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Comparative Study Of The Results Of Treatment With A Modern Modified Method Of Separating Lymph Nodes For Throat Cancer

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ABSTRACT

The results of studies conducted to date worldwide show that one of the most important prognostic signs of head and neck squamous cell carcinoma is the presence of metastases. Tumours of the oropharynx are complex anatomically and histologically because of the specificity for the detection of metastases in the thorax, computed tomography or magnetic resonance imaging of the chest is performed. In malignant tumours of head and neck organs spread locally, then metastasise to adjacent lymph nodes in the neck. Spread to local lymph nodes is partly related to tumour size, grade and aggressiveness.

Keywords: *head and neck tumours, regional metastases, treatment*

1. INTRODUCTION

Today, a number of research projects are being conducted in the world to develop new approaches to effective diagnosis and treatment of complications of oropharyngeal tumours, including justification of its metastases to lymph nodes, development of a new method of extended lymphadenectomy with resection of the nervous and vascular system in metastatic lesions of lymph nodes of head and neck tumours improvement of modern methods of measures to reduce disability and mortality of patients with oropharyngeal tumours. Cervical lymphodissection was performed according to the standards accepted in Russia and Uzbekistan. Patients were operated on 4-6 weeks after the end of remote radiotherapy in case of complete response of the primary tumour. In case of incomplete effect of the primary focus on radiotherapy or chemoradiation therapy, as well as in case of residual tumours, one-stage operations were performed on the primary focus and on the areas of regional metastasis. Clinical effect was assessed on the basis of direct examination data in case of nasopharyngeal, laryngeal and pharyngeal tumours on the basis of endoscopic examination with biopsy. Cervical lymphodissection was performed in the presence of metastatic lesions of lymph nodes, incomplete regression of metastases after irradiation. If treatment was started with surgical intervention, cervical lymphodissection was performed simultaneously with removal of the primary tumour or delayed lymphodissection was performed. In case of bilateral metastatic lymph node involvement

The technique of performing extended lymphodissection. After general endotracheal anaesthesia, the patient's position on the operating table is lying down with a roll under the shoulders, head tilted and turned to the opposite side of the tumour.

T-shaped skin incision. The horizontal part of the incision is made 2 cm below the chin, parallel to the edge of the mandible to the posterior edge of the sternoclaviculo-osceous muscle, the vertical part - from the intersection of the horizontal part with the anterior edge of the sternoclaviculo-osceous muscle down to its lateral stem. The skin together with subcutaneous fatty tissue is cut off to the sides to the levels of the anterior edge of the trapezius muscle, clavicle, midline of the neck and I cm above the lower edge of the mandible. The external jugular vein is ligated and crossed.

The skin flaps are cut off to the sides on the same borders as at the fascial-futlar excision of the neck fibre and lymph nodes. Above the clavicle from the sternum to the trapezius muscle dissect the superficial fascia with the saphenous muscle and the own fascia of the neck. Mobilise the tissues of the supraclavicular region and expose the legs of the sternoclavicular-papillary muscle. The legs of this muscle are crossed and ligated at the place of attachment to the sternum and clavicle. The internal jugular vein at the level of the clavicle is ligated and crossed, its stump is additionally sutured with silk ligature.

The tissues are dissected along the midline of the neck. After dissecting the tissues along the trapezius muscle, the fibre of the lateral triangle of the neck is isolated. Expose the ladder muscles

Next, the adventitia of the common carotid artery is dissected along the line running from the medial wall of the internal carotid to the lateral wall of the common carotid 1 cm below the branch of the trunk of the external carotid artery. After separation of the adventitia from the media, a direct vascular clamp is applied, and the lymph node block with the mouth of the external carotid artery is severed. A continuous vertical vertical return suture with 4/0 prolene thread is applied, thus creating a direct blood flow from the common carotid to the internal carotid with cone-shaped modulation of the vessel lumen. The mouth of the external carotid artery with its branches and the surrounding fibre is mobilised distally upwards to the submandibular region. The branches of the external carotid artery are ligated and resected and sutured. Removal of the entire tissue block is completed in the jawline region. After haemostasis, a rubber drain is inserted into the wound through the contraperitoneum and active aspiration is established for 2-3 days.

