis and shedding, and increased vascular permeability. Leukocytes leak out of the blood vessels and gather at the site of infection and injury; releasing proteolytic enzymes and chemical mediators (tumour necrosis factor, interleukin-1, nitric oxide 5-hydroxytryptamine, histamine, etc.). In addition, oxygen free radicals play a role in phagocytosis and immunity, and cause normal tissue damage[18]. When the tissue damage is serious, a large amount of fibrinogen leaks out, but the leaking cellulose cannot be completely absorbed and gradually continues to deposit in the extracellular matrix, leading to mechanization. Over time, some blood vessels degenerate and the elasticity of the soft tissue disappears, which seriously affects the neck activity function. According to the criteria of late radiation injury, the degree of cervical fibrosis can be divided into the following categories: grade 0, no fibrosis; grade I, mild fibrosis; grade II, moderate fibrosis, no symptoms; grade III, severe fibrosis; and grade IV, tissue necrosis.

6) Laryngopharyngeal mucosa damage: the effects are similar to those of oral mucositis, the laryngopharyngeal mucosa will be damaged after radiotherapy[19]. The clinical manifestations are pharyngeal pain, dysphagia and hoarseness, which can form protracted radioactive pharyngitis. There are mucinous glands in the submucosa of oropharynx and laryngopharynx. The latter can secrete mucus and play a role in moistening mucosa. After irradiation, the secretion function of the salivary gland is inhibited. The mucous membrane is dry and it loses the ability to self-clean, so it is easily infected. Radiation may also directly damage the mucous membrane, resulting in erosion and ulceration of the mucous membrane. Different from the whole neck prophylactic irradiation group, the lower boundary of the target area in the selective high-risk area irradiation group is higher, so the damage to the throat mucosa is avoided. Through laryngoscopy, we can clearly and accurately evaluate the influence of different radiotherapy targets on the mucosa after radiotherapy. The grades of the oropharyngeal mucosa reaction are as follows: grade 0: normal mucosa; grade I: slight congestion of the pharyngeal mucosa; grade II: moderate congestion of the pharyngeal mucosa with edoema; grade III: severe congestion of the pharyngeal mucosa with scattered erosion of the oral mucosa; and grade IV: lamellar ulcer, haemorrhage and necrosis of the pharyngeal mucosa.

Results

Patients and treatment:

Between February 2010 and March 2015, a total of 181 patients who met the standard were identified. The clinical features are listed in Table 1. Among them, 100 patients received whole neck prophylactic irradiation and 81 patients received selective high-risk area irradiation. After radiotherapy, the two groups were given 4-6 cycles of TP sequential chemotherapy. All patients completed the treatment cycle.

Survival and failure:

The median follow-up time was 38.5 months, and there were 8 cases of distant metastasis, 4 cases of local recurrence, 6 cases of lymph node recurrence and 58 cases of death, as shown in Table 2. The five-year OS, PFS and NFS were 67.9%,58.1%,64.6%, respectively. In addition, we also recorded 1 case of tracheoesophageal fistula and 1 case of reflux oesophagitis. According to the data, the main causes of treatment failure are local recurrence, lymph node recurrence, distant metastasis and haemorrhagic shock caused by tumour rupture.

Table 1 Patient characteristics

		Number	Percentile (%)	Selective high risk area irradiation	Whole neck prophylactic irradiation	P
Sex	Male	145	80.1	61	84	0.145
	Female	36	19.9	20	16	
Age	Median	54		53	55	0.775
	Range	31-75		31-72	34-75	
Stage	[illegible]	126	69.2	54	72	0.438
	[illegible]	55	30.8	27	28	

Table 2 Types of treatment failure

	Selective high risk area irradiation	Whole neck prophylactic irradiation
Distant metastasis	2	6
Local recurrence	2	2
Recurrence of lymph nodes	4	2
Deaths	26	32

As shown in Fig. 2, P = 0.9161 was calculated, indicating that there is no significant difference between the two groups in five-year OS (67.9% vs. 68%).

