The Quantification of Salivary Flow and pH and Stomatognathic System Rehabilitation Interference in Patients with Oral Diseases, Post-Radiotherapy

Bogdan Petru Bulancea 1,*, Laura Elisabeta Checherita 2,*, Carmen G.; Carmen, G.; Postolache, M.; R.; Carmen, G.; Postolache, M.; et al. The Quantification of Salivary Flow and pH and Stomatognathic System Rehabilitation Interference in Patients with Oral Diseases, Post-Radiotherapy. 

Abstract: Xerostomia is a common complication post-radiotherapy in patients with oral cancer. The acute and long-term side effects can considerably reduce the patient’s quality of life. The aim of our study was to perform analysis of salivary flow and pH in patients after radiotherapy. Methodology: Clinical and laboratory evaluations were conducted in the 2014–2019 period; out of a total 58 subjects aged between 45 and 84, 28 individuals with oral cancer were selected from St. Spiridon Hospital, Clinic of Maxillo-facial Surgery and Oncology Hospital, Iasi post-radiotherapy. Results: Significant downsized mean values of the hydrogen ion concentration (pH) in saliva (p < 0.001) were recorded in patients after radiotherapy, pH value = 4.580 (±1.051). The mean value of resting salivary flow (MRSF) was significantly lower for the group of patients with radiotherapy (MRSF) = 0.145 mL/min. In 89.29% of cases (25 post-radiotherapy cases), in order to perform oral complex rehabilitation treatment, several endodontic and periodontal treatments were performed. A total of 78.57% of the cases received complex oral rehabilitation as mobile or hybrid prostheses or fixed solutions. Conclusion: Understanding post-radiotherapy salivary biochemic modifications in patients with oral cancer could be of critical importance, in view of related oral disorder prevention.

Keywords: oral cancer; post-radiotherapy (RT); salivary pH; salivary flow rate (SFR); intraoral complex rehabilitation treatment; stomatognathic system (SS); temporomandibular joint (TMJ); temporomandibular disorder (TMDs)
1. Introduction

Oral cancer is one of the sixteen most common cancers worldwide [1]. Most patients are treated with chemotherapy, surgery, and radiotherapy. Ionizing radiation, which is used for treating head and neck cancers, produces oral side effects such as saliva quality variations, mucositis, and destruction of dental structures. In these cases, infections of dental origin in compromised patients are potentially lethal [2]. Radiation therapy techniques have steadily improved over the last few decades. Treatments now target the cancers more precisely, and more is known about setting radiation doses. These advances are expected to decrease the number of secondary neoformation pathologies and other complications that result from radiation therapy [3].

Oral fluid that lubricates the oral cavity, in case of xerostomia, hyposalgia, and sicca syndrome (decreased or absent salivary flow measured by tests), may induce burning sensations. Decreased salivary flow and dry mouth (xerostomia) can have consequences on both mastication and speech. In addition, less saliva means less protection of the teeth and oral cavity.

Hyposalgia promotes the appearance of infections, caries, and alteration of the oral tissues. Hyposalivation can have serious negative effects on the patient’s quality of life by affecting eating habits, nutritional status, phonation, taste perception, and prosthesis tolerance, as well. Xerostomia, caused by dysfunction of the salivary gland, is a common complication in oral cancer patients after radiotherapy [4], and it increases the risk of infections at the level of the oral cavity, causing the appearance of candida albicans.

Saliva is presented as an aqueous, hypotonic solution, which protects all the tissues of the oral cavity. It is secreted by numerous minor salivary glands and predominantly the major salivary glands- the parotid, submandibular or submaxillary, and sublingual. Saliva is critically important in oral homeostasis [5]. Physiologic salivary functions include maintenance of oral soft and hard tissues’ homeostasis, bacterial modulation, or support for other oral functions. Saliva assists in digestion (both in the mouth and gastro-intestinal tract), taste, and swallowing, as well [6,7]. It plays an essential role in oral tissue lubrication and the adjustment of the salivary potential of hydrogen (pH) [8]. The effects of a loss or reduction in salivary function can be severe, and can have a significant impact on common activities [9].

Salivary secretory disorders, xerostomia and sialorrhea, can be caused by a wide range of factors, including drugs and radiotherapy [10]. There are few studies in the literature related to the alterations of saliva, in the context of systemic diseases [11]. The usefulness of saliva in the diagnosis of diseases of the oral cavity, the risk of caries, and the monitoring of oral pathology is an ever-growing area of active investigation [12,13]. So, salivary tests can be used for diagnosis as well as to monitor the status of disease.

According to the literature, patients with oral saliva pH values ≤ 5.3 nine months after radiotherapy presented significantly higher risks for radiotherapy-related caries (RRCs) [14]. Another study found that patients suffering from radiotherapy-related caries (RRCs) displayed low levels of oral salivary pH values (4.3–5.0) for a long period after radiotherapy and had a slow rate of recovery. Patients without dental caries showed a decrease in saliva pH to 5.0–5.5 but recovered quickly to 5.5–6.0. The persistence of a steady state, which no longer decreased, indicated that increasing the oral saliva pH value to >5.3 could be a new target to prevent or reduce the occurrence of RRCs [13].

Some changes related to oral–systemic conditions, such as the increased prevalence of dental caries [14] and, consequently, oral infections, patients with xerostomia [15] represented a challenge for dental practitioners. Consequently, in order to control decay control in long-term therapy, a method of performing prosthetic restorations, including the occlusal pathology managements, ulcers of the oral mucosa, and oral cancer, could be assigned.

2. Aim of the Study

As the importance of the saliva in the protection of the dental hard and soft tissues is well known, the association of the salivary functions and oral morbidity determined by
dental caries, oral mucosa, and oral tissue injuries could be of great interest. We aimed to explore stomatognathic system (SS) changes and salivary gland functionality in patients affected by oral disorders, post-radiotherapy.

