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ABSTRACT

of the dissertation for the degree of Doctor of Science

EVALUATION OF SURGICAL RECONSTRUCTION MEASURES BASED ON QUALITY OF LIFE IN THE TREATMENT OF PATIENTS WITH ORAL CANCER

Speciality: 3226.01- Stomatology

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Applicant: **Mahammad Mirabdulla Davudov**

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Dissertation has been fulfilled in the departments of Oral and maxillofacial surgery and Oncology and Cancer Institute of Tehran University of Medical Sciences

Scientific advisor: professor **İraj Harirchi**

Official opponents: doctor of medical sciences, professor
Zohrab İslam Garayev

doctor of medical sciences, professor
Afat Rashid Aghazada

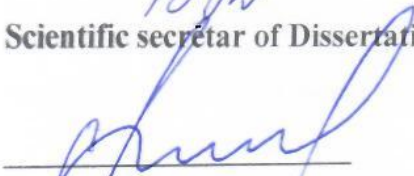
doctor of medical sciences, professor
Sergei Oleqovich Podvyaznikov

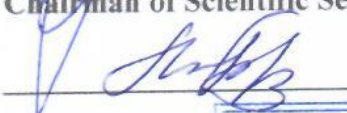
doctor of medical sciences
Mikhail Alekseievich Kropotov

Dissertation council of Supreme Attestation Commission under the (BED 2.05) President of the Republic of Azerbaijan operating at Azerbaijan Medical University

Chairman of Dissertation council: doctor of medical sciences,

Vafa Mustafa Panahian

Scientific secretar of Dissertation council:
doctor of medical sciences,
professor

Agha Chingiz Pashayev

Chairman of Scientific Seminar: doctor of medical sciences,
professor

Rizvan Movsum Mammadov



GENERAL CHARACTERISTICS OF RESEARCH

Actuality of the problem: According to world statistics, 640,000 people are diagnosed with head and neck cancer each year.¹ Among other oncological diseases, this figure ranks 6th (5-8%) and about 350,000 people die from this disease.² Among them, cancer of the mucous membranes of the lips and mouth is more common, and according to the International Agency for Research on Cancer (IARC), this figure is the 10th highest among all tumors (2-5%). With the application of modern treatment methods, mortality rates in these diseases have recently decreased, and survival rates have increased significantly.³ However, long-term survival alone is not sufficient to assess treatment success.⁴ This is especially true for tumors of the maxillofacial region: after extensive surgery, there is a loss of both vital functions and aesthetic indicators. In addition, side effects of radiation and chemotherapy (xerostomia, etc.) are intolerable for patients.⁵ Due to the lack of adequate rehabilitation measures for these patients, their quality of life decreases, affecting their physical, mental and social conditions, leading to great suffering.

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Oral cancer refers to cancer of the oral cavity and adjacent anatomical structures. According to the frequency of occurrence, oral cancer is a systemic cancer and ranks sixth among head and neck cancers.⁶

The incidence of oral cancer is increasing globally, and developing countries have a higher incidence and mortality rate of oral cancer than in developed countries.⁷

As for the specific location and structure that characterizes the condition of oral cancer, both the disease process and its treatment can significantly affect the appearance of the body and the life activities of patients, including the most important functions such as breathing, speaking, swallowing and eating.⁸ For example, in a study comparing quality of life (QOL), variables such as pain, speech, and shoulder function in the selective neck dissection and non-dissection groups showed that the neck dissection group had a weak QOL.⁹ In the last six decades, the mortality rate among these patients has decreased, while the five-year survival rate has increased.

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For this reason, the development of QOL has attracted the attention of the health community.¹⁰

In addition, HK assessment has been shown to be important in assessing patients' living conditions and providing clinical strategies. Primary tumor resection is the treatment of choice for the treatment of oral cancer and complex jaw defects involving soft tissues, bones, and teeth. Treatment can cause severe injuries, as it can disrupt the function of the oral masses, destroy beauty lines, and thus result in poor QOL. However, reconstruction can help patients overcome these problems to some extent. Reconstruction significantly aids oral functions such as speaking, swallowing, and chewing.

There are different methods of resection and reconstruction for the treatment of oral cancer. However, the quality and quantity of defects is one of the main factors in the choice of technique and indicates the success of tissue reconstruction treatment. The size of the jawbone, in addition to its main function, significantly affects the appearance of the human body. Reconstruction can cause changes by improving facial appearance and individuals' QOL.¹¹ Mandibular resection is an expensive and clinically difficult procedure. The lack of evidence-based guidelines prevents the comprehensive use of this therapeutic approach.¹²

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Many cross-sectional and longitudinal studies have been conducted on the subject (repeated collection of data for the same subject over a period of time), but only a few retrospective studies have been performed to compare QOL results after implant-based rehabilitation. Quality of life is a criterion that encompasses many of these variables and can be considered a specific criterion for factors such as death, illness, survival, and re-examination.

In recent years, the patient's quality of life has played a very important role in monitoring the success of treatment and its process.¹³

This is an important factor in evaluating the treatment process, and for the first time, the patient may be able to evaluate the treatment himself. Oral cancer is 10 times more common in men. Assessment of quality of life should reflect the success of multidisciplinary therapy and refer to areas where people need protection.¹⁴

Many QOL studies in the field of head and neck cancer are based on the patient's heterogeneity according to the location and stage of tumor development and are usually retrospective. Only a few perspective studies are focused on the anatomical field. Other information on HK parameters, in the form of individual or clinical observations, was placed post-operatively at retail based on important factors in the literature, and a small portion was supported by statistical analysis.¹⁵

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Cancer and the side effects of its treatment often lead to a decrease in quality of life.¹⁶ Although advances in cancer treatment have improved outcomes, the disease still has a significant impact on patients' physical and psychological well-being.¹⁷

It can also affect patients' social performance and mental health.¹⁸ First of all, it is argued that even if the tumor is completely cured, the quality of life of cancer patients can be severely impaired. This is especially true for some cancers of the spinal cord, cerebellum, salivary glands, eye socket, inner ear, jaw, and mouth.

Treatment and surgery for head and neck cancers often result in anatomical changes in the oral cavity that can lead to severe dysfunction such as speech, chewing, and swallowing. In addition, such treatment can affect patients' appearance, pain, and suffering in a way that can change the quality of life in these patients. These undesirable conditions often occur due to postoperative radiotherapy, which requires application. Until recently, neither rehabilitation nor reconstruction or conventional prosthetics have been able to solve these problems successfully. Therefore, the selection of appropriate reconstruction techniques when treating these patients seems to be an important parameter.

However, improving health-related quality of life remains important for these patients, regardless of different treatment regimens and reconstructive procedures. A study of patients with head and neck cancer showed that even higher than the treatment regimen, the basic quality of life and complications affected the quality of life after treatment.

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In addition, a long-term multicenter study of quality of life and psychosocial outcomes after oropharyngeal cancer surgery and free flap reconstruction of the mandible stated that psychosocial difficulties were a key determinant of long-term quality of life and suggested multidisciplinary management of these patients. Thus, this study aimed to obtain a more careful and detailed approach to assessing quality of life in different patient groups in addition to existing knowledge on the subject.

Thus, the selection of appropriate surgical rehabilitation measures for patients from this contingent remains relevant, and as a direction of research we set the following goal.

The object and subject of the research. In the research work, "Ablative and reconstructive surgery in oral mucosa cancer patients as a result of clinical and anamnestic examinations from 2012 to 2018 at the Departments of Oral and Maxillofacial Surgery and Oncology of AMU and the Cancer Institute of Tehran University of Medical Sciences operations are scheduled according to the instructions. 261 patients were involved in the research process. The patients' quality of life was studied, and psychometric analysis of the Azerbaijani version of the quality of life questionnaire was conducted. The results of different types of flap methods used for the elimination of soft tissue and mandibular defects after ablative operations were comparatively evaluated based on quality of life indicators.

The aim of study. To improve the quality of life by improving rehabilitation measures in the treatment of patients with oral cancer

The study objectives included:

1. Study of the life quality of patients treated with the diagnosis of oral mucosal cancer;
2. Assessment of the effect of various methods of flap repair on the quality of life indicators used in the treatment of patients with oral mucosal cancer to reconstruction of soft tissue defects caused by the resection of main (primary) tumor;

3. Experimental study of the effect of Diltiazem medicine on flap microcirculation after flap surgery;
4. Comparative assessment of the effect of results on quality of life indicators in cases of reconstruction and non-reconstruction with auto and allograft used for recovery after resection of the main (primary) tumor and resection of the jawbone in the treatment of patients with oral mucosal cancer invading the jawbone;
5. Assessment of oral, neck and shoulder functions after surgery and radiotherapy of patients treated with diagnose of oral mucosal cancer;
6. Choosing an effective treatment algorithm based on the results of medical rehabilitation measures in the treatment of patients with oral mucosal cancer.

Methods of research. The research work was performed from 2012 to 2018 at the Departments of Oral and Maxillofacial Surgery and Oncology of AMU and the Cancer Institute of Tehran University of Medical Sciences. Examination and treatment of 261 patients diagnosed with oral mucosa cancer was carried out. The following methods were used to fulfill the aims and objectives: Questionnaires prepared by the European Organization for Research and Treatment of Cancer were translated into Azerbaijani, culturally adapted, approved after being applied to 141 patients, and the Azerbaijani version of the questionnaire of this organization was registered. Then, psychometric test was conducted with the participation 96 patients to confirm the correctness of these questionnaires. Patients with soft tissue defects after resection of the main (primary) tumor in oral mucosal cancer patients were divided into 3 groups according to the type of reconstruction: patients undergoing reconstruction with primary wound closure, reconstruction with local flaps and reconstruction with distant-pedicle flaps. Oral mucosal cancer patients were divided into 3 groups according to jaw resection and reconstruction of jaw defects besides resection of primary tumor: patients without any reconstruction, reconstructed with a titanium plate and reconstructed with free vascular pedicle flaps and their treatment results were comparatively evaluated on the basis of

quality of life indicators. The effectiveness of the Diltiazem, which is used in reconstruction operations with free vascular pedicle flaps, was studied in experimental conditions. At the same time, dysfunction of oral, neck and shoulder functions after oncological operations was evaluated.