As shown in Fig. 3, the five-year PFS of the two groups was 58.02% and 58%, respectively. After analysis, P = 0.8916 was determined, indicating that there is no significant difference between the two groups in five years PFS.

As shown in Fig. 4, the five-year NFS for the two groups was 62.9% and 66%, respectively. After analysis, P = 0.7333 was determined, indicating that there is no significant difference between the two groups at five years.

Late toxicity

Table 3

	Selective high risk area irradiation	Whole neck prophylactic irradiation	P
Radiation stomatitis	4	6	0.756
Dry mouth	5	3	0.302
Loss of taste	2	3	0.828
Difficulty in opening mouth	1	2	0.688
Fibrosis of neck tissue	2	10	0.043
Laryngeal mucosa injury	5	24	0.001

According to our statistics, pharyngeal and laryngeal mucosal injury was the most common late toxicity in the two groups; 29 people presented this symptom. In addition, cervical fibrosis was also common. The late toxicity is shown in Table 3. All the adverse reactions were mild; i.e., grade I or II. However, the obvious side effects of the two targets were neck fibrosis (P = 0.043) and throat mucosa damage (P = 0.001). There was no significant difference in the frequency of other side effects.

Recurrence of lymph nodes:

During the follow-up period, 6 cases of lymph node recurrence were observed, all in area II and III, as shown in Fig. 5. Among them, there were 4 cases of selective high-risk area irradiation and 2 case of total neck prophylactic irradiation.

Discussion

Supraglottic carcinoma is a kind of malignant tumour with strong infiltration and rapid growth. Because of the abundant supraglottic lymphatics, bilateral cervical lymphadenopathy is very common in local advanced patients, which seriously affects the prognosis of patients[20].

Anatomically speaking, the vocal cords are the boundary between the supraglottic region and the infraglottic region, thus the two regions drain to different lymph nodes. Unlike the development of the glottic and subglottic areas, the lymphatic vessels of the supraglottic area do not anastomose with those of other areas. The main drainage sites of supraglottic laryngeal carcinoma are the deep upper neck and the deep middle neck lymph group (areas II and III). Zhang Lipeng and Wang Xiaolei, of the Head and Neck Surgery Department of Cancer Hospital of Peking Union Medical College, Chinese Academy of Medical Sciences, collected retrospective data for the confirmation of cervical lymph node metastasis after selective neck dissection in areas II, III and IV for patients with supraglottic cancer designated as stage cN0[21]. The same conclusion was reached with anatomy. Sanabria[22] studied the incidence of occult lymph node metastasis in primary laryngeal squamous cell carcinoma (LSCC) and concluded that postoperative prophylactic radiation in areas I, IV and V should not be routinely performed in patients with supraglottic laryngeal carcinoma. Xu[23] analyzed retrospectively the patterns of cervical lymph node metastasis in locally advanced supraglottic laryngeal carcinoma. In 62 patients with unilateral lesions, the occult lymph node metastasis rates of ipsilateral neck II, III and IV were 21%, 11.1% and 1.6%, respectively, while those of contralateral neck were 6.3%, 4.8% and 0%, respectively. Based on the above analysis, the most commonly involved areas of cervical lymph node metastasis in patients with stage cN0 supraglottic cancer are area II and area III, and area III is often associated with area II; area I is rarely involved in cervical lymph nodes; and area V is almost never involved. This provides a theoretical basis for selective high-risk area irradiation of supraglottic laryngeal carcinoma with only positive lymph nodes in areas II and III.

Our study showed that the five-year OS, PFS and NFS were 67.9%,58.1%,64.6%, respectively. The expected effect was achieved. There was no significant difference in OS and PFS between the selective high-risk area group and the whole neck group. As shown in Figure 1-2, the OS and PFS of the two groups are 67.9% vs. 68%, 58.02% and 58% respectively, and the P values are 0.9161 and 0.8916, respectively.