Our research targeted the evaluation of saliva rest flow drooling (RSF), rate of stimulated saliva (MRSF), and salivary pH in patients following radiotherapy for oral cancer. The results for these patients were compared to cancer-free subjects that were included in a control group.

Statistical analysis of RSF, MRSF, and pH associated to clinical examination and treatment rehabilitation was performed in order to achieve stomatognathic system (SS) homeostasis in the study cases compared to a control group.

The SS component involvement and stability through oral complex rehabilitation, periodontal, endodontic interventions, prosthetic treatments, and temporomandibular reconditioning is regularly performed for functional and aesthetical purposes, considering the biochemical and morphological aspects related to maintenance of the stomatognathic system homeostasis.

3. Materials and Methods

The clinical and paraclinical evaluation was conducted in the 2014–2019 period in a group of 58 patients aged between 45 and 84 years old, out of which 28 patients that received head and neck radiotherapy for oral cancer were selected from St. Spiridon Hospital, Clinic of Maxillofacial Surgery and Oncology Hospital, Iasi, Romania.

3.1. Study Design

The study design was built according to case-control study methodology. We used clinical and paraclinical data extracts from the paper observation documents of the patients present at the request of our study to which we added information from measurements recorded for pH and salivary flow, respectively. These data are important for dentists because a post-radiotherapy cancer patient often requires complex oral rehabilitation.

The methodology of case-control studies is where the selection of patients is conmsecutive to those presented in person for oral rehabilitation therapy.

- Inclusion criteria for the cases were as follows: patients suffering from oral cancer post-radiotherapy, that had a dose of irradiation between 60 Gray (Gy) and 70 Gy, depending on the specifics of each patient, presenting after a minimum interval of 2–3 months post-radiotherapy cure.

In our area, NE part of Romania, the external beam radiation therapy (EBRT) with IMRT (intensity modulated radiotherapy) technique is commonly used. Doses are reported in 60 Gy/30 fractions/6 weeks, 70 Gy/35 fractions/7 weeks, or 66 Gy/33 fractions/6.5 weeks, 2 Gy/fraction [16,17].

- The exclusion criteria for the cases were as follows: non-cancer patients (other pathologies might exist); non-cooperating patients; patients with advanced or terminal illnesses; incapacitated patients for scheduled procedures; and patients with medication that induces hyposalivation.

The SFR is an indicator of xerostomia after radiotherapy in patients with oral cancer. Sialometry encompasses a range of diagnostic tests aimed at evaluating the rate of salivary secretion (quantitative sialometry) and analyzing its composition (qualitative sialometry), it is an important tool in the rehabilitation treatment plan.

After radiotherapy, in patients with oral cancer, sialometry and salivary pH monitoring were necessary for estimating the risk of dental caries and to establish a complex oral rehabilitation plan. Prior to saliva harvesting, subjects were instructed to refrain from eating, drinking, and smoking.
3.1.1. The pH Measurement

Determination of the salivary pH was carried out directly using a digital pH meter (APH 20 model). The accuracy of the pH meter was calibrated using standard buffers (pH 4.7 and 10) to ensure the correct measured values.

3.1.2. The RSF Measurement

Determination of RSF rate (the procedure was realized in triplicate, recording the mean value) was performed by the following method: the patient sat in the dental chair with their head was slightly bent forward, and then they were asked to swallow the saliva accumulated in their oral cavity, after which the timer was started. The patient removed accumulated saliva every minute into a beaker; after 5 min, the amount of accumulated saliva was measured. Normal values range between 0.25–0.35 mL/min according to data in the literature [18].

3.1.3. The SSF Measurement

Determination of stimulated salivary flow (SSF) rate (the procedure was realized in triplicate, recording the mean value) was carried out according to the following method: the patient was sitting in the dental chair as in the previous test and was asked to chew for 60 s, and then swallow the accumulated saliva. The timing started after one minute, leaving the patient to evacuate saliva in a graduated beaker for 5 min. The volume was expressed as mL/minute. Normal values lie in the range 1–1.5 mL/min [18,19].

3.2. General Clinical Investigation Methods Used for Stomatognatic System Area

The clinical methods used in our study were important for periodontal status analysis, caries detection, endodontic evaluation, and prosthetic treatment staging, established for the achievement of homeostasis in the post-radiotherapy context.

3.2.1. Periodontal Indexes Quantification

Clinical periodontal data are, in general, presented on Ramfjord teeth (1.6, 2.1, 2.4, 3.6, 4.1, and 4.4): silliness and low gingival index (GI), gingival bleeding index (GBI), community periodontal index of treatment needs (CPITN), probing depth (PD), and clinical attachment loss (CAL), all of which offer an in-depth view of present periodontal damage.

3.2.2. Caries Indexes Quantification

The level of oral hygiene and estimation of saliva characteristics responsible for the occurrence of dental caries, for example, can be detected by special indexes such as the Decayed, Missing, and Filled Teeth (DMFT) index.

3.3. For a General Complex Rehabilitation Frame, Clinical Examination Methods Consist of the Following

3.3.1. Extraoral Examination with the Following

- temporomandibular joint (TMJ) inspection, palpation, and auscultation,
- palpation of the stomatognathic system muscle,
- the head and neck area lymph node system,
- superficial palpation of temperature, humidity, and sensitivity constants,
- posture relation (PR) and centric relation (CR),
- the evaluation by anthropometric adjuvant methods.

3.3.2. Intraoral Clinical Examination with the Following

- inspection, palpation and percussion of odonto-parodontal examination,
- occlusal relation from static and dynamic terms of gnathological-perceived concepts.
3.3.3. Paraclinical Investigative Methodology Support

Paraclinical examination can be performed to different degrees of complexity, from simple retro-dental-alveolar radiographs (RDR) and orthopantomography (OPG) to computer tomography (CT) and cone beam computer tomography CT (CBCT), as well as TMJ tomographkinesimandibulographies (KMG) and electromyography (EMG); however, study models or photographs have to display the necessary details for parameter restoration.