The main statements submitted for dissertation defense:

1. The C 30 (30-question questionnaire) assessing the general state of patients and H&N 35 (35-question questionnaire) and the new H&N 43 (43-question questionnaires) including local functional head and neck complaints prepared by the European Organization for Research and Treatment of Cancer to assess the life quality of patients with oral mucosal cancer were prepared in Azerbaijani for the first time, adapted and psychometric analysis of these questionnaires was carried out.

2. Different types of reconstruction methods used during surgical treatment of patients with oral mucosal cancer were compared based on quality of life indicators and a more efficient reconstruction method was proposed.

3. More common complaints and local dysfunction have been found after surgery, especially reconstructive surgery in patients with oral mucosal cancer.

4. The effect of Diltiazem medicine on microcirculation in transplanted tissue flaps was studied in experimental conditions and used clinically.

Scientific novelty of the research.

- Various types of reconstruction methods were comparatively assessed in terms of the effect on quality of life indicators in recovery surgeries performed to resection of soft tissue defects after the resection of the main (primary) tumor in the treatment of patients with oral mucosal cancer.

- The results of reconstruction of a jaw defect without reconstruction, with reconstruction with a titanium plate and a free vascular pedicle graft in patients with resection of the jawbone in the surgical treatment of the oral mucosa cancer were comparatively assessed based on quality of life indicators.

- The results of the use of Diltiazem in flap repair after the resection of the main (primary) tumor in the treatment of patients with oral mucosal cancer were assessed in experimental conditions.

- Oral, neck and shoulder functions were assessed based on quality of life indicators after treatment of patients with oral mucosal cancer.

Practical significance of the work. The results of different reconstruction methods in the treatment of oral mucosa cancer were evaluated based on quality of life indicators. It was determined that the reconstruction methods proposed in the treatment of oral cavity mucosa cancer improve the quality of patients' life. The Azerbaijani version of the questionnaire (EORTC QLQ-C30, EORTC H&N 43) presented by the European Organization for Research and Treatment of Cancer for the assessing the life quality of patients treated with the diagnosis of oral mucosal cancer was developed, clinically and psychometrically validated.

The Azerbaijani version of the questionnaire of life quality was approved and put into practice by the European Organization for Research and Treatment of Cancer.

Apobation of study results. The author has given papers on the topic of the dissertation at the following scientific conferences: the 10th International Congress of Otorhinolaryngology Head and Neck Surgeons of Turkey (2012), Ankara, Turkey; Scientific-practical conference dedicated to academician R.N. Rahimov's 90th anniversary (2013), Baku, Azerbaijan; "The 3rd Azerbaijan Plastic Surgery Days and ISAPS course" conference of Azerbaijan Public Union of Plastic Surgery (2014), Baku, Azerbaijan; The 8th congress of oncologists and radiologists of the CIS countries (2014), Kazan, Russia; Scientific conference on "Current Problems of Medicine" (2014), Baku, Azerbaijan; The 16th International Conference of Iranian Maxillofacial Surgeons (2018), Tehran, Iran; Scientific and practical conference dedicated to the National Leader H. Aliyev's birthday (2018), Baku, Azerbaijan; The 13th international congress of the Turkish Association of Oral and Maxillofacial Surgeons together with the European Society of Craniofacial Surgeons (2019), Belek,

Turkey; The 1st International Conference of the Society of Oral and Maxillofacial Surgeons of Azerbaijan (2019), Baku, Azerbaijan; The 5th conference of the Russian Society of Specialists in Head and Neck Tumors (2019), Moscow, Russia; The 1st International Conference “Oral Cancers”, Eskishehir, Turkey (2020).

The dissertation was defended at the specialized Defense Council at Cancer Research Center of the Tehran University of Medical Sciences on January 22, 2020. The preliminary discussion of the finished dissertation was held at the extended meeting dated 11.03.2022 (Protocol No.6) with the participation of researcher of other specialty departments of Azerbaijan Medical University, and its preliminary approval was held on 14.09.2022 at the meeting of the Approval commission (Protocol No 16), which hold scientific seminars, of the One-time Dissertation Council BED 2.05 under the Azerbaijan Medical University.

Applying the results scientific work. Patients diagnosed with oral mucosa cancer were treated at the Departments of Oral and Maxillofacial Surgery and Oncology of AMU, Cancer Institute of Tehran University of Medical Sciences. The Azerbaijani version of questionnaire of the life quality was used in the Departments of Oral and Maxillofacial Surgery and Oncology of AMU. Based on the results of the dissertation work, the choice of the reconstruction method is included in the daily practical scope of the Department the Oral and Maxillofacial Surgery of AMU.

Published scientific works related to the dissertation work. 28 scientific works – 15 of them foreign (10 of them international summaries) and 13 local, 22 scientific journal articles and 6 theses (4 of them in the materials of international scientific-practical conferences) were published related to the topic. 7 scientific presentations were made at local and international scientific-practical conferences, symposia and congresses on the topic of the research work.

One authorship certificate was received on the dissertation work: The 30-question questionnaire assessing the general state of cancer patients and the 43-question questionnaires assessing head

and neck complaints prepared by the European Organization for Research and Treatment of Cancer were prepared in Azerbaijani, and they were officially registered by the organization and a certificate was issued to the author after cultural adaptation and clinical use of them.

The volume and structure of the dissertation: The dissertation consists of 396.993 characters without spacing, an introduction (22.463 characters), a reference review (61.750 characters), material and methods of research (42.639 characters) 3 chapters (20.883+185.521+14.558 characters), a conclusion, results, practical recommendations (49.179 characters) and a list of references, written on 307 standard computer pages. The dissertation includes 33 tables and 61 figures. The reference list includes 301 sources.

RESEARCH MATERIALS AND METHODS

The study material consisted of 261 patients with oral mucosal cancer. In 2012-2018, these patients were treated in the oral and maxillofacial surgery departments of the Clinical Medical Center, AMU Teaching Surgery Clinic, AMU Oncology Clinic and the Cancer Institute of Tehran University of Medical Sciences. The treatment regimen in all patients was in accordance with the NCCN (National Comprehensive Cancer Network - USA) protocol. Plastic after tumor removal in 216 patients reconstructive operations were carried out.

The research was conducted in several areas:

1. The Azeri Version of European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30): Translation and Validation.

The European Organization for the Research and Treatment of Cancer (EORTC) is a group of international researchers who study the quality of life and create a questionnaire to assess the quality of life of patients with cancer. With the increasing number of international clinical trials, the consistency of translations and the

cultural equivalence of interventions are critical to assessing patients' quality of life in different cultures and in different countries.

In this survey system, the EORTC applied a modular approach with a basic questionnaire (QLQ-C30) covering the symptoms and problems observed in the general population of cancer patients, and the modules accompany the main questionnaire and address the location, symptoms, and treatment. are special.

All EORTC QOL questionnaires have been developed in accordance with EORTC Guidelines (Johnson 2011), including four stages of the creation process. All stages are prepared in an international environment and require translation into different languages. Translations using modular preparation should be prepared according to standard EORTC translation procedures as described in this Translation Guide.

In this survey system, EORTC applied a modular approach with a basic questionnaire (QLQ-C30) covering the symptoms and problems observed in the general population of cancer patients, and the modules accompany the main questionnaire and are specific to location, symptoms, and treatment.

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Depending on the status of the module, Questionnaires can be used by external users. Only fully approved and partially approved modules (Final Phase 3) are available for use in research.

All EORTC queries are copyrighted. The European Organization for the Study and Treatment of Quality of Life in Cancer Patients (EORTC QLQ-C30) is a key tool for assessing quality of life in cancer patients. It consists of 30 items and

consists of 5 activity subdivisions (physical, role, emotional, cognitive, and social activities), a global quality of life subdivision, and a number of symptom subdivisions such as fatigue, pain, nausea, and vomiting. Scores on activity and global quality of life range from 0 to 100, where a higher score indicates a better situation. Scores in symptom subdivisions also range from 0 to 100, but higher scores here indicate more severe symptoms.

Translation

First permission was asked from the EORTC Study Group on Quality of Life. Then forward-backward translation procedure was applied to translate the English-language version of the questionnaire into Azeri as recommended (Cull et al., 2002). As such two independent experts translated the questionnaire into Azeri. Consequently after reviewing both translations a single Azeri version was provided. Then, two other bilingual physicians not connected to the study back translated the questionnaire into English. Subsequently a single English version was provided and checked with original questionnaire. Finally the provisional Azeri version of the questionnaire was pre-tested and its final form was approved by the EORTC Study Group on Quality of Life and was administered in this study

Validation

A cross section study was conducted on a sample of Azeri patients with confirmed diagnosis of oral cancer attending to a teaching hospital affiliated to Azerbaijan Medical University in Baku, Azerbaijan from January 2017 to December 2018. All patients were candidate for surgery. There were no restrictions for including patients in the study with regard to age, gender and disease stage unless they did not wish to participate. Patients completed the Azeri version of the EORTC QLQ-C30 and then the following procedures were applied: Construct validity: it was assessed using known groups comparison where the disease stage was utilized as known groups indicator. In addition we performed item-scale correlation matrix. As such we hypothesized that items belonging to a subscale should have higher correlation with own

subscale. Reliability: internal consistency was estimated in order to examine reliability.

