Review Article

IMPACT OF RADIATION-INDUCED TRISMUS ON PATIENTS' LIFE QUALITY

ABSTRACT

Head and neck cancers (HNC) account for 10–15% of all cancers globally. Curative radiation therapy (RT) and concurrent chemoradiotherapy (CCRT) with or without surgery are widely accepted standard treatment modalities for these patients. Radiation-induced fibrosis is one of the side effects of these treatments, and it causes degeneration, inflammation, pain, and atrophy of the masticatory muscle fibers and the temporomandibular joint, resulting in trismus. Trismus, also known as hypomobility of the mouth, is defined as a restricted opening of the mouth. Radiation-induced trismus (RIT) can occur within the first three months of treatment or up to 12–48 months later during the follow-up period. It has a significant negative influence on daily activities and vital oral functions, including speech problems, difficulty eating or drinking, psychological problems, malnutrition, dehydration, and difficulty with oral hygiene, reducing the quality of life (QoL). Given the underappreciated nature of trismus and its negative consequences in HNC patients receiving RT or C-CRT, the purpose of this review was to provide a concise review of the physical, social, and emotional implications of RIT and their impact on QoL measures, as well as the available evaluation methods for physicians in the related medical fields.

Keywords: Head and neck cancer, radiation-induced trismus, radiotherapy, assessment tools, quality of life.

Introduction

Each cancer patient goes through a traumatic and life-changing experience that affects their mental, emotional, and sexual functions, as well as their family life and socioeconomic status (1). Previous research has shown that emotional distress, the severity of disease symptoms, treatment-related complications, and their management all harm QoL measures (2).

Head and neck cancers (HNC) account for 4% of all cancers worldwide (3), with radiotherapy (RT) being an essential component of treatment for nearly 80% of patients. Despite significant advancements in RT planning and delivery systems, a considerable percentage of patients still suffer from radiation-induced acute and chronic toxicities, particularly those receiving concurrent systemic agents (4). Although there are numerous efficient therapies for acute RT-related toxicities, treatment options and their benefits for chronic toxicities are much more limited. Impaired function of the salivary glands, swallowing muscles, and masticatory apparatus are among the most problematic late complications in the head and neck region (4).

Trismus, derived from the Greek word "trismos," which means "grill, grind, or squeak," is a late sequela of RT that lowers the QoL of difficult-to-treat patients (5). RT-induced trismus (RIT) develops as a result of fibrotic changes and related contracture in masticatory structures such as the masseter and pterygoid muscles, as well as damage to their neural innervation and vasculature, and temporomandibular joint degeneration (TMJ) (6).

Trismus prevalence may vary widely depending on tumor location and size, treatment(s) used, and patient selection criteria in different studies with distinct evaluation methods (7,8). RIT rates for patients with maxillary sinus cancer, oral and oropharyngeal cancer, and nasopharyngeal cancer have been reported to be 5-32%, 0-69%, and 0-36%, respectively (7, 9-13). RIT adversely affects oral health and daily oral function, interferes with speech, drinking, and eating, and makes maintaining proper oral hygiene difficult, which

can harm the immune system (14). Physical limitations caused by this severe complication can eventually affect patients' dietary, sexual, mental, emotional, social, and emotional functions, including mood, pleasure, and amusement (15).

Despite the fact that many validated questionnaire systems have been used to assess the QoL of HNC patients with RIT, the exact impact of this devastating complication has yet to be defined in the literature. Hence, the present review desires to comprehensively review the effects of RIT on the physical functions and psychosocial status of the affected patients and compare the efficacy of various assessment tools, which may hopefully serve usefully in oncology clinics.

The Impact of Radiation-Induced Trismus on Patients' Life

Trismus following RT has been associated with numerous debilitating health consequences, including decreased nutrition due to impaired mastication, difficulty in communication due to articulation difficulty, and compromised oral hygiene (16). Jaw opening limitations have been reported with varying frequency and severity in patients who have received RT to the TMJ and/or masseter/pterygoid muscles, representing the most vital components of the masticatory apparatus (17). RIT can interfere with patients' daily activities in the following ways:

A. Medical
B. Physical
C. Psychological and Social
D. Sexual

A. Medical effects

Patients presenting with tumors of the nasopharynx, oral cavity, oropharynx, base of tongue, salivary gland, maxilla, or mandible that invade or reside near the TMJ, pterygoid muscle, or masseter muscle are more likely to develop RIT (16,17). Patients who have previously been irradiated and are being treated for a recurrence appear to be more vulnerable to RIT than

patients who receive RT for the first time (18,13). This evidence indicates that the detrimental tissue effects of RT are cumulative, even over long periods. RIT can begin near the end of RT or at any time in the next 24 months. Limitations in mouth opening frequently develop gradually over several weeks or months. The symptoms of RIT may get worse with or without medical intervention, or they may eventually get better or stay stable (19). Oral side effects from radiation therapy are intricate, dynamic pathological processes that lower QoL and put patients at risk for severe clinical dysfunction. Poor nutritional status and resultant weight loss (WL) is frequently associated with RIT (20), which is well-recognized as a poor prognostic factor for many cancers when WL exceeds 5% over the past six months (21).