3.3.4. Rehabilitation Stadialisation

Oral rehabilitation can be initiated by cranio-mandibular reposition and can be performed by establishing the principles of treatment through classical methods-preparation, impression, stage checks of prosthetic framework, and final adaptation, depending on the clinical situation and individual criteria.

3.4. The Statistical Analysis

A database was created using Microsoft Access for Windows. The statistical analysis was performed with the SPSS 20.0 software package for Windows. It was used to assess the central tendency indicators.

The following factors were considered dependent variables: salivary pH, RSF, and SSF, which were important issues that were discussed in our study by their influence on the functionality of the SS in the context of oral rehabilitation viability.

A statistical descriptive methodology was used to evaluate the central tendency indicators for RSF and SSF.

Statistical analytic methodology (Pearson χ² test) was used to evaluate the statistical significance of observed differences.

3.5. Ethical Considerations

All study patients were evaluated by a multidisciplinary head and neck oncology team and were subjected to a physical examination, biopsy of the primary lesion for histologic confirmation, and computed tomography (CT) or magnetic resonance (MRI).

All patients signed an informed consent for the procedures and gave their written consent to participate in this study for complex oral rehabilitation. The study was approved by the Ethics Committee of Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, and Apollonia University Iasi, Romania, also. All protocols were in accordance with the provisions of the Declaration of Helsinki.

4. Results

For paraclinical and clinical assessment, patients were divided into two groups, as follows:

- Group A consisted of 28 patients that followed radiotherapy for oral cancer (cases group);
- Group B, non-cancer cases, consisted of 30 patients (control group).

4.1. General Characteristics of the Studied Groups

The gender distribution was as follows: 23 women in total, 9 in the radiotherapy and 14 in the control group; 35 men in total, 19 in the radiotherapy group and 16 in the control group (Table 1). During the study, 3 patients from the cases group were removed.

<table>
<thead>
<tr>
<th>Gender</th>
<th>N/(%)</th>
<th>Group A Cases of Radiotherapy</th>
<th>Group B Controls</th>
<th>χ²</th>
<th>Liberty Degrees (LD)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>23 (39.66)</td>
<td>9 (32.14)</td>
<td>14 (46.67)</td>
<td>1.277</td>
<td>1</td>
<td>0.25845</td>
</tr>
<tr>
<td>Male</td>
<td>35 (60.34)</td>
<td>19 (67.86)</td>
<td>16 (53.33)</td>
<td>0.588</td>
<td>0.101</td>
<td>0.46712</td>
</tr>
<tr>
<td>Total</td>
<td>58 (100.0)</td>
<td>28 (48.28)</td>
<td>30 (51.72)</td>
<td>0.588</td>
<td>0.101</td>
<td>0.46712</td>
</tr>
</tbody>
</table>

The gender structure of the batches was homogeneous. All the values calculated for χ² ≥ up to 3.841 were considered statistically significant for p < 0.05.
Associated Pathological Features Description

In terms of the description of associative pathological features, according to the anamnesis we could mention the following, presented in Table 2: hypertension (HTA) and cardiovascular pathologies, metabolic impairment and/or diabetes, osteoporosis, Alzheimer’s disease, stroke, minor to moderate psychiatric pathologies such as depression and anxiety.

Table 2. The associative pathological features of the study groups.

<table>
<thead>
<tr>
<th>Associated Pathological Feature</th>
<th>N/(%)</th>
<th>Group A Cases of Radiotherapy</th>
<th>Group B Controls</th>
<th>$\chi^2$</th>
<th>LD</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTA and cardiovascular diseases</td>
<td>25 (34.10)</td>
<td>15 (53.37)</td>
<td>10 (33.33)</td>
<td>2.419</td>
<td>1</td>
<td>0.11987</td>
</tr>
<tr>
<td>Metabolic disorder/diabetes</td>
<td>14 (24.14)</td>
<td>9 (32.14)</td>
<td>5 (13.33)</td>
<td>1.894</td>
<td>1</td>
<td>0.16875</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>10 (17.24)</td>
<td>8 (28.57)</td>
<td>4 (13.33)</td>
<td>2.049</td>
<td>1</td>
<td>0.1523</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>10 (17.24)</td>
<td>6 (21.42)</td>
<td>4 (13.33)</td>
<td>0.665</td>
<td>1</td>
<td>0.4148</td>
</tr>
<tr>
<td>Stroke</td>
<td>5 (8.62)</td>
<td>3 (10.71)</td>
<td>2 (6.6)</td>
<td>0.301</td>
<td>1</td>
<td>0.58325</td>
</tr>
<tr>
<td>Psychiatric pathologies</td>
<td>14 (24.14)</td>
<td>9 (32.14)</td>
<td>5 (13.33)</td>
<td>1.894</td>
<td>1</td>
<td>0.16875</td>
</tr>
</tbody>
</table>

From the point of view of living and work conditions, post-radiotherapy cases were in first place, and control cases were in second position and the antecedents were as follows: 6/6 (21.42%/20%) alcohol consumers ($\chi^2 = 0.018$, DL = 1, at $p = 0.89327$); 10/8 (35%/26%) smokers ($\chi^2 = 0.554$, DL = 1, at $p = 0.45668$); 15/14 (53%/46%) patients that did not have a regular meal schedule ($\chi^2 = 2.322$, DL = 1, at $p = 0.12755$); and 22/7 (78.57%/23.22%) disbalanced dietary food principles at ($\chi^2 = 17.678$, DL = 1, at $p = 0.00002619^*$), with sedentary habits in the profile description cases.

4.2. The Study of Salivary pH

The statistical indicators of salivary pH are presented in Table 3.

Table 3. The central tendency indicators on salivary pH.