Descriptive statistics was used to explore the data. Since the quality of life data was not distributed normally, Kurskal-Wallis test was used for known groups comparison. The Spearman correlation coefficients were estimated in order to provide item-scale correlation matrix. Reliability was estimated using the Cronbach's alpha coefficient. The alpha value of 0.70 and above was considered as acceptable.

2. Quality of life in patients with oral cancer treated by different reconstruction methods as measured by the EORTC QLQ-H&N43

This was a descriptive clinical study in patients with oral cancer. The study included patients who referred to department of oral and maxillofacial surgery in Azerbaijan Medical University. All patients who underwent tumour ablative surgery, and had primary reconstruction were entered into the study. Surgery included resection of the primary tumour and neck dissection. Depending on the tumour localisation, tumour size, and neck lymph nodes (clinically positive or negative) radical, modified, selective or elective neck dissection was also done. Patients also did or did not have reconstruction (no flap, local flap, distant-regional flap) depending on defect size, localisation, and functional-aesthetics, and the subsequent treatment (adjuvant radiotherapy, chemotherapy). For patients who did not have a flap depending on tumour size and tumour site after primary tumour resection, the wound was closed primarily. They had early stages of the disease and had little problems with oral function. Local flaps were used as an alternative to distant flaps based on the patient's overall condition and tumour stage. The local flap included nasolabial, tongue, and facial artery musculomucosal flaps. These patients had only skin, and mucosal defects, and for these patients local flaps were used for reconstruction of skin, mucous membrane, and the lower lip defects.

Distant-regional flaps were used for composite defects in advance stages of the disease and included pectoral major myocutaneous flap, deltopectoral flap, cervical flap, and free flap (fibular free flap, radial forearm free flap, and latissimus dorsi free flap). The evaluation was made by a trained surgeon six months following surgery in the outpatient clinic using the Azeri version of two well known questionnaires to compare QoL in patients who received local, distant-regional or no flap reconstruction.

The questionnaires

1. The EORTC QLQ-C30: it is a well-known core cancer QoL questionnaire. It consists of 30 items that cover a number of functioning and symptom subscales. Each item is rated on a 5-point Likert scale and scores range from 0 to 100 where higher scores for functioning and global QoL subscales indicate better conditions and for symptom subscales indicate worse symptoms.¹⁴

2. The EORTC QLQ-H&N43: it is the extended version of the previously developed questionnaire QLQ-H&N35 (see Table 1 for similarities and differences). It is a supplementary module for the EORTC QLQ-C30 that measures QoL in patients with head and neck cancers. It contains 43 items tapping into six multi-item and 13 single-item symptom subscales: namely pain, swallowing, problems with senses, speech problems, trouble with social eating, less sexuality, teeth, dry mouth/sticky saliva, body image, shoulder pain, skin problems, anxiety, trouble with social contact, opening mouth, coughing, lymphoedema, problems with wound healing, weight loss, and neurological problems.¹⁵ Each item is rated on a four-point Likert scale and scores for each subscale range from 0 to 100 where higher scores indicate more serious symptoms.

Statistical analysis. The quantitative indicators were reported using numbers, percentages, and median and range. Since the data were not normally distributed, the Kruskal-Wallis test was used to compare QoL data among three groups. In addition to adjustment analyses for age, stage and types of reconstruction,

the generalised linear model was used to compare QoL data in three groups using SPSS (version 13). The generalised linear model procedure provides regression analysis and analysis of variance for dependent variables by one or more fixed factor variables or one or more covariates. As such the QoL variables were considered as dependent variables, and reconstruction types (no flap, local flap, and distant-regional flap) and disease stage were considered as fixed factors and age as covariate. The level of probability was set at $p < 0.05$

3.Evaluation of quality of life in patients with oral cancer after mandibular resection: Comparing no reconstruction, reconstruction with plate, and reconstruction with flap.

This was a cross-sectional study of quality of life in patients with oral cancer referred to Tehran Cancer Institute, affiliated to Tehran University of Medical Science during year 2017 and 2018 in Iran. All patients who received oral cancer surgery at the study period were identified and entered into the study if they survived 12 months following surgery. In all patients, the tumor was spread to the mandible bone, so that the treatment plan involved a resection of the mandible and the loss of bone continuity. Based on patients' conditions including age, stage of the disease, postsurgical treatment, and clinical decision making, 3 groups of patients were identified: patients who underwent reconstruction with plate, patients who underwent reconstruction with flap, and those who did not receive any reconstruction. As indicated all patients completed a demographic and quality of life questionnaire at the end of 12 months follow-up. Clinical information was extracted from case records.

Quality of life was measured using the following questionnaires.

1. The EORTC QLQ-C30. European Organization for Research and Treatment of Cancer core quality of life questionnaire (EORTC QLQ-C30) is a core questionnaire for measuring quality of life in patients with cancer. It consists of 30

items tapping into 6 functioning and a number of symptoms subscales. Scores for each subscale range from 0 to 100 where for the functioning subscales, the higher scores indicate better conditions and for the symptoms it is vice versa. The psychometric properties of the Iranian version of the questionnaire are well documented.

2. The EORTC QLQ-H&N35. European Organization for Research and Treatment of Cancer head and neck cancer-specific quality of life questionnaire-35 items (EORTC QLQ-H&N35) is the early version of a specific questionnaire for measuring quality of life in head and neck cancer. The questionnaire consists of 35 items measuring a number of symptoms including pain, swallowing, sense problems, speech problems, trouble with social eating, and trouble with social contact. Scores for each symptoms range from 0 to 100, where the higher scores indicate worse conditions. The questionnaire is validated in Iran and its report is available elsewhere.

Analysis. Descriptive statistics were used to explore the data. Given that the distribution of data was not normal, thus nonparametric test (Kurskal–Wallis test) was performed for comparing quality of life among 3 groups of patients. Since there were no significant differences among 3 groups with regard to age, gender, and tumor stage, we did not control for any confounding variables. Data were analyzed by SPSS software.

Use of the pectoralis major skin flap (PMMF) in the treatment of advanced oral cancer

Between 2011 and 2019, 71 PMMF were reviewed retrospectively. The underlying pathology was oral and oropharyngeal squamous cell carcinoma (SCC). Among the pathologies, stage 4 primary HCC (57.7%), large recurrent (14%) or isolated neck metastases (12.6%) prevailed. PMMF was applied in the reconstruction of 54 of them, and the main indication for this was concomitant pathologies in addition to the advanced phase of the pathology. Most of the patients belonged to

AAC (American Society of Anesthesiologists) class 3 and had received prior surgical and/or radiotherapeutic treatment.

Most resections were performed in the lower jaw (32.4%) or tongue/oropharyngeal region (26.7%). Mandibular defects were repaired with an PMMF as a primary choice in 19.7% of cases and after failure of a free flap in 12.7% of cases.

The outcomes of free-flap surgery in head and neck postoperative defects

This study is an intervention “experimental quasi”. The study population is 39 patients of subspecialty plastic surgery clinic and department of oral and maxillofacial surgery of Azerbaijan Medical University that with final diagnosis they need surgical removal of cancer tissue. The number of cases are between 2009 till 2016 is 39. The surgery is consisted of a simultaneous group work of plastic and oncologic surgeon, their work is included of free flap removal of different parts of body according to defect extent of cancer tissue resection in patient’s head or neck. After the surgery, they have been observed for 3 months and their surgery results have been evaluated. The age average of this patients was 59.8 ± 15.1 meanwhile they were between 15 and 82 years old. 26 patients (68.6%) were male and 13 patients (31.4%) female. 29 patients (82.8%) were Iranian and 10 patients (17.2%) were Azerbaijanian. Only 7 patients (17.9%) had smoking antecedent and the others (82.1%) didn’t. Altogether, there has been co-diseases in addition to head & neck cancer. 6 patients (15.4%) had diabetes, 2 patients had hypertension, 3 patients (7.6%) had heart valve disease and 3 patients (7.6%) had other diseases (malnutrition and COPD). There has been previous surgery operation antecedent in 12 (30.8%) patients. The usage of Anti-coagulation during the surgery has reported in 37 patients (93.1%), while its post-surgery usage has been in 21 patients (72.4%). Lidocaine has been used during the surgery for 27 patients heparinized saline in surgery process was prescribed for all patients. There have been 31 free flap surgeries in which two simultaneous flap were used for 2 patients, thrombotic events

were not seen in any patients. There were fl ap complete loss in 4 patients (10.3%) and partial fl ap loss (fl ap necrosis) in 4 patients (10.3%) in the report. The ischemia average time in operation time has been 105.6 ± 35.8 minutes (1.76 ± 0.59 hour) and the anesthesia average time in patients has been 547.7 ± 82.7 minutes (9.12 ± 1.37 hour). Pre-operation PT mean was 13.8 ± 2 seconds, PTT mean 42 ± 14.9 seconds, INR mean 1.2 ± 0.36 and ACT mean 80.2 ± 20.1 seconds.

Oral, neck and shoulder functions after oncological intervention in the oral cavity

In 2012-2018, 120 patients with primary cancer of the tongue or floor of the mouth and 60 healthy people were selected according to the age criteria of this study. Patients with recurrent cancer of the head and neck and impaired perception were not included in this study. 73 patients received only surgery, 47 patients received both surgical and radiotherapeutic treatment.