During the fascial-futlar excision of subcutaneous fatty tissue of the neck, Kreil's operation and our method sometimes complications develop. Most often nerve trunks are injured: the marginal branch of the facial, hyoid, lingual, vagus, diaphragmatic, sympathetic nerves. With trauma to the vagus nerve, there are dysfunctions of many organs. In traumatic release of the nerve is recommended to inject into its sheath 0.5% solution of Novocain. Cases of cardiac arrest during induction anaesthesia have been described. In this case, it is necessary to carry out vigorous resuscitation measures. When isolating subcutaneous fat.

Small tumours were cured by surgery or radiation with equal efficacy. However, the radiation method allowed for a better functional outcome. The irradiation fields were the same as for the root of the tongue, but the posterior border of the field was in the middle of the vertebral bodies. Taking into account the fact that most tumours of this localisation are located close to the midline, irradiation of lymph nodes on both sides (levels II, III, IV) was performed in all patients. In case of tumours of the posterior pharyngeal wall the pharyngeal lymph nodes were additionally irradiated. Areas of regional metastasis were irradiated from anterior or anteroposterior fields. For multiple metastases of posterior pharyngeal wall and soft palate cancer, lymph nodes including levels I, II, III, IV, An one or both sides of the neck) and pharyngeal lymph nodes were irradiated. Patients with advanced disease were treated with combination and chemoradiation. Surgical interventions were performed in the presence of residual tumour and/or metastases after treatment. The main treatment modalities for nasopharyngeal cancer are radiation and chemoradiation. The cervical lymph nodes were always irradiated bilaterally for curative or prophylactic purposes. Surgical interventions were used very rarely (removal of recurrent tumours in case of impossibility to perform repeated irradiation or radical cervical lymphodissection in case of incomplete regression of metastases after chemoradiation treatment).

Purpose of the study: to improve the results of surgical treatment of patients with oropharyngeal tumours with regional metastases to the neck lymph nodes by improving the extended lymphadissection with resection of the neck vascular-nervous structures.

Material and methods: The study included 615 patients who received treatment in RSNPMCRC of MH RUz (84 patients), P.A. Herzen Research Institute (388 patients) and Bukhara regional branch of RSNPMCRC (143 patients) from 2000 to 2012 with squamous cell cancer of oropharyngeal region with metastases to lymph nodes of the neck. Patients with malignant tumours of oropharyngeal organs with metastases to lymph nodes of the neck, taking into account the tumour prevalence and the location of the primary tumour. Clinical, laboratory, radiological, ultrasound, morphological, MRI and MSCT studies, surgical, chemotherapeutic, combined treatment and statistical methods were used in the study.

2. RESULT

In this chapter, we will present the results of combined and complex treatment of pharyngeal cancer. When evaluating the treatment results, we will take into account not only the immediate and distant results of the combined treatment, but also the severity of pathomorphosis, immediate and distant complications, the percentage of disability and measures for their prevention. In accordance with the aim and objectives of the study, we will focus on the comparative results between the two methods of neck lymph node dissection (radical and modified).

As it was mentioned in the previous chapter, our study is based on retrospective and prospective study of treatment results of 258 patients from 2002 to 2012 who were treated in RSNPMCRC of MH RUz, P.A.Herzen MNIOI and Bukhara regional branch of RSNPMCRC for pharyngeal tumours.

Under the conditions of our study, all patients had their diagnosis confirmed by morphological methods. A 100% correct result was obtained by taking three biopsies. The histological structure of the tumour is shown in Table 1.