<table>
<thead>
<tr>
<th>Group of Study</th>
<th>Mean Value</th>
<th>Std. Dev.</th>
<th>Std. Error</th>
<th>CI 95%</th>
<th>Min. Value</th>
<th>Max. Value</th>
<th>Q25</th>
<th>Median</th>
<th>Q75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A: Radiotherapy</td>
<td>4.580</td>
<td>±1.051</td>
<td>0.25</td>
<td>4.059</td>
<td>5.102</td>
<td>3.00</td>
<td>5.50</td>
<td>5.00</td>
<td>5.50</td>
</tr>
<tr>
<td>Group B: Controls</td>
<td>6.259</td>
<td>±0.152</td>
<td>0.04</td>
<td>6.180</td>
<td>6.340</td>
<td>6.00</td>
<td>6.50</td>
<td>6.20</td>
<td>6.35</td>
</tr>
<tr>
<td>Total</td>
<td>5.350</td>
<td>±0.871</td>
<td>0.10</td>
<td>5.149</td>
<td>5.551</td>
<td>3.00</td>
<td>6.50</td>
<td>5.30</td>
<td>6.00</td>
</tr>
</tbody>
</table>

As was observed in our study, the oral pH in patients with radiotherapy was 4.580 (±1.051), and in the control group the oral pH value = 6.259 (±0.152).

4.3. The Study of Salivary Flow

The assessment of the function of the salivary glands was mainly based on the measurement of the saliva flow. Statistical indicators of RSF in mL/min are presented in Table 4.

Table 4. The central tendency indicators of resting salivary flow (RSF).

<table>
<thead>
<tr>
<th>Group of Study</th>
<th>Mean Value</th>
<th>Std. Dev.</th>
<th>Std. Error</th>
<th>CI 95%</th>
<th>Min. Value</th>
<th>Max. Value</th>
<th>Q25</th>
<th>Median</th>
<th>Q75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A: Radiotherapy</td>
<td>0.145</td>
<td>±0.051</td>
<td>0.011</td>
<td>0.091</td>
<td>0.131</td>
<td>0.030</td>
<td>0.160</td>
<td>0.105</td>
<td>0.130</td>
</tr>
<tr>
<td>Group B: Controls</td>
<td>0.503</td>
<td>±0.071</td>
<td>0.021</td>
<td>0.461</td>
<td>0.541</td>
<td>0.401</td>
<td>0.601</td>
<td>0.461</td>
<td>0.501</td>
</tr>
<tr>
<td>Total</td>
<td>0.385</td>
<td>±0.271</td>
<td>0.031</td>
<td>0.330</td>
<td>0.440</td>
<td>0.031</td>
<td>0.800</td>
<td>0.123</td>
<td>0.305</td>
</tr>
</tbody>
</table>
The mean value of SSF was significantly lower (at \( p < 0.001 \)) for the cases group with radiotherapy (MRSF = 0.145 mL/min) compared to the control group (MRSF = 0.503 mL/min). Statistical indicators for SSF, in mL/min, are presented in Table 5.

### Table 5. The central tendency indicators of stimulated salivary flow (SSF).

<table>
<thead>
<tr>
<th>Group of Study</th>
<th>Mean Value</th>
<th>Std. Dev.</th>
<th>Std. Error</th>
<th>CI 95%</th>
<th>Min. Value</th>
<th>Max. Value</th>
<th>Q25</th>
<th>Median Value</th>
<th>Q75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A: Radiotherapy</td>
<td>0.513</td>
<td>±0.387</td>
<td>0.091</td>
<td>0.321 - 0.706</td>
<td>0.150</td>
<td>1.130</td>
<td>0.375</td>
<td>0.890</td>
<td></td>
</tr>
<tr>
<td>Group B: Controls</td>
<td>1.475</td>
<td>±0.311</td>
<td>0.078</td>
<td>1.309 - 1.641</td>
<td>1000</td>
<td>2.000</td>
<td>1.450</td>
<td>1.750</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0.813</td>
<td>±0.393</td>
<td>0.038</td>
<td>0.738 - 0.889</td>
<td>0150</td>
<td>2.000</td>
<td>0.520</td>
<td>1.000</td>
<td></td>
</tr>
</tbody>
</table>

The salivary flow changes were important in the cases group of patients with RT (MSSF = 0.513 mL/min) compared to the control group (MSSF = 1.475 mL/min), at \( p < 0.001 \).

After completed radiotherapy, 10.71% (\( n = 3 \)) of the studied patients refused or did not show up to the complex oral rehabilitation treatments.

The identified location of the tumor lesions was as follows: six cases (21.42%) lower lip; three cases (10.71%) upper lip; three cases (10.71%) jugal zone; two cases (7.14%) tongue area; five cases (17.86%) posterior palate; seven cases (25.00%) buccal floor; and two cases (7.14%) had another combined localization (inferior or superior gingival and alveolar mucosa, s.o.).

Out of the total number of cases group, among subjects with squamous cell carcinoma, the representation of well-differentiated squamous cell carcinoma was 14.28% (4 cases), moderately differentiated squamous cell carcinoma 39.28% (11 cases), and poorly differentiated squamous cell carcinoma 46.42% (13 cases).

The oncologic irradiation protocol was made according to the thickness of the tissue through the radiology objected by a fractioned radiotherapy device, in correlation with other clinical parameters (Table 6).

### Table 6. Distribution of applied irradiation from the cases group.

<table>
<thead>
<tr>
<th>Localization</th>
<th>N/(%)</th>
<th>Cases Group Radiotherapy Applied (Gy)</th>
<th>Cases Group Stadium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip tumor</td>
<td>9 (32.14)</td>
<td>Bilateral ganglion 50-60 Gy</td>
<td>II and III</td>
</tr>
<tr>
<td>Jugal tumor</td>
<td>3 (10.71)</td>
<td>66 Gy</td>
<td>II and III</td>
</tr>
<tr>
<td>Tongue, posterior palate, oral floor tumors</td>
<td>14 (50.00)</td>
<td>60-66-70 Gy</td>
<td>I, II and III</td>
</tr>
<tr>
<td>Combined tumors</td>
<td>2 (7.14)</td>
<td>60 Gy/70 Gy</td>
<td>II and III</td>
</tr>
</tbody>
</table>

The lymph node irradiation protocol was applied for 9 (32.14%) cases of lip cancer, which received 50 Gy, the minimum doses applied, and the remaining 19 (67.25%) cases received different irradiation treatment doses adjusted according to the specific type and clinical situation of each case from the cases group.