First of all, the conditions of healthy people were noted, and these changes were identified as follows:

- Thermal sensitivity
- Sense of touch
- Protrusion of the tongue
- Lateralization of tongue

Sensory function of the tongue: Thermal (thin sensory fibers) and tactile (thick sensory fibers) sensory functions were randomly tested with true and false stimuli, provided that the patient's eyes were closed. After each pair of true and false irritants, patients had to report irritability (mandatory selection procedure). Irritant pairs were applied 3 times. The level of irritants was determined for healthy people, so patients were able to respond correctly in uninjured areas. The inspection area (right and left) was determined at a distance of 10 mm from the tip of the tongue and the right and left edges, if possible. For the analysis, we used the results of the most affected areas. A 2 mm diameter heat-conducting aluminum rod (22° C; tactile sensation with cold sensation) was used as a true irritant to test thermal

sensory function. Heat-resistant Perspex rods were used for the false irritant. The tactile sense function was measured using Semmes - Weinstein monofilament (Semmes - Weinstein Aesthesiometer, Stoelting Co., Wood Dale, IL) with index number 3.22. Touching this filament (fiber) was really irritating. The false stimulus was to bring another instrument closer to the patient instead of the filament. Thermal and tactile sensations were measured as a decrease in function and 0 as normal.

The study included 120 patients diagnosed with oral cancer and 60 healthy controls. The patients were treated from January 2011 to January 2017 at the Department of Oral and Maxillofacial Surgery of AMU and the Cancer Institute of Tehran University of Medical Sciences.

The patient group included 59 patients from the surgical group alone, 66 patients from the surgical radiation therapy group, and 20 patients from the radiation therapy group alone. collected from medical data.

Patients were assessed no more than 4 weeks before the oncology intervention, at least 4-6 weeks after the intervention, at least 6 and 12 months after surgery, or 6 and 12 weeks after radiation therapy, when patients were treated only with radiation therapy.

Eighty-three patients were treated with ND and 62 patients were not treated with ND. Fifty-five patients were treated with unilateral SND, 16 patients with unilateral MRND, and 3 patients with unilateral RND and 10 patients with bilateral ND. Due to the low number of RND patients, such patients were grouped together with patients with MRND in a group called (M) RND.

Features of the tumor stage (T of TNM), regional lymph node metastases (TNM of N), oncological intervention, and the type of reconstruction listed in Table 1 were noted. Chi-squea tests showed that the number of patients varied significantly ($p < 0.005$) for 4 patient groups (without ND, SND, (M) RND, and bilateral ND) in relation to regional lymph node metastases, oncologic intervention, or oral cavity reconstruction. The mean

age of 145 patients (65.3 ± 13.0 years) was slightly higher in the control group (60.3 ± 7.2 years). Twenty-five patients refused to participate in the study, 19 patients died within a year after surgery, and 4 patients were excluded from the study for complications and as a result of ND protection.

Material and methods of experimental study

Experiment was performed in Central Research Laboratory of Azerbaijan Medical University, Baku, Azerbaijan in 2018. Thirty 1-2 yr old rabbits with a weight of 2,1-3,0 kg were used for the experiment. The ischemia model on the flaps were formed in all subjects. For this purpose, 1.0 gr of calypsol solution was applied to the subjects via intramuscular injection. The hairin the abdominal skin of the subjects has been cleared and the crescent-shaped section which encompasses skin and subcutaneous tissue was applied. The right and left branches of the arteria epigastrica inferior were dissected. The left vascular pedicle was ligated and the blood flow was stopped. An ischemia model has been created for 1 hour on the right vascular pedicle. For this purpose, the intermittent clamping method was used and the vascular pedicle was tightened 3 times with 10 min intervals and 10 min each. Following the successful application of the ischemia model, the skin margins were adapted to each other and they were mended with silk thread No 4. Surgical wounds were cleaned with antiseptic solutions. 0.3 gr ceftriaxone was applied via intramuscular injection to prevent infection complications. The Ethics Committee of Azerbaijan Medical University approved the study in accordance with the tenets of the Helsinki Declaration and national ethical guideline for medical research. Ethics Approval Code: AZ. AMU.06072018.05. The ischemia model-created skin was removed with surrounding healthy tissues by excision after 2 wk (14 d) upon completion of the experiment. For this purpose, 1.0 gr of calypsol solution was applied to the subjects via intramuscular injection. Euthanasia was performed in all subjects via injection of 20.0 mg air to auricular vein. The experimental animals were divided into three groups, each

containing 10 rabbits after the creation of the ischemia model in the skin flap: First group (control group) - consists of 10 rabbits who underwent ischemia model, but no medication were used in the duration of the experiment. Second group (comparative group) - consists of 10 rabbits who underwent ischemia model, and during 14 d, a daily dose of 60 mcg Nitroglycerin had been applied. Third group (main group) -consists of 10 rabbits who underwent ischemia model, and during 14 d, a daily dose of 45 mg diltiazem was applied. Histologically, some morphological parameters of the microcirculation such as endothelial hyperplasia, thickening of the arterial vessel wall, thrombosis, congestion and edema were evaluated with a semiquantitative method of 4 degrees [0-3] for their intensity. Statistical calculations were made on the results obtained after this evaluation. In the statistical evaluation, the average size of various parameters, their mean standard deviation, P-value between the different groups were calculated using SPSS (ver.15.0, Chicago, IL, USA). The variance analysis (ANOVA test) was used to measure the P-value and the significance threshold was accepted as $P \leq 0.05$

RESEARCH RESULTS AND THEIR DISCUSSION

The Azeri Version of European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30): Translation and Validation In all 141 patients with confirmed diagnosis of oral cancer were entered into the study and completed the Azeri version of the EORTC QLQ-C30. The mean completion time for the questionnaire was 9.5 (SD = 1.31) minutes ranging from 8 to 15 minutes. The mean age of patients was 59.5 (SD = 10.7) years. Most patients were male (n = 111, 78.7%) and had stage I of the disease (n = 59, 41.8%). The characteristics of patients are shown in Table 1.

Table 1.

Quality of Life among the Study Samples by Stage of the Disease as Measured by the Azeri Version EORTC QLQ-C30 by Stage (Known Groups Comparison)

	Stage 1	Stage 2	Stage 3	Stage 4	P*
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Functioning**					
Physical	98.5 (2.7)	83.7 (8.7)	53.9 (6.6)	29.5 (12.1)	< 0.001
Role	87.5 (15.1)	73.3 (17.8)	59.5 (17.9)	33.3 (19.2)	< 0.001
Emotional	74.1 (14.5)	68.1 (18.6)	46.8 (27.3)	41.6 (22.1)	< 0.001
Cognitive	90.1 (15.8)	64.2 (24.8)	23.8 (13.1)	80.2 (25.1)	< 0.001
Social	82.2 (19.5)	67.3 (24.7)	50.1 (22.3)	47.6 (29.5)	< 0.001
Global quality of life	62.1 (14.7)	53.6 (14.7)	38.1 (11.9)	33.3 (9.6)	< 0.001
Symptoms ***					
Fatigue	19.7 (19.7)	40.4 (20.9)	61.9 (16.6)	68.2 (11.8)	< 0.001
Nausea and vomiting	11.1 (19.7)	4.3 (9.9)	10.3 (16.2)	9.5 (16.2)	0.17
Pain	29.1 (17.9)	45.3 (19.3)	68.2 (20.3)	83.3 (13.6)	< 0.001
Dyspnea	15.8 (21.7)	28 (25.5)	42.8 (12.5)	61.9 (12.5)	< 0.001
Sleep difficulties	9.1 (20.3)	20.6 (25.9)	33.3 (31.6)	42.8 (16.2)	< 0.001
Appetite loss	18.1 (25.1)	20 (24.2)	38.1 (28.4)	57.1 (16.2)	< 0.001
Constipation	33.8 (30.6)	30 (29.5)	34.9 (32.4)	19.1 (17.8)	0.58
Diarrhea	23.1 (28.5)	20 (26.1)	17.4 (27.1)	9.5 (16.2)	0.57
Financial difficulties	32.2 (25.4)	52.6 (23.4)	57.1 (23.9)	66.6 (27.2)	< 0.001

* Derived from Kurskal-Wallis test; ** Higher scores indicate better conditions; *** Higher scores indicate worse conditions.

Construct validity

The results obtained from known groups comparison are presented in Table 2. As expected the questionnaire well differentiated between patients who differed in the disease stage. Those with higher stage of the disease scored lower on functioning

subscales and scored higher on symptom subscales. In addition performing item-scale correlation analysis the results found to be satisfactory. There were higher correlation between items and its own hypothesized subscale as expected.

Reliability

The internal consistency of the questionnaire as assed by the Cronbach's alpha coefficient ranged from 0.68 to 0.94 indicating acceptable results.

This study reported on translation and validation of the EORTC QLQ-C30 in Azerbaijan and proved that the Azeri version of the questionnaire is valid. With one exception (Camran et al., 2018) we could not identify any other studies that report on psychometric properties of patient-reported outcomes from Azerbaijan. Thus one should bear in mind that such studies in Azerbaijan are at their early stages. Perhaps with introducing this questionnaire for measuring health related quality of life in cancer patients we could see more publications from Azerbaijan on this topic in the future.

This study took a very straightforward procedure in translating and validating the EORTC QLQ-C30 in Azerbaijan for use as a standard and valid benchmark in clinical and epidemiological studies. In general patients did not report any serious problems while completing the questionnaire and hopefully we could find all equivalent words in Azeri for the English expressions. Sometimes one major problem in translating well-known questionnaires into other languages of the origin is the fact that findings equivalents are very difficult (Kleijn et al., 2006). Know-groups comparison was performed to assess discriminant validity. Almost in all measures significant differences were observed among patients with different stages of the disease. However, the result for three symptom subscales (nausea and vomiting, constipation and diarrhea) among patients who differed in disease stage was not significant. It seems that since the first line treatment for patients was surgery (surgical resection and flap reconstruction), thus these three symptoms (usually seen among patients who receive chemotherapy)

did not show significant differences. In addition the findings showed a good item-scale correlation for all functioning and multi-item symptom subscales, which lend support to the hypothesized scale structure of the questionnaire

The Azeri version of the EORTC QLQ-C30 showed good internal consistency where all Cronbach's alpha coefficients exceeded the expected threshold value ($\alpha \geq 0.7$). However the Cronbach's alpha coefficient for pain subscale was 0.68, which seems acceptable. The finding from our study was almost similar to other studies carried out in different countries (Kobayashi et al., 1998; Montazeri et al., 1999; Zhao and Kanda, 2000; Arraras et al., 2002; Guzelant et al., 2004; Awad et al., 2008; Wan et al., 2008).