In terms of lymph node recurrence, 6 out of 181 patients had a recurrence rate of 0. Among them, there were 4 cases of selective high-risk area irradiation and 2 case of total neck prophylactic irradiation. As shown in Figure 3, the five-year NFS of the selective high-risk area irradiation group was 62.9%, while it was 66% for the total neck prevention irradiation group ($p= 0.7333$), indicating that both groups could better control the recurrence of lymph nodes.

In terms of late toxicity, the incidence of throat mucosa injury in patients in the selective high-risk area irradiation group was significantly reduced (6.17% vs. 24%, $P = 0.001$); the selective high-risk area irradiation group also avoided the occurrence of late cervical tissue fibrosis to a certain extent (2.47% vs. 10%, $P = 0.043$), as shown in Table 3. There was no significant difference in the incidence of radiation-induced oral mucositis, xerostomia, loss of taste and difficulty in opening the mouth; the P values were 0.756, 0.302, 0.828 and 0.688, respectively. An analysis of the causes suggests selective high-risk area irradiation and whole neck prophylactic irradiation. Targeting the two areas has no effect on the oral mucosa, parotid gland, salivary gland, temporomandibular joint and the normal tissue of masseter muscle, so there is no significant difference in the incidence of the abovementioned adverse reactions.

In conclusion, our study is the first report of selective high-risk area irradiation after supraglottic laryngeal cancer with positive lymph nodes in areas II and III. In terms of OS, PFS and relapse free survival rate of lymph nodes (NFS), the effect of selective high-risk area irradiation is not inferior to that of whole neck pre-irradiation. We have reason to believe that selective high-risk area irradiation is safe and feasible for patients with supraglottic laryngeal cancer only accompanied by positive lymph nodes in areas II and III. In addition, selective high-risk area irradiation can reduce the amount of normal tissue, reduce long-term adverse reactions and improve the quality of life.

Because of the relatively small sample size and relatively short follow-up time, this study can only be used as a preliminary study at present. A larger number of patients and a longer follow-up time are required to evaluate the safety and feasibility of selective high-risk area irradiation.

Abbreviations

OS :overall survival rate;

PFS:progression-free survival;

NFS:nodal recurrence-free survival;

LSCC: laryngeal squamous cell carcinoma;

HNSCC :head and neck squamous cell carcinoma ;

CT: Computed Tomography;

MRI: Magnetic Resonance Imaging;

PET-CT: Positron Emission Tomography-Computed Tomography;

PTV: Planning target volume;

PTVtb:Planning target volume tumor bed;

ROM :Radiation-induced oral mucositis;

WHO :World Health Organization ;

RTOG;Radiation Therapy Oncology Group;

EORTC:The European O-rganization for Reasearch and Treatment of Cancer;

Declarations

Ethical Approval and Consent to participate

The ethical committee of the second hospital of Jilin University approved the research plan. Informed consent application has been exempted.

Consent for publication

Not applicable.

Availability of supporting data

The datasets are available to all interested researchers on reasonable request from corresponding author.

Competing interests

The authors declare that they have no competing interests.

Funding

No fundings.

Authors' contributions

Jianfeng Zhou and Hongyong Wang take responsibility of the content and writing of manuscript. These authors contributed equally to this study and share first authorship. Li Bian collected data. Tiejun Wang reviewed manuscript and approved fnal manuscript.

Acknowledgements

Authors wish to thank numerous individuals participated in this study.

Authors' information (Optional)

[1] Department of radiotherapy,Jilin University Second Hospital,218 Ziqiang street, Changchun, 130000, China.

References

1. Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 2017; 3(4):524-548.
2. McDermott JD, Bowles DW. Epidemiology of Head and Neck Squamous Cell Carcinomas: Impact on Staging and Prevention Strategies. Curr Treat Options Oncol. 2019; 20(5):43.
3. Yılmaz T, Süslü N, Atay G, Günaydın RÖ, Bajin MD, Özer S. The effect of midline crossing of lateral supraglottic cancer on contralateral cervical lymph node metastasis. Acta Otolaryngol. 2015;

135(5):484-8.