Squamous cell carcinomas are sensitive to radiation therapy and non-keratinizing carcinomas respond better to chemotherapy, although they have a poorer prognosis.

### 4.4. Complex Rehabilitation Landmark

Histological evidence data have been considered from the beginning, therefore justifying the investigated neof ormation pathology before radiotherapy, which completed the paraclinical investigative dimension of the thematic study.

Also, important sequences of the clinical examination of the cases were represented by the initial aspects of the maxillary and mandibular arches, dental caries, periodontal affection, randomly presented edentation and aspects of malocclusion, interferences in
dynamic occlusion, limitation of mouth opening, and cranio-mandibular malrelations in posture (RP) or centric relation (RC), also.

The adjuvant paraclinical investigation tools used were the documentary casts, OPG, TMJ-tomography, KMG, and CBCT, as well as the evolution in the context of oral rehabilitation treatments, which offered the opportunity to change the situation in a more functional and desirable aesthetic form, according to objective and subjective criteria considered of each individual case.

During the extraoral examination, at the TMJ level, through the classic investigative methods such as inspection, auscultation, and stomatognathic muscle palpation, the ganglionic head and neck area system palpation, superficial palpation of temperature, humidity, and sensitivity constants, the important justification of clinical sign elements were revealed and also correlated with sedentary habits combined with malnutrition and psychiatric disorders and general associative pathology.

The following information, by comparison, is presented in Table 7: TMDs, with asymmetry and asynergistic signs on right sight, with crackles and crepitation, asymmetry and asynergism on left side and crepitation and lateral deviation in both studied groups.

The muscular system, methodologically palpated, by the two inseparable methods and registered hypertonicity, being quantitatively represented both numerically and as a percentage, for the cases of post-radiotherapy in the first place, and for the control cases in the second position were 6/4 (42%/13.33%), and hypotonia 6/1 (42%/3%), in both groups.

Clinically palpable lymph nodes in the submental, submandibular regions, and along the central sternocleidomastoid axis could be identified at 9/1 (32.14%/3%).

From the cases groups, detected bone deficiencies were influenced by the measurements from anthropometrical clinical methodology, in posture and centric landmark relations at 10/2 (35.71%/6.67%) and recordings related to the mouth opening deficiencies. During superficial palpation, with clinical methods applied, we noticed a lower sensitivity in 3/2 (10.71%/6.67%) patients. Important dental screenings were documented in both groups’ data files (the cases group were more affected): severe caries; periodontal disease (teeth with periodontal pockets, \( p > 6 \) mm) 5/1 (17.85%/3.33%) measured by PD clinical methodology; periapical dental pathology, (partially) impacted teeth; residual root tips; radiographic abnormalities, such as root resorption and dental oral cysts.

Oral candidiasis was reported in three patients from cases group (Table 8).

The muscular system, methodologically palpated, by the two inseparable methods and registered hypertonicity, being quantitatively represented both numerically and as a percentage, for the cases of post-radiotherapy in the first place, and for the control cases in the second position were 6/4 (42%/13.33%), and hypotonia 6/1 (42%/3%), in both groups.

Clinically palpable lymph nodes in the submental, submandibular regions, and along the central sternocleidomastoid axis could be identified at 9/1 (32.14%/3%).

From the cases groups, detected bone deficiencies were influenced by the measurements from anthropometrical clinical methodology, in posture and centric landmark relations at 10/2 (35.71%/6.67%) and recordings related to the mouth opening deficiencies. During superficial palpation, with clinical methods applied, we noticed a lower sensitivity in 3/2 (10.71%/6.67%) patients. Important dental screenings were documented in both groups’ data files (the cases group were more affected): severe caries; periodontal disease (teeth with periodontal pockets, \( p > 6 \) mm) 5/1 (17.85%/3.33%) measured by PD clinical methodology; periapical dental pathology, (partially) impacted teeth; residual root tips; radiographic abnormalities, such as root resorption and dental oral cysts.

Oral candidiasis was reported in three patients from cases group (Table 8).
From a qualitative point of view only, for evaluation of the damaged dental-periodontal status condition, we used systematization through mean value indices.

Regarding the intraoral clinical examination of the patient, the first important sign observed was periodontal damage, with horizontal bone line, 43.10%, and vertical bone line, 37.93%.

Severe inflammation (for post-radiotherapy cases the values were placed first, and in control cases, in second position) presented with symptoms marked by redness edema, tendency to spontaneous bleeding, ulceration; also, GI index and CAL index, both scored three, were observed on mandibular teeth at 22/1 (78.57%/3.33%), and GBI index of two at 20/1 (71.42%/3.33%).

On examination of the maxilla, an increased GI index value of two was demonstrated at 25/6 (89.29%/20.00%), and at 25/3 (89.29%/10.00%), which represented severe levels of inflammation. Value two in the CAL index at 25/5 (89.29%/16.67%) and value two in the GBI index at 25/4 (89.29%/13.33%) were recorded. The level of gingival damage was dependent on the amounts of bacterial plaque and the level of oral hygiene. A plaque index of two and three were recorded at 25/3 (89.29%/10.00%).

In the radiotherapeutic frame, periodontal rehabilitation consisted of aetiologic therapy in combination with minimally invasive techniques, considering the field of radiotherapy, and a 3-month follow-up. Post-radiotherapy there were 18 cases (64.29%) of mucositis, which were treated with benzocaine and lidocaine, but also with anti-inflammatory and opioid products in severe cases, as well as with polyvinylpyrrolidone and sodium hyaluronate (compounds that maintain tissue hydration, reduce pain, protect and lubricate tissues). Two patients (7.14%) reported taste disorders, three patients (10.71%) reported ulcerations; antifungal agents and topically applied antiseptic solutions were administered to five (17.86%) cases in the study group.