We studied a cohort of oral cancer patients. The descriptive findings indicated that overall the score for global quality of life subscale was the lowest and score for the physical functioning was the highest. Perhaps this indicates that although patients who diagnosed with oral cancer might have good physical functioning or physical health, they suffer from low global quality of life and emotional functioning as reflected by patients. Also patients relatively scored higher on pain subscales compared to other symptom subscales, which confirms such observation. There is evidence that cosmetic appearance, and psychological well-being can become compromise during the diagnosis, treatment, and survivorship of patients with oral cancer (Valdez and Brennan, 2018).

This was a preliminary validation study and surely might have some limitations. Limited psychometric evaluations, studying only oral cancer patients, and lack of follow-up information are among important shortcomings with this study. However, we are very optimistic that such studies could introduce patient-reported outcomes to the Azeri medical professionals and might help clinicians and medical investigators to consider patients' voice and concerns. The EORTC QLQ-C30 has been approved for clinical use and scientific interpretation in numerous studies and has proven to be an important link between patient and physician. In conclusion, the findings from this preliminary validation study indicated that the

Azeri version of the EORTC QLQ-C30 is a valid core instrument for measuring quality of life in cancer patients in Azerbaijan.

For psychometric evaluation of Azeri version of the head and neck cancer specific quality of life questionnaire (EORTC QLQ-H&N43) total of 96 patients (67 men and 29 women) who underwent flap reconstruction for oral cancer in Azerbaijan were studied. The mean age of patients was 59.6 (SD = 10.7) years ranging from 30 to 82. In 47 cases, age was lower than 60 years.

Validity was examined using known groups comparison. We hypothesized that the questionnaire should be able to differentiate between patients who are differing in stage and metastasis. In fact we hypothesized that patients with lower stage and no metastasis should score better than patients with higher stage and having metastasis. For comparison the Mann-Whitney and Kruskal Wallis tests were used. In addition convergent and divergent validity (discriminant validity) was examined by estimating correlation coefficient between the EORTC QLQ-C30 and the EORTC QLQ-H&N43 scores. Due to skewed distribution of the data we used the Spearman's rho coefficient. Correlation coefficients ranging 0.1–0.3 were considered low, 0.31–0.5 as moderate, and those exceeding 0.5 as high. Internal consistency reliability for multi-items subscales (having at least 3 items) was assessed using the Cronbach's alpha coefficient. Alpha coefficient equal or greater than 0.7 was thought satisfactory. The Cronbach's alpha coefficient for the multi-item scales of the QLQ-H&N43 ranged from 0.66 to 0.78 indicating that the internal consistency of the Azeri version of the questionnaire was acceptable.

The findings from this study indicated that the Azeri version of the EORTC QLQ-H&N43 is a valid instrument for measuring quality of life in head and neck cancer patients. The internal consistency in five out of seven multi-item subscales was good and only the Cronbach's alpha for social eating (0.66) and body image (0.69) were slightly lower than acceptable threshold (0.7). Perhaps these could be due to cultural differences that exist among different nations. For instance, social eating is less common in Azerbaijan.

The authors of the original study that introduced the EORTC QLQ-H&N43 indicated that they analyzed the data in accordance with the EORTC Quality of Life Group QLG Module Development Guidelines. Thus, to retain an item in the module, they used 8 predefined criteria such as relevance, floor and ceiling effects, item difficulty, and compliance. They also used additional measures including the Cronbach's alpha coefficient to assess internal consistency for multi-item subscales. The Cronbach's alpha for hypothesized subscales they included in the module ranged from 0.77 to 0.87 that were well above acceptable values.

To the best of our knowledge contrary to expectation other than the original study, the current study is the second independent one that reports on psychometric properties of the QLQ-H&N43. The Serbian version of the QLQ-H&N43 was the first study that reported on psychometric evaluation of the questionnaire. The study included 170 patients and found good internal consistency for 5 out of 7 multi-item subscales. The study also showed that the questionnaire had acceptable validity (known groups validity) where patients who differed in type of laryngectomy, adjuvant therapy or 5-year survival scored differently in the expected directions. We used known groups comparison for the validity purpose. As expected the Azeri version of the questionnaire well differentiated among patients who differed in stage and metastasis, although in most instances the differences among patients were not significant. For instance as reported in Table 5, only 8 out of 19 subscale showed statistically significant difference between the two groups, and in Table 6, only 2 out of 19 subscale showed statistically significant difference. One explanation for such observation might be related to the small sample size in each group. In addition since we analyzed the data for all types of oral cancers, therefore one might argue that if there was an opportunity to analyze the data for each sub-types of oral cancer, then it was possible to obtain significant results for all measures assessed. Finally as pointed out by Polit and Yang when performing known groups validity the direction of differences for

scores among sub-groups (as hypothesized) are more important than statistical significant level values

Interestingly the authors of the QLQ-H&N43 stated that the QLQ-H&N35 could still be used in ongoing or future studies if the investigators prefer to use this head and neck module version. However, they believe in studies investigating multimodal treatment or targeted therapies, the QLQ-H&N43 might be more suitable to detect differences between patient groups. This study has some limitations. The sample size was relatively small. Secondly we did not perform test-retest analysis to investigate the stability. It seems that for using the Azeri version of the QLQ-H&N43 in future outcome studies we still need to perform further psychometric evaluations. However, one should note that the QLQ-H&N43 should be used with conjunction of the EORTC QLQ-C30 core cancer questionnaire, which is now available in Azeri version, too.

Quality of life in patients with oral cancer treated by different reconstruction methods as measured by the EORTC QLQ-H&N43

In all 120 patients were approached. Of these, 24 patients died within three months and so the remaining 96 patients (67 men and 29 women) who underwent surgery for oral cancer were studied (Fig. 1). Thirty-six patients received no flap, 31 patients received a local flap, and 29 patients a distant or regional flap. The mean (SD) age of patients was 60 (11) years, range from 30 -82 years.

As shown, unregulated baseline operative scores were lower in patients treated with local flaps than in other patients. In addition, the global QoL score was the lowest compared to other operational scores. The QoL information as measured by the EORTC QLQ-C30 are presented in Table 3. As shown, unadjusted core functioning scores in patients with local flaps were lower compared with other patients. In addition, the global QoL score was the lowest score compared with other functioning scores. However, of these, only physical functioning differed significantly among three groups ($p = 0.003$). Similarly these patients scored higher for symptoms as measured by the QLQ-C30. Of these fatigue ($p < 0.001$), nausea and

vomiting. (p = 0.01), pain (p = 0.035), and dyspnoea (p = 0.002) differed significantly among the three groups (table 2).

Table 2.
Quality of life among patients by type of flap as measured by the EORTC QLQ-C30. Data are median (range).

	No flap (n=36)		Local flap (n=31)		Distant-regional flap(n=29)	p*
Functioning**						
Physical	93.3	(46.6-100)	86.6	(46.6-100)	100 (66.6-100)	0.003
Role	83.3	(50-100)	66.6	(33.3-100)	100 (66.6-100)	0.060
Emotional	75.0	(33.3-100)	75.0	(25-100)	83.3 (25-100)	0.100
Cognitive	100 (16.6-100)		100 (33.3-100)		100 (50-100)	0.844
Social	83.3	(33.3-100)	83.3	(33.3-100)	91.6 (33.3-100)	0.263
Global quality of life	66.6	(33.3-83.3)	66.6	(8.3-83.3)	66.6 (33.3-91.6)	0.253
Symptoms ***						
Fatigue	22.2	(0-66.6)	44.4	(0.0-77.7)	11.1 (0-66.6)	< .001
Nausea and vomiting	0	(0-66.6)	0 (0-66.6)		0 (0-66.6)	0.010
Pain	33.3	(0-66.6)	33.3	(16.6-83.3)	16.6 (0-66.6)	.035
Dyspnea	0	(0-66.6)	33.3	(0-66.6)	0 (0-33.3)	0.002
Sleep difficulties	0	(0-100)	0 (0-66.6)		0 (0-66.6)	0.083
Appetite loss	0	(0-100)	0 (0-66.6)		0 (0-66.6)	0.749
Constipation	33.3	(0-100)	33.3	(0-100)	33.3 (0-100)	0.297
Diarrhea	0	(0-100)	33.3	(0-100)	33.3 (0-100)	0.132
Financial difficulties	33.3	(0-100)	66.6	(0-66.6)	33.3 (0-66.6)	0.233

* Derived from Kruskal-Wallis test.

** Higher scores indicate better conditions.

*** Higher scores indicate worse condition

Further analyses using the generalised linear regression while adjusting outcomes for age, reconstruction types and the disease stage showed that significant difference remained for physical function ($p = 0.007$) and fatigue ($p < 0.001$) but not for nausea and vomiting and pain. However, dyspnoea ($p = 0.004$), and insomnia ($p = 0.026$) emerged as significant after adjustment.

Quality of life among patients by type of flap as measured by the EORTC QLQ-H&N43*. Data are median (range)..