4. PRESSMAN JJ, SIMON MB, MONELL CM. Anatomic studies related to the dissemination of cancer of the larynx. Cancer. 1961; 14:1131-8.
5. Lim YC, Choi EC, Lee JS, Koo BS, Song MH, Shin HA. Is dissection of level IV absolutely necessary in elective lateral neck dissection for clinically N0 laryngeal carcinoma. Oral Oncol. 2006; 42(1):102-7.
6. Maria OM, Eliopoulos N, Muanza T. Radiation-Induced Oral Mucositis. Front Oncol. 2017; 7:89.
7. Redding SW. Cancer therapy-related oral mucositis. J Dent Educ. 2005; 69(8):919-29.
8. Wang Y, Zhou X, Xu X. Oral microbiota: an overlooked etiology for chemotherapy-induced oral mucositis. J Formos Med Assoc. 2015; 114(4):297-9.
9. Vikram B, Mishra UB, Strong EW, Manolatos S. Patterns of failure in carcinoma of the nasopharynx: I. Failure at the primary site. Int J Radiat Oncol Biol Phys. 1985; 11(8):1455-9.
10. Cooper JS, Fu K, Marks J, Silverman S. Late effects of radiation therapy in the head and neck region. Int J Radiat Oncol Biol Phys. 1995; 31(5):1141-64.
11. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995; 31(5):1341-6.
12. Conger AD, Wells MA. Radiation and aging effect on taste structure and function. Radiat Res. 1969; 37(1):31-49.
13. Shatzman AR, Mossman KL. Radiation effects on bovine taste bud membranes. Radiat Res. 1982; 92(2):353-8.
14. Tomita Y, Osaki T. Gustatory impairment and salivary gland pathophysiology in relation to oral cancer treatment. Int J Oral Maxillofac Surg. 1990; 19(5):299-304.
15. Mossman KL. Frequent short-term oral complications of head and neck radiotherapy. Ear Nose Throat J. 1994; 73(5):316-20.
16. Bhatia KS, King AD, Paunipagar BK, et al. MRI findings in patients with severe trismus following radiotherapy for nasopharyngeal carcinoma. Eur Radiol. 2009; 19(11):2586-93.
17. OuYang PY, Shi D, Sun R, et al. Effect of intensity-modulated radiotherapy versus two-dimensional conventional radiotherapy alone in nasopharyngeal carcinoma. Oncotarget. 2016; 7(22):33408-17.
18. Greenleaf JF, Fatemi M, Insana M. Selected methods for imaging elastic properties of biological tissues. Annu Rev Biomed Eng. 2003; 5:57-78.
19. Sangthawan D, Phungrassami T, Sinkitjarurnchai W. A randomized double-blind, placebo-controlled trial of zinc sulfate supplementation for alleviation of radiation-induced oral mucositis and pharyngitis in head and neck cancer patients. J Med Assoc Thai. 2013; 96(1):69-76.
20. Thompson CF, St John MA, Lawson G, Grogan T, Elashoff D, Mendelsohn AH. Diagnostic value of sentinel lymph node biopsy in head and neck cancer: a meta-analysis. Eur Arch Otorhinolaryngol. 2013; 270(7):2115-22.

21. Zhang L P, Wang X L. The research progress of cervical lymph node metastasis in supraglottic cancer patients with cN0. Chinese Journal of coal industry medicine. 2018; 21(01):91-94.
22. Sanabria A, Shah JP, Medina JE, et al. Incidence of Occult Lymph Node Metastasis in Primary Larynx Squamous Cell Carcinoma, by Subsite, T Classification and Neck Level: A Systematic Review. Cancers (Basel). 2020; 12(4).
23. Xu Y, Zhang Y, Xu Z, et al. Patterns of Cervical Lymph Node Metastasis in Locally Advanced Supraglottic Squamous Cell Carcinoma: Implications for Neck CTV Delineation. Front Oncol. 2020; 10:1596.