Tooth loss can be avoided with certain strategies, including fluoride trays in the clinical phase, for a proper management of severe caries due to xerostomia. Low salivary flow rate and poor buffering capacity have been suggested as dental carie-activity indicators.

Carious lesions were both, medium and deep in severity in the cases group with predominant localization in the cervical area (9, 32.14%), while in the control group they were found to be small and medium (5, 16.67%) with localization on the occlusal and proximal surfaces. Class I SI II Black and combined one, as well as the presence of incorrect dental restorations, were performed in both study groups.

In addition, to the appearance of ulceration aspects by decreased salivary secretion and the poor adaptation of existing mobile prostheses, cervical caries with a constant effect of hyposialia were also registered. In this context of salivary imbalance, the level of cervical caries was recorded in the initial stage before radiotherapy and showed a high level.

The appearance of the edentation arches’ pathological clinical signs was noticed in rehabilitation in a significant percentage, especially in the category of the extended I, II Kennedy classes in 17/6 cases (60.71%/20%) and partially reduced in percentage in 11/9 cases (39.29%/30.00%) in the modified Kennedy classes I, II, III.

In the context of oral rehabilitation fixed prostheses were applied in 21.43% (six cases) of the specific group of cases after radiotherapy, compared to eight cases (26.67%) in the control group, accompanied by appropriate endodontic treatment in four (14.29%) cases, compared to two (6.67%) cases in the control group.

The oral rehabilitation treatment performed by means of mobile prosthesis in 12 cases (42.86%) represented a significant percentage, performed after periodontal specific mucosal treatments and improvement of mucosal resilience adjuvant, and 4 (14.29%) cases in mixed rehabilitation, including specific treatments of the dysfunctional syndrome of the somatogenic system, with their associated pathology, compared to the control group.

The patients with TMDs, pain, occlusal interferences, mandibular imbalances, and muscle hypertonia or hypotonia, also benefited from complex treatment based on occlusion mouthguards.
Myorelaxant drug treatment, at specialist indications, was subsequently accompanied by associated fixed and removable prosthetic devices, related endodontic reconstructions, and restoration of gnathological dental arch parameters within the periodontal and dental support tissues, at the same time as existing malposition and malocclusion, associated periodontal stabilization, and contention (Table 9).

<table>
<thead>
<tr>
<th>Complex Oral Rehabilitation Feature</th>
<th>N/(%)</th>
<th>Group A Cases of Radiotherapy</th>
<th>Group B Controls</th>
<th>$\chi^2$</th>
<th>LD</th>
<th>$p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed prosthesis</td>
<td>14 (24.14)</td>
<td>6 (21.43)</td>
<td>8 (26.67)</td>
<td>0.217</td>
<td>1</td>
<td>0.64133</td>
</tr>
<tr>
<td>Endodontical treatments</td>
<td>6 (10.34)</td>
<td>4 (14.29)</td>
<td>2 (6.67)</td>
<td>0.906</td>
<td>1</td>
<td>0.34117</td>
</tr>
<tr>
<td>Mobile prosthesis</td>
<td>16 (27.59)</td>
<td>12 (42.86)</td>
<td>4 (13.33)</td>
<td>6.32</td>
<td>1</td>
<td>0.01193</td>
</tr>
<tr>
<td>Mixed rehabilitation</td>
<td>9 (15.52)</td>
<td>4 (14.29)</td>
<td>5 (16.67)</td>
<td>0.063</td>
<td>1</td>
<td>0.80181</td>
</tr>
<tr>
<td>Mouthguard appliances</td>
<td>8 (13.79)</td>
<td>4 (14.29)</td>
<td>4 (13.33)</td>
<td>0.011</td>
<td>1</td>
<td>0.91647</td>
</tr>
</tbody>
</table>

The cases with chronic TMDs were usually associated with local factors (e.g., uncomfortable dental materials used to restore teeth), systemic factors (including lack of minerals, vitamins, etc.), and irritating psychological factors (stress, life events, etc.). Mastication difficulties could be minimized by maintaining the dentition and using different types of suitable prostheses, such as fixed, mobile, or mixed.

5. Discussion

The pathological complexity of neoformation generally resonates in the area of mental disorders and, in addition to the physical and functional impairment of the individual, there are emotional imbalances quantified on all kinds of diagnostic tools. In the case of oral cancer, there is also a local quantification that accompanies these assessments, according to recent literature [20] on the correlations between certain parameters and their impact on quality of life.

The research data revealed that salivary gland hypofunction and xerostomia induced by cancer therapies could be prevented or symptoms minimized to some degree [21], depending on the type of cancer treatment [22], through effects of gustatory and masticatory stimulation, specific oral mucosal lubricant formulas, submandibular gland transfer, acupuncture, etc.

Clinical results, accompanied by the radiological examinations revealed by the present study results at the level of TMJ, with asynergism, asymmetry, and laterodeviation, showed joint pathological signs and muscle imbalances related to general associated pathologies, such as depression, neurological disorders, and Alzheimer’s disease.

The inflammatory signs of lymph nodes accompanying bone deficiencies with changes in the opening of the mouth, and trismus, were certified by crano-mandibular malrelations, which indicated the interaction and interdisciplinary aspects of therapeutic management. Both dental caries and periodontal diseases [23] can affect anyone, and selecting healthy subjects was a complicated issue. The reduction in salivary functions had important effects, as shown by issues observed in the present study, because of the impact on individual normal activities. Considering the central role that saliva plays in the oral cavity, alterations in salivary functions can be found in most oral diseases; however, there are few studies showing salivary gland alterations in primary oral diseases. Since the critical role of adequate saliva on dental hard tissues has been recognized, some researchers have examined the association between salivary functions and the prevalence of oral diseases [24].

The literature points out that in oral cancer patients [25], salivary changes in quantitative, qualitative, and microbial composition are presented.