Table 1:Histological structure of nasopharyngeal tumours included in the study

Histological structure of the tumour	Number of incidents	
	Main	Control

Squamous cell carcinoma	44 (39,9%)	41 (28,3%)
Neocorneal carcinoma: without lymphoid stroma with lymphoid stroma	 23 (20,4%) 12 (10,6%)	 32 (22,1%) 35 (24,1%)
Undifferentiated carcinoma: without lymphoid stroma with lymphoid stroma	 13 (11,5%) 10 (8,8%)	 25 (17,2%) 20 (13,8%)
Total n = 258	n = 113	n = 145

The table1 shows that 1/3 of all patients had squamous cell tumour structure, and the most common tumour found in patients was neorhoveal carcinoma (43.4%). Approximately the same results were obtained by conventional and posterior rhinoscopy. The incidence of ipsilateral recurrence with or without tumour recurrence elsewhere in patients who had viable tumour cells in histological preparations of cervical lymph nodes was 14%, and in patients who did not have viable tumour cells in histological preparations the recurrence rate was 2.5%. The risk of ipsilateral recurrence was almost the same in patients with complete effect as in those with incomplete or no effect.

The incidence of ipsilateral and overall recurrence in patients with viable tumour cells in biopsy specimens from cervical lymph nodes was twice as high as in patients in complete remission after chemoradiation or distant radiotherapy (80%). There was a significant difference when comparing the two groups with respect to specific causes of death ($p = 0.014$).The incidence of cause-specific mortality was 73% in patients with complete effect and viable tumour cells compared with patients with partial effect or no effect and viable tumour cells 43%. Overall survival was 62% and disease-specific survival was 76%. There were no significant differences in disease-specific survival between N1 patients (23.5%) and patients with N2-3 (23.8%) ($p = 0.91$). There were also no differences between groups when comparing only patients with complete effect ($p = 0.95$).

Patients with tumours of the tonsils or base of the tongue, had a significantly better clinical outcome with a disease specific survival rate of 87.3% compared to 67.9% of patients with tumours of all other localisations.

Patients after remote radiotherapy who had viable tumour cells in biopsy specimens from cervical lymph nodes had a worse prognosis in terms of mortality as a result of disease progression by 52%, compared with 10% of patients without viable tumour cells in the neck region.

Outcome of complications

We studied the difference in neck movement volume and mouth opening between the modified cervical lymphodissection and radical lymphodissection groups from the start of radiotherapy and chemoradiotherapy to 12 months after treatment. There was a significant reduction in all three parameters of neck movement volume and mouth opening in patients, after modified and radical cervical lymphodissection, at two months after treatment ($p<0.001$). Twelve months after treatment, there was still a significant reduction in neck rotation, but other parameters were at nonsignificant levels. In addition, no significant difference in lymphatic circulation was found between the two groups after 12 months.

Treatment outcomes

There was no difference in neck movement volume and mouth opening between patients who underwent radical cervical lymphatic dissection (RCLD) and modified cervical lymphatic dissection (MCLD), from the start of treatment to CRT or DLT until 12 months after treatment. There was a significant reduction in all three parameters of neck movement volume and mouth opening ability in patients after modified and radical cervical lymphatic dissection at 2 months after treatment ($p<0.001$). At 12 months after treatment, there was still a significant reduction in rotational movements in the neck, but its effect on other parameters was negligible.

There was also no effect on the assessed parameters at any time point during the first year of radical cervical lymphodissection. In addition, there was no significant difference in the duration of lymphedema between the two groups after 12 months.

The patient groups after 12 months became smaller than initially due to loss of patients from recurrence or death (N = 33), and from unknown causes (N = 24). Recurrence of the primary focus was equally frequent in both the primary (7.9%) and control groups (8.9%). The development of metastases in deeper layers of the neck occurred mainly in patients with RSLD

(11.7%) and exceeded three times in comparison with MSLD (2.7%).

The total number of patients with shoulder dysfunction in patients after cervical lymphodissection was 17.0%. There was a large numerical difference between patients who underwent MSLD (12.4%) and those who underwent RSLD (20.7%). But there was no significant difference in the prevalence of swallowing disorders between patients of RSLD (32.4%), and patients after MSLD (30.1%) (p = 0.053).