Figures

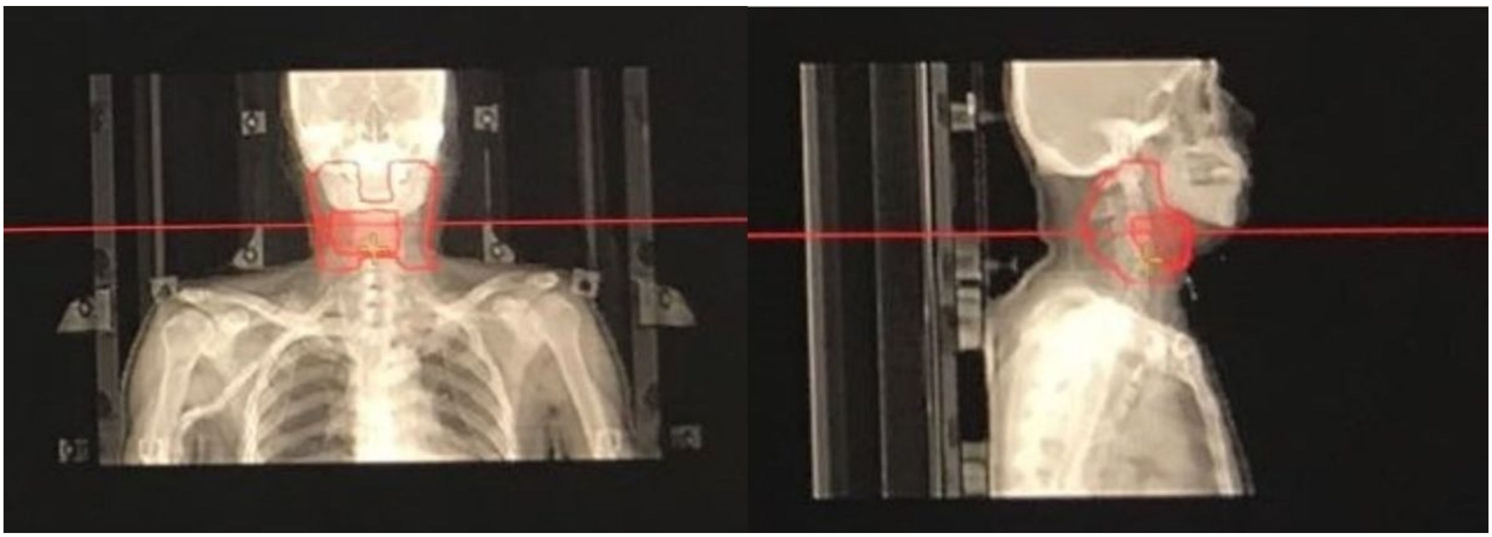

Figure 1

PTVtb includes the primary tumour bed area with the prescription dose DT: 60 Gy/30 F; PTV is a selective high-risk area, i.e., areas II and III, with the prescription dose DT: 50 gy/25 F. Patients were treated once a day, five times a week. The other conditions were the same as the whole neck prophylactic irradiation group.