The comparison of QoL among three groups as assessed by the specific head and neck cancer QoL questionnaire (EORTC QLQ-H&N43) are presented in Table 5. For most measures patients who received local flaps scored higher, indicating that they had poorer QoL. However, after using the generalised regression model to adjust outcomes based on age, type of reconstruction and the disease stage, eight of the 19 QoL variables including problems with senses ($p = 0.012$), speech problems ($p = 0.005$), trouble with social eating ($p = 0.027$), teeth function ($p = 0.005$), skin problems ($p = 0.038$), wound healing problems ($p = 0.038$), weight loss ($p = 0.020$), and neurological problems ($p = 0.009$) showed significant differences. The results are shown in Table 3.

This was a study of QoL in head and neck cancer patients operated on who received no reconstruction, reconstruction with a local flap, or reconstruction with a distant-regional flap. The most important finding was the fact that, although not consistent for all measures, patients who received a local flap reported poorer QoL compared with those who received distant-regional flap or no reconstruction at all. However, a study comparing local flap with microvascular reconstruction using the EORTC QLQ-H&N35 reported that overall patients who received microvascular reconstruction showed better functioning but significantly worse symptoms such as swallowing, chewing, speech problems, taste, and pain. The findings from this study indicated that the opening of the mouth was poorer in the local flap group compared with other groups. However, this was not significant. Similarly we found that patients in the local flap group suffered more than other groups.

Table 3.

Quality of life among patients by type of flap as measured by the EORTC QLQ-H&N43*. Data are median (range)

	No flap (n=36)		Local flap (n=31)		Distant-regional flap(n=29)		<i>p</i> **
HN pain	25.0	(0-100)	33.3	(0-83.3)	16.6	(0-58.3)	0.035
HN swallowing	41.6	(0-66.6)	25.0	(0-50.0)	16.6	(0-58.3)	0.010
HN senses problems	16.6	(0-66.6)	16.6	(0-33.3)	0	(0-50.0)	0.018
HN speech problems	33.3	(0-60.0)	33.3	(0-60.0)	20.0	(0-53.3)	0.005
HN trouble with Social eating	33.3	(0-66.6)	25.0	(0-66.6)	16.6	(0-53.3)	0.010
HN Less sexuality	0.0	(0-100)	0	(0-66.6)	0	(0-66.6)	0.841
HN teeth	44.4	(0-77.7)	55.5	(22.2-100)	33.3	(0-88.8)	0.12
HN dry mouth / sticky saliva	0	(0-100)	0	(0.0-50.0)	0	(0.0-33.3)	0.077
HN body image	22.2	(0.0-100)	11.1	(0-66.6)	22.2	(0.0-88.8)	0.125
HN shoulder pain	0	(0.0-66.6)	9.0	(0-66.6)	0	(0-33.3)	0.052
HN skin problems	0	(0-100)	0	(0-44.4)	0	(0-44.4)	0.087
HN anxiety	50.0	(0-100)	66.6	(0-100)	33.3	(0-100)	0.168
HN trouble with social contact	0	(0-100)	0	(0-100)	0	(0-100)	0.710
HN opening mouth	0	(0-100)	33.3	(0-100)	33.3	(0-100)	0.124
HN coughing	0	(0-100)	0	(0-100)	0	(0-33.3)	0.007
HN lymphoedema	0	(0-66.6)	0	(0-66.6)	0	(0-66.6)	0.068
HN problems wound healing	0	(0-100)	0	(0-33.3)	0	(0-100)	0.005
HN weight loss	0	(0-100)	0	(0-66.6)	0	(0-33.3)	0.029
HN neurological problems	0	(0.0-100)	0	(0-66.6)	0	(0-33.3)	0.090

The problem of swallowing was most commonly seen in non-flap groups. In the local flap group, however, this problem was more common than in the distant regional group. The findings of the

current study indicated that although patients are relatively high on functioning subscales of the EORTC QLQ-C30, the score for global QoL in these patients was low. Similarly a retrospective study of QoL in patients who received distant flaps reported that patients had poor global QoL, role functioning, and social functioning. Patients also reported high symptom burden as measured by the EORTC QLQ-H&N35.

To explain why global QoL score was low when other functioning scores were satisfactory, one might argue that this was the result of several factors including the fact that an individual who develops cancer might suffer from different problems and perhaps his or her future perspectives are ambiguous. This is why supportive care including social support and in case of oral cancer the issue of rehabilitations are very important. The findings from advanced analyses of the data (i.e. the generalised linear model) showed that type of reconstruction (the effect of flap) was more apparent than age and the disease stage. To explain such findings it is possible to point out that since there were no great age differences among the three study groups then it is obvious that age did not emerge as a significant contributing factor to QoL in these patients. However, as could be seen in Table 1, because there were apparent differences in the disease stage among patients, this factor showed more influence on patients' QoL. This study compared QoL in a group of patients with oral cancer who received no flap, local flap, and distant regional flap using the EORTC QLQ-H&N43. In general using the EORTC QLQ-H&N43 could be a novelty for our study since only a few studies have been published using this new version of the questionnaire. In addition comparing three groups could be considered as an advantage for this study since most existing studies on QoL in patients with head and neck cancer are either simple descriptive studies or at most compare QoL for different distant-regional flap techniques. 6 Limitations This study had some limitations. Firstly this was a cross sectional study measuring QoL at one point in time. Perhaps future studies need to collect data before and after any given intervention or interventions and then compare

QoL in different groups at pre- and post-treatment periods. In fact since we did not collect QoL data at baseline, the observed differences could be due to the surgical procedures, but could equally well have been caused by differences at baseline. This has a significant impact on the interpretation and generalisability of the results. Secondly we included patients with different histopathology (90 patients with squamous cell carcinoma and six patients with adenocarcinoma and adenocystic carcinoma). The behaviour of these tumours is different and so might have affected the results. However, because of the small sample size it was not possible to carry out a separate analysis for different subgroups of patients who differed in histopathology or in case of distant-regional flap for different subgroups of patients for whom how many different flaps were used. Thus due to small sample size in each group we only could adjust quality of life measures for age, type of reconstruction, and the disease stage. However, the adjusted R², which only exceeded 0.2 on one occasion, indicated that the models explain little or none of the variation. Perhaps the sample size was modest for this type of analysis. Multi-centre studies are therefore recommended to include baseline QoL (preoperative QoL assessment) and other influencing factors to avoid bias in interpreting the findings

Evaluation of quality of life in patients with oral cancer after mandibular resection (Comparing no reconstruction, reconstruction with plate, and reconstruction with flap).

In all, there were 170 patients. Of these, 50 patients were died at 1-year follow-up. Thus, the remaining 120 patients were entered into the study (no reconstruction: 40, reconstruction with plate: 41, and reconstruction with flap: 39). The mean age of patients was 50.4 (standard deviation=15.9) years, ranging from 22 to 85 with a median of 49 years. There were no significant differences among patients in age ($P=.12$), gender ($P=.52$) and stage of the disease ($P=.78$). Most patients presented with advanced stage (III and IVA) and all underwent mandibular resection. The characteristics of patients are presented in Table 4.

Table .4

Quality of life among study samples as measured by the European Organization for Research and Treatment of Cancer core quality of life questionnaire (EORTC QLQ-C30).

Mean (SD) Mean (SD) Mean (SD) P

	No reconstruction (n =40)		Reconstruction with plate (n =41)		Reconstruction with flap (n =39)		P
	Orta (SD)		Orta (SD)		Orta (SD)		
Functioning†							
Physical	82.5	(24.2)	84.1	(23.7)	86.6	(13.8)	.76
Role	87.0	(30.7)	93.8	(20.2)	96.5	(12.7)	.33
Emotional	62.1	(25.6)	66.8	(22.2)	69.4	(24.8)	.37
Cognitive	62.1	(25.6)	66.8	(22.2)	69.4	(24.8)	.37
Social	83.7	(27.5)	85.9	(29.1)	90.0	(19.9)	.77
Global quality of life	60.7	(21.3)	58.9	(18.0)	61.0	(20.8)	.79
Symptoms‡							
Fatigue	13.6	(19.4)	8.7	(19.1)	19.8	(15.1)	.23
Nausea and vomiting	2.8	(11.7)	4.8	(12.7)	1.2	(4.4)	.35
Pain	17.5	(26.4)	12.2	(21.1)	11.5	(16.2)	.67
Dyspnea	12.5	(20.9)	9.6	(25.5)	8.5	(16.6)	.31
Sleep difficulties	22.5	(27.6)	15.7	(24.1)	14.5	(22.6)	.38
Appetite loss	11.4	(20.9)	12.5	(22.2)	11.9	(17.9)	.58
Constipation	18.6	(21.1)	18.4	(21.5)	13.3	(19.6)	.39
Diarrhea	1.6	(7.2)	2.7	(12.1)	0.8	(5.2)	.78
Financial difficulties	21.9	(34.6)	14.9	(30.7)	20.8	(30.3)	.55

SD = standard deviation. *

Derived from Kurskal–Wallis test. † Higher scores indicate better conditions.

‡ Higher scores indicate worse conditions.

Finally, quality of life as assessed with the EORTC QLQ H&N35 did not show any significant differences among the study samples except for speech problems ($P=.04$), dry mouth($P=.03$), and feeling ill ($P=.04$). In general, patients who did not receive reconstruction scored higher on symptoms as measured by the EORTC QLQ-H&N35, indicating lower quality of life compared to patients who received reconstruction with plate or reconstruction with flap. The detailed results are presented in Table 5.

The findings from the current study did not show significant differences among patients who received different reconstructions for oral cancer. Unfortunately, there is a wide range of contradictions on reconstruction for cancers of oral cavity in the literature. Few studies reported on the type of complication with respect to the reconstruction parameters.