Comparisons of cervical movement volume and mouth opening between post-RSLD and MSLD patients were as follows. Cervical movement volume and mouth opening volume at 12 months were satisfactory 67 and 52 patients, respectively (p>0.05). There were no significant differences in weight loss between the main (-5.9 kg) and control groups (-6.2 kg). There was a slight difference in the frequency of patients with weight loss >10%, in the control group, but this difference was not significant. The overall 2-year survival rate for all patients in the study (of n = 258 at the beginning of the second year, n=194 patients) was 74.7% (n=145). There was a significant difference in 2-year survival between the main (n = 89; 78.8%) and control groups (n=105, 72.4%) (log rank, p = 0.49). The difference of 5% is due to the fact that the patients subjected to RSCLC more often had recurrence of metastases in deep layers of the neck. 5 - year survival rate of the patients differed significantly. In patients of the control group this index did not exceed 52,2% (83 patients), whereas in the main group this index was 78 patients (69%) (p<0,01)

Table 2: Results of 5 - year survival of patients with pharyngeal tumours in patients of the main and control groups

Surgical treatment	3-year survival rate	5-year survival rate
Radical cervical lymphodissection n=145	105 (72,4%)	83 (52,2%)
Modified cervical lymphodissection n=113	89 (78,8%)	78 (69%)
Total n=258	194 (75,2%)	161 (62,4%)

The best indicators as expected were registered in patients with modified SHLD, which is associated with the low traumatic nature of this operation and the possibility of more radical removal of lymph nodes from the deep layers of the neck.

3. FUNCTIONAL IMPAIRMENT

Patients in the modified lymphodissection group had significantly less difficulty swallowing than those in the main group, with a proportional odds ratio (OR) of 2.3 (95% CI: 1.3-4.0). In the main group, 58% responded that they could swallow food of any consistency compared with 35% in the main group (p < 0.001).

There were significantly more patients using increased calorie and protein supplements in the study group (60%) than in the control group (32%) (p<0.001) (p<0.001). The overall incidence of swallowing disorders was 61% and the number of patients presenting complaints of dry mouth was 92%; the number of ‘very huge’ problem with dry mouth, was 41%. The severity of these complications depended on the mode and regimen of chemotherapy and radiotherapy.

There was a significant difference in the extent of neck and shoulder stiffness problems at 6 months after stopping treatment. The odds ratio was 1.9 (95%) with an increased risk of reduced ability to open the mouth in the main group compared to the control group.

4. QUALITY OF LIFE AND DEPRESSION

There were no significant differences between the study groups 6 months after treatment discontinuation according to the parameters of the EORTC questionnaires. After six months post-treatment, the overall rate of depression of any severity (mild and severe) was 27%.

5. CONCLUSIONS

In conducting this work, we complied with all the terms of the Helsinki Agreement on the Conditions for Conducting Clinical Trials. Only treatments recognised as effective by international standards were performed.

The choice of treatment for oropharyngeal tumours is always based on the possible risk of residual tumour after radiotherapy and the reduced risk of recurrence with possible disease progression induced by LD. The earliest studies on morbidity and clinical outcomes from neck dissection are retrospective and therefore have a low level of evidence, whereas our study is both retrospective and prospective, including long-term follow-up data on patients, making adjustments to baseline values possible.

The patients were divided according to the method of combined and complex treatment into three treatment groups. The patients underwent a course of radiation or chemoradiation therapy before or in the postoperative period, both in the zone of the primary focus and in the zone of the regional lymphatic collector. Various operations on the primary focus with one-

stage or delayed cervical lymph node dissection were performed.

According to the aim and objectives of the study, we studied in a comparative aspect the method of modified lymph node dissection developed by us and the classical variant of lymphodissection.

We studied not only the peculiarities of the course of the operative and postoperative period, but also the influence of various factors on the immediate and long-term results of treatment, on the quality of life. In order to develop specific recommendations on the application of this or that method of dissection, the peculiarities of metastasis to regional lymph nodes of tumours of different localizations were studied. In this case the affection of regional metastatic nodes on the side of the primary focus was noted in 68,9% of patients, on the side opposite to the process - in 12,2% of patients and bilateral metastases were revealed in 18,9%.

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