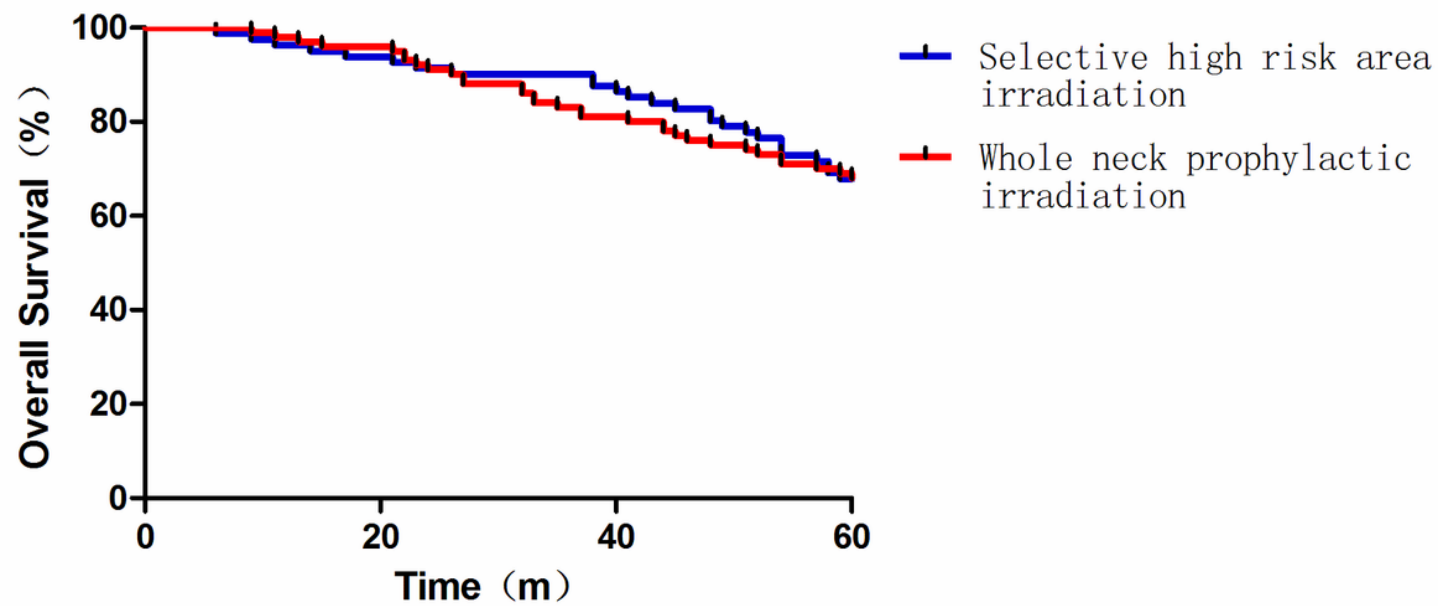

Fig.2

Figure 2

P = 0.9161 was calculated, indicating that there is no significant difference between the two groups in five-year OS (67.9% vs. 68%).