Low levels of cariogenic and periodontopathogen species, lower pH and SRF, were detected in our research also, combined with an increased number of lactobacilli acids and acidogens. This indicated a higher risk of caries that required prevention and therapeutic RT to reduce the quality and quantity of saliva in oral cancer patients [26], which was associated
with an increased risk of the appearance of fungal candida albicans. Other authors [27] identified that age, xerostomia, an oral pH level lower than 5.3, type of RT, drinking habits, and dose to sublingual glands are potential predictors of RRC. The limitations indicated by studies of irradiation doses lower than 32.53 Gy to the sublingual gland suggest the existence of a protection against RRC, comparative with the present study that irradiation doses were more positioned at values about 50 Gy to 70 Gy, and a pH value = 4.580 (±1.051) at the lower level in the cases group, whereas the control group had an oral pH value of 6.259 (±0.152) [28].

It was revealed that saliva secretion follows the circadian rhythm, with the lowest secretion rate occurring during sleep, and the highest rate in the late afternoon. However, most of the flow rates were measured for whole saliva or saliva from major salivary glands, but there also exist minor salivary glands, and researchers proposed that they have an important contribution also. No statistical difference was seen in the flow rates between male and female subjects, whereas other research [29] concluded that there were gender differences; it was shown that saliva flow rates had lower values in women. Higher values, compared with the controls, were recorded for patients with poor hygiene, and, in general, with a preponderant food imbalance (MSRF = 0.77 mL/min). It was indicated [30] that chemotherapy radiation induced periodontal inflammation [31], which was also suggested in our research. This could be exacerbated, even if the oral hygiene levels were good. In agreement with previous studies, we considered that it was fundamental to control plaque accumulation by related indexes in irradiated patients to prevent colonization of periodontal pockets of pathogens [32] and in patients with a decreased local defense and permanent salivary changes.

All cancer patients experienced a certain degree of mucositis, but some of them had severe, advanced mucositis of grade three or four, or, more precisely, 85% of those receiving RT orally (in the case of those with advanced carcinomas, the percentage was even 100%). The lesions usually healed in about 4–7 weeks after the last dose.

In our study, the prevalence of mucositis was 64.29%. Intensity-modulated radiation therapy (IMRT) in oral cancer, after the correlation observed between variables, especially mucositis and SFR. During week 2 and 5 of treatment, our results indicated that it was registered severely deteriorated the patients’ quality of life and general health status, which was quantified by the Karnofsky performance status scale (KPS) [33].

Hyposalivation was identified in 78.41% of the sample and the mean radiation dose applied was 63.01 Gy (±9.58). Hyposalivation was associated with higher doses of radiation ($p = 0.038$), which had the potential to increase the chance of presenting hyposalivation by 4.25 times. In terms of this issue, concomitant chemotherapy and RT therapeutic procedures did not seem to increase the chances of hyposalivation compared to radiotherapy alone, and time elapsed since the end of radiotherapy had a protective effect, which was quantified at 75% ($p = 0.025$) [34].

The literature suggests [34] that salivary hypofunction and xerostomia are induced by RT in the head and neck region, depending on the cumulative radiation dose to the gland tissue and the new approaches to further reduce the dose to the parotid [35], and in particular, the submandibular and minor salivary glands, as these glands are major contributors to the lubrication of oral tissues.

The way each type of radiation behaves is important in planning radiation treatments. A radiation oncologist selects the type of radiation that is suitable for each patient’s cancer type and location. Radiation-induced xerostomia has been a common complication in RT of oral cancer patients, despite the advancement in RT techniques [36]. After RT, low values of SRF appear in oral cancer patients [37] due to changes in salivary gland parenchymal [38] assigned to microvascular glandular inflammation and oedema; patients have difficulties in chewing, swallowing, and speech. When radiation exposure exceeds 50 Gy the reduction in salivary flow is profound, and it dwindles over 90%, in our present study the indication value was around 60–70 Gy.
Stimulated salivary flow was lowest in the cases group (MSSF = 0.51 mL/min) compared to the control group (MSSF = 1.47 mL/min). In patients with oral cancer, after RT, the low stimulated salivary flow was explained by secretion hypofunction, severe atrophy, interstitial fibrosis, and loss of parenchyma of salivary glands [39,40]. This underlined that all patients in the xerostomia [41] group had a decreased SSF, which was considered an important marked sign in patients with oral cancer after RT treatments [42,43]. At 3 months, there was a significant reduction in unstimulated (0.346 mL/min) and stimulated (0.80 mL/min) SRF, the unstimulated flow rate continued to decrease further until 6 months (0.295 mL/min), and an increase in SFR (0.91 mL/min) was recorded. After a period of time, 12 months, minimal recovery was detected in both unstimulated (0.362 mL/min) and SFR (1.09 mL/min), facts also revealed by literature confirmation [44,45].

Despite advances in new RT techniques, patients with oral cancer were registered with oral complications regarding mean stimulated whole salivary flow decreasing from 1.09 to 0.47 mL/min; mean maximal mouth opening, reducing from 45.58 to 42.53 mm at 6 months (at \( p < 0.001 \)); and the presence of 8.10% oral mucositis and 3.80% with oral ulceration [46]. Palliative radiation can help relieve symptoms such as pain, swallowing, or breathing problems that can be caused by advanced cancer. These tumors can be treated, even if they spread quickly, to make them smaller, so that the patients can feel better and lead a normal life.

Oral diagnostic tools, dedicated to oral health-related quality of life (OH-QO) being reduced [47], can detect changes related to dry mouth, sticky saliva, swallowing solid foods, and sense of taste at 6 months after RT, with resulting negative impacts on oral function and quality of life. Regarding quality of life, it was observed that emotional dimensions were the most affected, and, also, there was a higher number of moderate mucositis correlations with quality of life in association with variables such as pain, saliva, swallowing, and anxiety.