Several studies have found that trismus negatively impacts oral function-related QoL, such as pain, eating, chewing, taste, saliva production, and dry mouth, as well as a higher incidence of jaw-related problems and eating limitations (22-24). RIT can also cause difficulties in proper mastication and airway clearance functions. To swallow normally, an individual must first manipulate the food into a cohesive bolus. There may be post-swallow excess residue if the tongue cannot move properly. The combination of poor bolus organization, poor mastication, and excess amounts of residual food in the oral cavity may result in aspiration problems, which may regrettably be fatal in some cases (19). Eisbruch et al. reported considerably higher rates of swallowing problems following RT (25,26). Hence, patients undergoing RT or CCRT frequently require feeding tubes, limiting their oral intake to mostly liquids during treatment. As a result, they may be unaware of the slow progressive onset of RIT until they attempt to resume soft or solid food consumption (27).

Finally, RIT can lead to poor oral hygiene. Patients who have received high doses of radiation to the salivary glands must practice good oral hygiene to avoid dental caries (cavities). Oral hygiene deficiencies can aggravate mucosal and dental problems, increasing the risk of mandibular osteoradionecrosis, another detrimental late toxicity of RT or CCRT

(28). Furthermore, the task of dentists and other oral health professionals, such as oral and maxillofacial surgeons, may become more difficult to carry out, potentially jeopardizing routine oncologic follow-up. RIT may also lead to multiple tooth deficiencies due to obligatory extractions. More than half of those patients with severe tooth deficiencies find it difficult to consume nutrients like nuts, apples, and raw carrots, and as a result, their daily intake of non-starch polysaccharides, protein, calcium, non-heme iron, niacin, vitamin C, intrinsic and milk sugar may be reduced to critical levels in this patient's group (29).

B. Physical effects

Jaw pain and cramps, difficulty biting, chewing, or brushing teeth, inability to swallow certain nutrients, headaches, and earaches are all reported physical symptoms of RIT (30). A soft diet is recommended for patients suffering from RIT. Soup, smoothies, yogurt, mashed potatoes, oatmeal, beans, steamed vegetables and fruits, cheese, fish, and omelets are all examples of soft foods. However, it should be remembered that these foods would be close to puree consistency. Another hard-to-solve problem in such patients is that effective brushing will be unattainable due to the restricted mouth opening, which may lead to poor oral hygiene and related dental caries, periodontal and dental infections. Thus, patients with RIT should be advised to use small-headed toothbrushes and antibacterial mouthwashes to avoid dental caries by maintaining good oral hygiene (31). Due to limited mouth openings, dental infections and caries may necessitate multiple tooth extractions because timely dental interventions are not conceivable (32). As a result, multiple tooth losses may unavoidably alter the physical appearance of the affected patient's face, potentially leading to mood and psychosocial issues. The systematic review and meta-synthesis of seven studies revealed that tooth loss was linked not only to compromised oral health but also to a decline in social standing and self-esteem. Of note, the authors came to the conclusion that oral rehabilitation has broad benefits for restoring quality of life and self-worth (33). Therefore, timely

interventions may prevent RIT-related tooth loss and improve almost all QoL metrics in these patients.

C. Psychological and Social effects

RIT hinders the development of "eating and the social habits". RIT-related restrictions in mouth and TMJ movements may also impair sufferers' speech and social communication abilities, which altogether increases the risk of social isolation, loneliness and lowers QoL in HNC patients (34). Besides, trismus frequently causes halitosis (35), a multifaceted medical condition that adversely alters the affected individuals' QoL and psychosocial profile. Halitosis is a humiliating condition that makes patients feel graceless around others and lowers their QoL. Because halitosis diminishes personal relations, it is also embarrassing for relatives and friends of such patients. Hence, halitosis should not only be considered a medical problem but must be recognized as a social impediment that is to be urgently coped with (36). Confirming this reality, a study by Elias and Ferriani found that patients with halitosis had a high risk of social anxiety disorder (37). Halitosis may become a significant factor in personal relationships, resulting in social isolation (38). Patients with halitosis create a social barrier between themselves and their friends, relatives, partners, or coworkers (39). It is self-evident that QoL will, without a doubt, be negatively altered if a person has physical and mental limitations that interfere with aspects of speech, social relationships, and self-esteem (40).