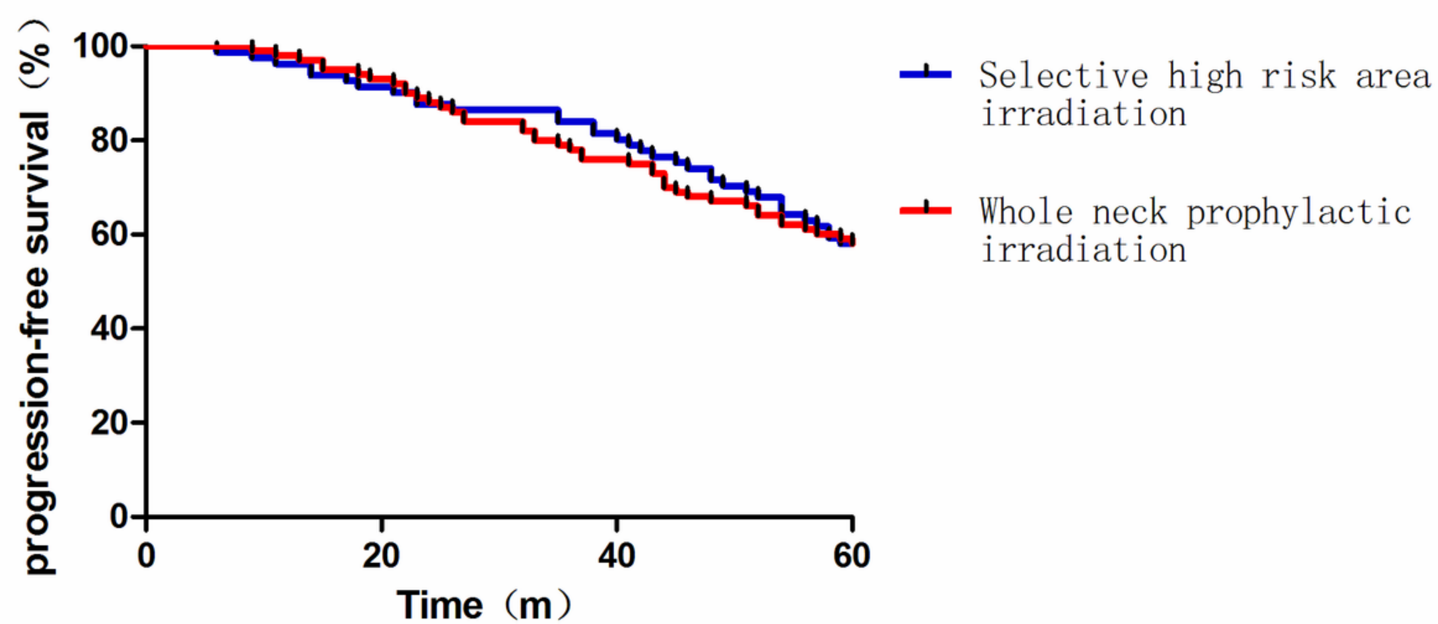

Fig.3

Figure 3

The five-year PFS of the two groups was 58.02% and 58%, respectively. After analysis, P = 0.8916 was determined, indicating that there is no significant difference between the two groups in five years PFS.

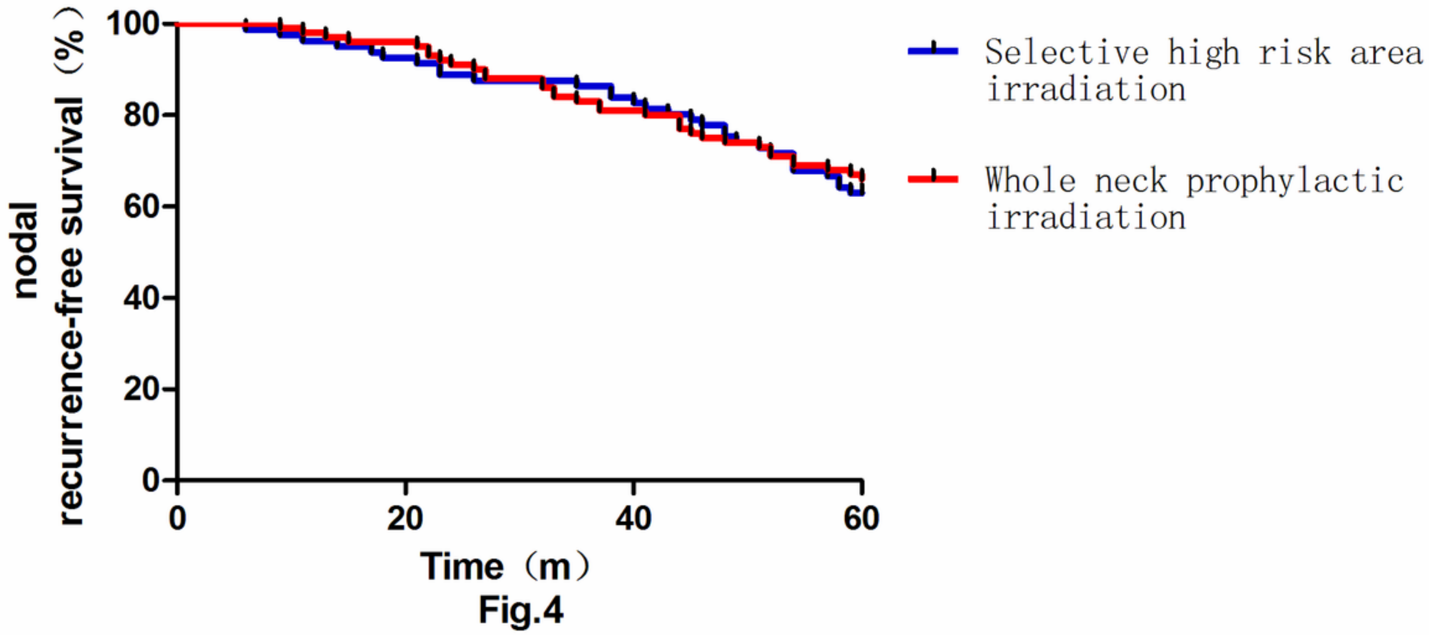

Figure 4

The five-year NFS for the two groups was 62.9% and 66%, respectively. After analysis, P = 0.7333 was determined, indicating that there is no significant difference between the two groups at five years.