A study examined depression and quality of life among survivors of head and neck cancers. A sample of patients with head and neck cancer with mean follow-up period of 38.7months were evaluated by the EORTC QLQ-30, QLQ H&N35, and the Hospital Anxiety Depression Scale. Significant pretreatment predictors of long-term depressive symptoms were cigarette smoking, alcohol use, T3 or T4 tumors, and more than 3 medications, while significant predictors of global quality of life were anemia, hypoalbuminemia, and T3 or T4 tumors.

Functioning scores for our patients were relatively high. Such observation might be due to the fact that patients in current study were relatively young (mean age 50.4 years). However, although younger age might not critically influence functioning in these patients, younger age patients might suffer more from other consequences such as facial appearance. A study of 25 young patients reported that mandible reconstruction with fibula flap significantly influenced young patients' quality of life.

Table . 5

Quality of life among study samples as measured by the European Organization for Research and Treatment of Cancer head and neck cancer-specific quality of life questionnaire-35 items (EORTC QLQ-H&N35)

	No reconstruction (n =40)		Reconstruction with plate (n =41)		Reconstruction with flap (n =39)		P†
	Orta (SD)		Orta (SD)		Orta (SD)		
Pain	15.4	(29.6)	11.1	(19.3)	10.8	(23.4)	.55
Swallowing	20.6	(26.9)	11.6	(15.4)	15.4	(19.1)	.31
Senses problems	12.9	(26.8)	7.6	(14.2)	4.6	(9.8)	.70
Speech problems	16.3	(25.7)	6.7	(16.2)	11.1	(23.2)	.04
Trouble with social eating	22.5	(29.9)	13.8	(21.6)	19.4	(28.6)	.42
Trouble with social contact	19.6	(26.1)	13.1	(19.8)	15.4	(24.7)	.50
Less sexuality	27.9	(39.6)	14.0	(25.5)	15.8	(34.8)	.22
Teeth	31.6	(37.7)	16.2	(27.4)	20.8	(30.9)	.12
Opening mouth	31.6	(37.7)	16.2	(27.4)	20.0	(30.9)	.12
Dry mouth	47.5	(40.5)	28.2	(37.1)	21.5	(34.4)	.03
Sticky saliva	14.1	(27.0)	5.1	(12.1)	13.3	(27.0)	.33
Coughing	16.6	(28.2)	9.4	(21.5)	13.3	(22.3)	.39
Felt ill	20.8	(28.9)	8.5	(16.6)	8.3	(16.4)	.04
Pain killers	20.8	(40.5)	15.7	(36.9)	20.5	(40.9)	.84
Nutritional supplements	20.8	(40.5)	10.5	(31.1)	10.2	(30.7)	.36
Feeding tube	10.2	(30.7)	7.8	(27.3)	2.5	(16.0)	.39
Weight loss	22.5	(42.2)	15.7	(36.9)	15.3	(36.5)	.65
Weight gain	10.0	(30.3)	10.5	(31.1)	13.1	(34.2)	.89

SD = standard deviation. *

Higher scores indicate worse conditions.

† Derived from Kurskal–Wallis test.

Bold values are significant.

However, a recent study reported that reconstructive microsurgery even can be proposed to older as well as younger patients because according to quality of life measures older patients can take advantage of this complex surgical technique.

Three quality of life parameters were found significantly differed among the patients groups. These were speech problems, dry mouth, and felt ill. Looking at the data, it seems that the difference mainly was originated from difference between no reconstruction group with the 2 other groups; otherwise, there was no significant differences between the group who received reconstruction with plate or reconstruction with flap. A findings from a prospective study showed that in general microvascular reconstruction after mandibular osteoradionecrosis may improve health-related quality of life with an emphasis on pain reduction, improved scores for feeling ill, and sexual difficulties as measured by the EORTC QLQ-H&N35.

Result of PMMF reconstruction

The pectoralis major muscle receives its blood supply from the thoracic branch of the thoracoacromial artery and the lateral pectoral artery. After dissection of the chest wall flap, a subcutaneous tunnel is formed under the skin between the neck and the chest and the flap is passed under the skin bridge. The flap is placed into the defect and secured with two layers of sutures.

The 5-year overall and cancer-specific survival rates were 11.0% and 65.5%, respectively. These results compare favorably with the literature for advanced and recurrent diseases, despite the fact that a large proportion of patients died due to other diseases associated with concomitant complications.

The results of free-flap surgery

The patients average age of those who have reported total flap loss was 65.5 ± 10.6 years and in other people was 59.4 ± 15.5 ($p=0.59$). There have been different side effects on 10 patients (34.5%). Hematoma was seen in 2 people (6.9%) and infection, slow wound healing and death each one were seen in 1 patient (3.4%). There wasn't any report of side effects like seroma, compartment syndrome pulmonary embolism in our patients. Some other effects

which haven't mentioned in the questionnaire, have been seen in 5 patients. The average age of those with partial fl ap loss was 49.6 ± 20.4 years and other patients average age was (61.1 ± 14.4 years) ($p=0.22$). The average age of those with hematoma was 67.5 ± 9.1 years. The patient with infection and slow wound healing were 52 and 68 years old. Comparing this cases showed no significant statistic difference ($p=0.88$). The anesthesia average time in patients with total fl ap loss was 495 ± 63.6 minutes and in the other patients was 552 ± 83.6 minutes ($p=0.25$). The anesthesia average time in patients with partial fl ap loss was 570 ± 108.1 minutes and in other patients was 545 ± 81.5 minutes ($p=0.63$). The operation progress ischemia average time in patients with total fl ap loss was 120 ± 84.8 minutes and in other patients was 104.3 ± 32.3 minutes ($p=0.56$). Ischemia average time in patients with partial fl ap loss was 116.6 ± 60.2 minutes and in other patients was 104 ± 33 ($p=0.58$). There was reported only one PT from 2 patients with total fl ap loss and that was 18.6 seconds. PT average in other patients was 13.5 ± 1.8 seconds. It has been a significant statistic difference in this case ($p=0.015$). PT mean in partial fl ap loss was 14.2 ± 0.98 seconds and in other patients was 13.7 ± 2.1 seconds ($p=0.78$). PPT in one that had total fl ap loss was 65 seconds and in others was 41 ± 14.3 seconds ($p=0.11$). PPT mean in those with partial fl ap loss was 29 ± 1.4 seconds and in other patients was 43.1 ± 15 seconds. There wasn't a significant statistic difference ($p=0.20$). INR in those with total fl ap loss was 202 and in other patients was 102 ± 0.3 ($p=0.006$). INR mean in partial fl ap loss was 1.2 ± 0.0 and in other patients was 1.2 ± 0.3 ($p=0.81$). ACT in one who had total fl ap loss was 46 and its mean in other patients was 82 ± 18.9 . It was almost a significant difference ($p=0.08$). ACT mean in patients with partial fl ap loss was 80 ± 5.6 and in others was 80.2 ± 21.2 ($p=0.98$). Both people with total fl ap loss were male. Other people were 29 (74.1%) male and 10 (25.9%) female ($p=0.56$). In partial fl ap loss, all people were male too. In other people, 19 (73.1%) were male and 7 (26.9%) were female. There was not seen any significant difference ($p=0.42$). Table 3 shows post-operation side effects frequency with

gender segregation. Also, there wasn't any significant statistic difference in this case ($p=0.26$). There was a smoker person and a no smoker person among the patients with total flap loss. On contrary, there were 7 smokers (17.9%) and 32 (82.1%) no smokers ($p=0.21$). All patients with partial flap loss were no smokers. On the other hand, 8 people (20.5%) were smokers and 31 people (79.5%) didn't use tobacco ($p=0.41$). Our studies shows that cigarette consumption didn't have influence on frequency of post-surgery side effects ($p=0.32$). There was a post-surgery Anti-coagulation consumption in one patient among those two patients with total flap loss, on contrary there was Anti coagulation consumption in 29 patients (74.1%) and 10 patients (25.9%) without this consumption($p=0.46$). in 3 patients with partial flap loss, there was a post-surgery Anti-coagulation consumption. In other patients, there was a post-surgery Anti-coagulation consumption in 20 patients (51.3%) and didn't use in 6 patients (15.4%) ($p=0.011$). Both patients with total flap loss had operation antecedent. In other patients 15 (37%) people had operation antecedent ($p=0.081$). Both patients with partial flap loss had operation antecedent and the other one didn't. There were 10 people with no operation antecedent among those with partial flap loss which didn't have operation antecedent ($p=0.34$). The operation antecedent didn't have influence on post-surgery side effects too. Also, the lidocaine consumption during surgery didn't have influence on total flap loss or partial flap loss ($p=0.58$ and $P=0.50$ respectively). We have the same situation in heparinated saline consumption too ($p=0.58$ and $P=0.50$ respectively). There wasn't a significant statistic difference of adjuvant therapy application in total flap loss or partial flap loss, although it was near to be significant in complete flap loss ($p=0.064$).

Results of assessment of oral and neck functions

The study included 45 patients with squamous cell carcinoma of the tongue and bottom of the mouth. 23 patients in the age group of 63.9 ± 14.0 (average \pm SD (standard deviation)), 9 women and 14 men, in the surgical group (SG), 6 patients, 16 men, 61 patients in the age group of 61.8 ± 10.0 , studied in the radiotherapeutic group

(SRG). Table 1 shows the characteristics of the stages of pathological tumor (pT), the area of resection and the type of reconstruction.

X² tests showed that the number of patients differed significantly in both groups according to the size of the primary tumor and the type of reconstruction. Due to time constraints, 2 patients could not be examined during the time between surgery and radiotherapy. In addition, 2 patients (SG) underwent additional resection for 1 month after surgery. One patient (SRG) underwent reconstructive surgery between 6 and 12 months after surgery due to extensive osteoradionecrosis.