Stomatitis, in its various clinical forms, can be found in most systemic diseases (respiratory, metabolic, cardiovascular, hepatic, renal diseases), which alter the local mucosal reactivity. The oral cavity reflects the existence of clinical manifestations caused by systemic risk factors, which can often become their “primary alarm signal” or “primary diagnostic key” [48]. In this context, after periodontal tissue integration the fixed and mobile prosthetic treatments were applied during the rehabilitation process, obtaining a minimal comfort. Patients in the present study generally had complex pathologies, such as coronal lesions, mixed edentations, periodontal, endodontics, occlusal disorders with a high degree of pathogenicity and a proportional degree of rehabilitation 89.29%, compared to the control group. This was demonstrated by evaluating the mentioned cario- and periodontal indexes and also by the numerous prosthesis applications [49].

Studies present the insufficiency of cohesion forces in situations where the lowest value of adhesion forces was caused by the reduction in salivation, showing that not only the quality but also the amount of saliva secreted was important in adults using mobile prosthetic restorations [50].

Drug support with sialagogue status, cranio-mandibular repositioning, and mental recovery, as well as specific rebalancing treatments, not only in the field of SS, but in the body, with SS being an integral biological system, shows the complexity, and the major impact of management in oral pathology rehabilitation treatments [50], in patients after RT [51].

Radiotherapy significantly improves a patient’s chances of survival, and it often coincides with side effects due to the unavoidable co-irradiation of normal tissues surrounding the tumor, which includes salivary glands [52].

Our study had some limitations. The study design was realized with some cases that affected the results’ generalization. However, difficulties in participant enrollment existed, as well as unfavorable economic criteria, accompanied by the small number of cases suitable for such research.

Quality of life is a desirable issue, and, in fact, is the practical target in these cases of complex rehabilitation treatment [53], in the management of oral cancer patients, and
beyond. Following the applied complex rehabilitation treatment, there was a slight improvement in the quality of life.

6. Conclusions

We can specify that there was a predominance of males in the present study, in the area of the place where the study was conducted, and in the period of time involved.

The multidisciplinary team management approach was guided by the presence of associative pathologies, according to the anamnesis, with hypertension having a quantified majority predominance, followed by metabolic diseases, osteoporosis, Alzheimer’s disease, stroke, and psychiatric pathologies, as well as the lifestyle standards and other habits reported. There existed important correlations between the severity of salivary gland dysfunction and the degree of radiation exposure by type, as well as with the location of the tumor, thus there were potential predictors of radiation-related caries and the impact of subsequent imbalances created in SS parameters and accompanying TMD symptoms.

Xerostomia, a RT complication, represents a challenge for a rehabilitation department, as researchers in caries and periodontal control, through the correlative prosthetic difficulties generated as well as the management of associated stress pathology. In patients with labial, jugal, lingual, palatal, or combined oral cancer, in the present study, according to the observations of calculated mean values, there was a decrease in salivary pH after RT (below 6.0): pH value = 4.580 (±1.0) and mean SSF value were significantly lower (at $p < 0.001$) after RT (MRSF = 0.145 mL/min), which caused demineralization of dental hard tissues and increased the risk of post-radiotherapy caries detected by oral screening. Impaired periodontal status after RT was assessed by several specific periodontal indices. It represented a major risk factor for further complications when accompanied by other pathologies, such as root resorption and oral dental cysts, as well as the occurrence of oral candidiasis.

The treatments applied were carried out with care and attention, given the sensitivity of oral tissues and the high risk of infection associated with the presence of mucositis, which is often followed by ulceration and taste disorders.

During clinical and paraclinical examination it was underlined that the manifestations of the dysfunctional syndrome of the stomatognathological system were particularly pronounced and present as TMJ deficiencies, asymmetries, cracking sounds or crepitation, hypertonia and hypotonia and bone deficiencies detected anthropometrically, mouth opening deficiencies, decreased sensitivity in association with the presence of clinically palpable lymph nodes in the submental and submandibular regions and along the central sternocleidomastoid axis.

Considering the type of applied treatments chosen, as well as the aesthetic, psychological, and functional impact of oral cancer, we could emphasize that the recovery of SS parameters represented a goal achieved through interdisciplinary efforts, additional efforts, additional experience, and ground covered, and a step forward in the management of the type of pathology in the study.

As far as oral rehabilitation treatment interferences is concerned, a common part of the dysfunctional syndrome of SS in the context of oral cancer pathology, the final desideratum was represented by the achievement of homeostasis, which is important for the each patient.


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Institutional Review Board Statement: The present study was approved by the Ethics Committee of Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, 19 July 2017, No. 547/1012012
and TD312/2008 and 1653/UA/26.11.2015 Apollonia University Iasi, Romania. All protocols were in accordance with the provisions of the Declaration of Helsinki.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** All data are available from the corresponding authors upon reasonable request.

**Conflicts of Interest:** The authors declare no conflict of interest.

**Abbreviation**

- RSF: salivary resting flow
- SFR: salivary flow rate
- OPG: orthopantomography
- SSGT: dysfunctional syndrome of stomatognathic system
- MRSF: the mean value of resting salivary flow
- SSF: stimulated salivary flow
- RRC: radiotherapy-related caries
- KMG: kinesiomandibulography
- RT: radiotherapy
- Yuu MJ: temporo-mandibular joint
- IMRT: intensity-modulated radiation therapy
- CBCT: cone beam computer tomography, dental tomography
- RC: centric relation
- HTA: hypertension
- \( p \) value: value for statistical significance level
- \( \chi^2 \): chi square calculated value
- GBI: index gingival bleeding
- PD: probing depth
- CPA-index: clinical attachment loss index
- DMFT index: carioreactivity index, the decayed, missing, and filled teeth index
- EMG: electromyographies
- CPITN index: Community Periodontal Index of Treatment Needs
- Gy: Gray
- \( pH \): potential of hydrogen
- OH-QO: oral health-related quality of life
- TMDs: temporo-mandibular disorders
- PR: posture relation
- KPS: Karnofsky performance status scale

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