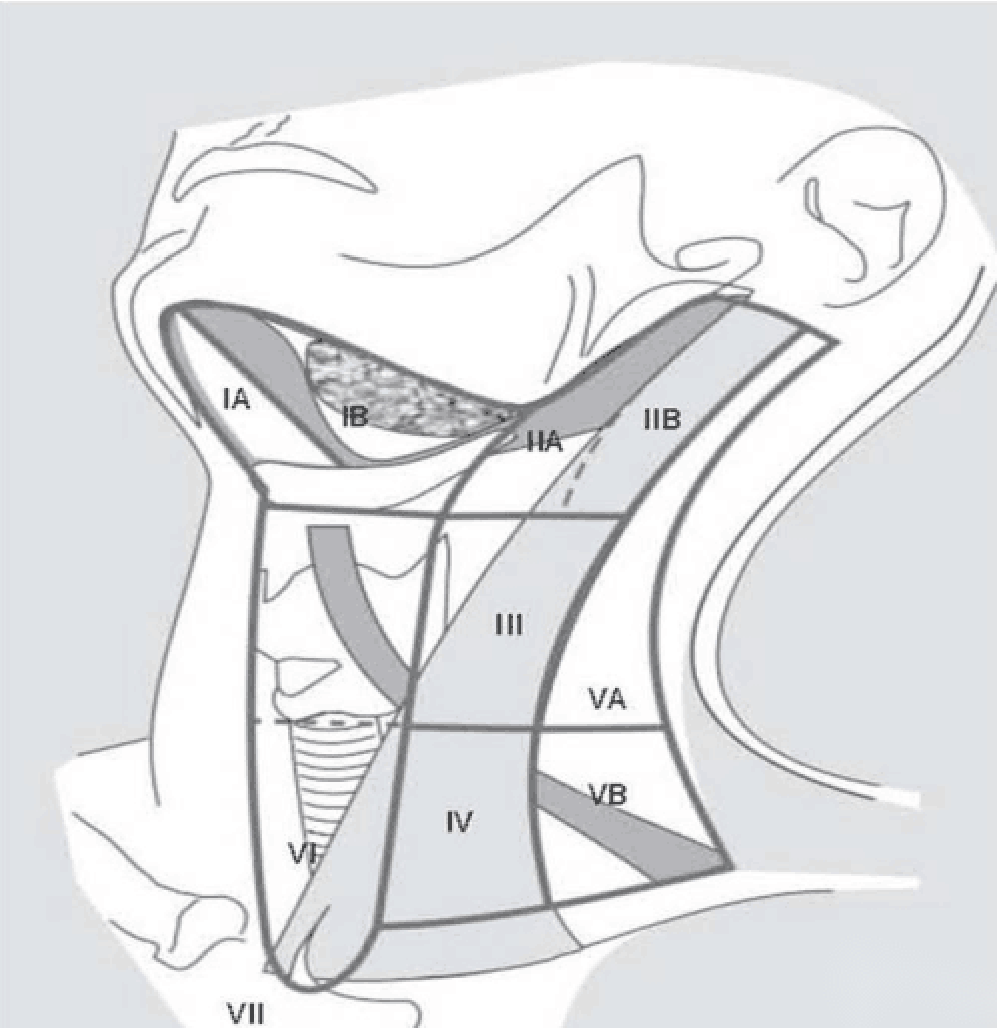

Figure 5

Among them, there were 4 cases of selective high-risk area irradiation and 2 case of total neck prophylactic irradiation.