The effect of tumor stage, resection site, and reconstruction on preoperative and postoperative functional changes of the tongue was examined by the Kruskal-Wallis test and one-way VAAN.

Maximal active lateral flexion of the neck. Maximal lateral flexions of the patients of the 4 neck dissection groups are depicted at the various measurement moments in Figure 2. The solid line represents the average angle of the neck movements of the healthy controls. The maximal lateral flexion showed a significant ($p < 0.05$) change at both the ipsi- and contra-lateral side of the SND group over the 1-year No ND SND (M)R ND bilateral ND p-value T umour stage (T of T NM) During the 1-year period a gradual recovery occurred. Patients of the SND group showed deterioration of maximal lateral flexion of the neck at both the ipsi- and contra-lateral side ($p < 0.01$) between half and one year after intervention. Patients of the bilateral ND group had low maximal lateral flexion values at all measurement moments. Before intervention no significant differences in maximal lateral flexion of the neck were observed between the patients of the 4 ND groups and the controls. Shortly after intervention lateral flexion to the contra-lateral side of the neck of the (M)RND group was significantly lower ($p < 0.05$) than the lateral flexion of the healthy controls, patients with no ND, and contra-lateral lateral flexion in the SND group. One year after intervention the bilateral ND group showed a significantly lower ($p < 0.05$) maximal lateral flexion of the neck than healthy controls and patients without a ND Maximum lateral flexion in patients from 4

neck dissection groups is described at different assessment points. The valid line represents the mean angle of neck mobility in healthy controls. Significant change in maximal lateral flexion ($p < 0.05$) was present in both the ipsi-lateral and counter-lateral side SND group for more than 1 year.

Maximum active posterior flexion of the shoulder showed significant ($p < 0.01$) changes in the ipsi-lateral side in both SND and (M) RND groups over a one-year period. Immediately after the intervention, a significant decrease in maximal posterior flexion ($p < 0.05$) was observed in all groups except the counter-lateral SND group.

Maximum shoulder abduction over a period of more than one year showed significant changes in all patient groups ($p < 0.05$), with the exception of the contralateral-lateral side in the (M) RND group. Maximum abduction worsened significantly ($p < 0.05$) in all patients, with the exception of contra-lateral abduction in patients with SBD and (M) RND groups. Significant reductions in abduction (M) were observed in the ipsi-lateral side of patients in the RBD group (about 60%) and in the ND group (about 50%) in all indications for abduction.

A significant increase in pain while moving the neck was reported shortly after intervention by the patients of the SND, (M)RND and bilateral ND groups. The pain scores decreased during the 1-year period for the patients of the SND and bilateral ND groups to the level of the controls, but remained significantly higher than the scores of the controls for the patients of the (M)RND group. The patients of the no ND group reported pain scores comparable to those of the controls. Before intervention no significant differences in pain while scores were observed between the patients of the 4 ND groups and the controls. Shortly after intervention the patients of the SND, (M)RND, and bilateral ND groups scored significantly higher ($p < 0.05$) on pain while moving the neck, than the healthy controls and the patients without a ND. Half a year after intervention the (M)RND and bilateral ND groups still significantly differed ($p < 0.05$) from the no ND group. One year after intervention the patients of the (M)

RND group scored significantly higher on pain ($p < 0.05$) than the healthy controls, the no ND and the SND group. Pain when moving the neck varied significantly ($p < 0.001$) over one year in patients with SND, (M) RND, and bilateral ND groups.

Result of experimental research

The study aims to determine the effect of Diltiazem on the microcirculation and vascular wall, as well as subcutaneous soft tissues and skin on the skin used during reconstructive and plastic surgery. Appropriate medication was administered and changes in skin and subcutaneous tissue were examined after 2 weeks (14 days) with histological examination.

Endothelial hyperplasia, thickening in the arterial vessel wall, and thrombosis were significantly lower in the main group. Endothelial thickening was seen mostly in control group, less in comparison group, and the least in the main group.

General hyperplasia, swelling, papillary proliferation of endothelial layer were evident in some samples of the control group. Although the findings are usually seen in the veins of the suture side of the tissue flap, various re active lesions were observed in the veins of the central part of the flap. In this group, endothelial lesions mainly were seen in arterial vessels. Endothelial lesions were more prominent in the areas of capillary proliferation (granulation tissue) in surgical section side of the flap. Lumen obstruction was seen in some vessels due to endothelial hyperplasia. Endothelial hyperplasia was seen just in some samples of the comparative group; it was total and flat type hyperplasia, and papillary proliferation has not been observed in any case. Vascular obliteration due to endothelial hyperplasia did not appear. Focal or total flat endothelial hyperplasia was identified in only a few of the main group samples. There was a statistically significant difference between the control and the main groups when comparing the mean values of endothelial hyperplasia ($P=0.001$). However, there was no statistically significant difference between the comparative and the main groups when comparing the same parameter ($P=0.096$).

As in our study, previous studies have also revealed that diltiazem can prevent vascular wall thickening and lumen obstruction by preventing smooth muscle tissue damage of vessel wall. A study on monkeys has highlighted that diltiazem successfully eliminated vasospasm in brain vessels. The concluded findings have also been elaborated on in studies with different experimental models. The main achievement of our study was to transpire the correlation between diltiazem and endothelial hyperplasia. This fact with morphological parameters may be very valuable in future studies with diltiazem. It can be conducive to coming up with more significant and solid findings in this respective area of observation.

According to final findings of the study on rabbits with a developed model of ischemia, with prescription of diltiazem, endothelial hyperplasia on microcirculatory system of skin, the thickening of arterial vessel walls and the thrombosis in vessel's passage were rarely observed through statistical differences. Diltiazem eliminates the factors, causes vessel occlusion and hypoxia as its sequence.

CONCLUSIONS

1. Among the groups of patients with soft tissue defect after resection of the primary tumor in oral cancer, only physical activity was significantly different between the three groups ($p = 0.003$). According to symptoms measured by QLQ-C30, fatigue ($p < 0.001$), nausea and vomiting ($p = 0.01$), pain ($p = 0.035$) and dyspnea ($p = 0.002$) were significantly different between the three groups. It has been shown that reconstruction with a distant-regional flap leads to a better quality of life in patients with oral cancer compared to no flap and local flap [25].
2. Sensory problems ($p = 0.012$), speech problems ($p = 0.005$), social eating problems ($p = 0.027$), teeth function ($p = 0.005$) after using a generalized regression model to correct the results based on age, type of reconstruction and disease stage, eight of the 19 QOL variables showed significant differences, including

skin problems ($p = 0.038$), wound healing problems ($p = 0.038$), weight loss ($p = 0.020$), and neurological problems ($p = 0.009$) [24,26].

3. According to the final results of the experimental study, in rabbits treated with diltiazem drug, endothelial hyperplasia in the vessels of the microcirculatory system, thickening of the arterial vessel wall ($p=0.000$), and thrombosis in the vessel port were recorded at a weaker level with a statistically significant difference ($p=0.000$). In contrast, venous congestion and perivascular hemorrhages, as well as edema, were more intense in this group [17,27].
4. The quality of life assessed by the EORTC QLQ-C30 among the groups of patients undergoing mandibular resection showed that the indicators of physical function ($p=0.76$), role function ($p=0.33$) and global quality of life ($p=0.79$) of the patients in the 3 groups were relatively high, at the same time showed lower results in emotional ($p=0.37$) and cognitive ($p=0.37$) function. Three quality-of-life parameters were significantly different between groups of patients undergoing mandibular resection. Quality of life assessed with the EORTC QLQ-H & N35 did not show significant differences between study samples, except for speech problems ($P = .04$), dry mouth ($P = .03$) and feeling unwell ($P = .04$). In general, patients without reconstruction had higher scores on symptoms assessed by the EORTC QLQ-H & N35, which demonstrated lower quality of life than patients who underwent plate reconstruction or flap reconstruction. [22].
5. Shortly after the intervention, SND, (M)RND and bilateral ND (ND) group patients had significantly higher pain during neck movement compared to the control group and patients without ND ($p < 0.05$). After half a year of intervention, (M)RND and bilateral ND groups differed significantly from the group without ND ($p < 0.05$) [11, 13].
6. Reconstruction in patients with soft tissue defect after removal of the primary tumor in oral mucosa cancer with distant pedicle flaps, and free vascular pedicle flaps in patients undergoing

mandibular resection gave more effective results in terms of quality of life indicators.

PRACTICAL RECOMENDATIONS

1. In order to assess the overall quality of life in patients with oral cancer, filling out a questionnaire by patients can be important.
2. After surgical treatment, repeated filling of the questionnaire by the patients is important to evaluate the effect of the applied treatment on the patient's quality of life.
3. Among the reconstruction methods used for the elimination of soft tissue defects in the surgical treatment of oral cancer, reconstruction with a distant pedicle flaps is more effective based on quality of life indicators.
4. Among the reconstruction methods used to eliminate mandibular defects in the surgical treatment of oral cancer, the use of free vascular pedicle bone autografts is more effective based on quality of life indicators.

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LIST OF ABBREVIATIONS AND TERMS

QOL- quality of life

H&N 43 – a 43-item head-length quality-of-life questionnaire

EORTC – European Organization for Cancer Treatment and Research

QLQ – C 30 – a 30-item quality of life questionnaire related to general health

QLQ – H&N 35 – a 35-question head-and-neck quality-of-life questionnaire

PMMF – pectoralis major myocutaneous flap

H&N – head and neck

ND – neck dissection

SND – suprahyoid neck dissection

MRND – modified radical neck dissection

RND - radical neck dissection

SAN – spinal accessory nerve (XI nerve)

SCC – squamous cell carcinoma

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