Depending on the extent of the RIT-related tooth loss, muscle tone loss and facial collapse may take place, leading to cosmetic problems (32). This atrocious situation may cause the patient to avoid social communities, which undermines self-esteem and leads to mental breakdown (29).

D. Sexual effects

As previously stated, RIT can cause dental caries, periodontal disease, and dental infections, leading to unwelcome halitosis (32, 41). Many researchers have examined the psychosocial effects of halitosis (37,42), but its impact on sexual health has usually been underestimated to date. In their study on the effect of halitosis on sexual function, Ozler et al. used the International Erectile Function Index (IIEF) to assess the sexual health of men with halitosis and compared the results to a similar group of healthy men (36). According to the results of the study, it was revealed that subjects with bad breath odor had significantly lower scores in all functional areas, which meant a worse sex life (36). Subjects with halitosis had significantly lower scores in all function domains, implying a poorer sex life (37). In a more recent study involving 100 patients, Olszewska-Czyz et al. found that higher halitosis levels resulted in lower SF-36 domain scores. Furthermore, the strongest relationship between intra-oral halitosis and decreased QoL was discovered in the domains of social functioning, vitality, emotional wellbeing, and general health perception (43).

In summary, RIT may cause halitosis, which may often lead to unpleasant alterations in the psychological, social, and sexual domains of QoL measures. Hence, every possible effort should be made to prevent the development of halitosis in RIT patients. For this purpose, it should be recognized as a condition that requires a multidisciplinary approach, including dental specialists, psychologists, and other members of a multidisciplinary oral care team (Figure 1).

Objective and Subjective Measures of Trismus-Related Quality of Life

Individuals' normal mouth openings range between 40 and 60 mm (44), with males typically being able to expand their mouths wider than females (45). Trismus is frequently measured objectively using the maximal mouth opening (MMO), the largest aperture between the upper and lower incisor margins (14,16,46). In the case of edentulous patients, the vertical distance between the opposing upper and lower alveolar ridges may be used instead (47). Calipers or

other measuring devices can be used to perform these measurements (14, 22). The MMO should be assessed before beginning of the therapy, and the patient or clinician should measure it frequently after treatment to monitor its maintenance (48) (Figure 2).

Trismus is commonly defined as MMO 35 mm or less (either the interincisal distance or the distance between the upper and lower alveolus) (18,23,47,49), which is also corroborated by Scott and colleagues' findings (16,23). A cut-off of ≤35 mm is mostly used for trismus in the literature (18,23,47,49). Patients suffering from trismus may nonetheless have an objectively "normal" MMO measurement. The primary or exclusive outcome measure of successful medical applications may no longer be death with the introduction of patient-reported outcome measures (PROMs) and QoL surveys. Subjective measurements can also be used to contrast various therapies, such as trismus, opening up new paths outside traditional outcome assessment approaches (50).

These subjective trismus assessments are either mouth-opening specific surveys, such as the Mandibular Function Impairment Questionnaire (MFIQ) (18), or a subset item in a general cancer QoL questionnaire, such as the Performance Status Scale (PSS) (51). The Mandibular Function Impairment Questionnaire, one of the mouth opening-specific questionnaires, was utilized in the first study that sought to establish the cut-off for trismus (MFIQ) (18). This questionnaire has 11 items that measure reported mandibular function issues during social interactions, speaking, taking large bites, chewing hard food, chewing soft food, working and/or everyday activities, drinking, laughing, eating food that is chew-resistant, yawning, and kissing. Additionally, six other items explained why some foods were difficult to consume, including hard cookies, beef, raw carrots, French bread, peanuts/almonds, and apples. Responses were graded as (1) no difficulty, (2) quite a bit of difficulty, (3) much difficulty, and (4) great difficulty or impossible without help. The scores

were totaled and ranged from 0 to 68, with a higher score representing more disability (18). The internal consistency of the questionnaire varies from 0.80 to 0.95. (52).

The Liverpool Oral Rehabilitation Questionnaire (LORQ v3) is another mouth-opening specific questionnaire (53) that includes 40 questions, 17 of which are related to oral functions, orofacial appearance, and social interactions. To analyze the influence of chewing skills on social life and food choice, five questions were included: (1) Did you experience difficulty chewing? (2) Did you have pain when you chew? (3) Did your chewing ability affect your social life? (4) Did your chewing ability influence your choice of foods? and (5) Did you experience difficulty with mouth opening? The answer choices were "always", "often", "sometimes", and "never" (23).

The Gothenburg Trismus Questionnaire (GTQ) is an additional mouth-opening-specific test (22). Although it has been researched only in one study, this trismus-specific questionnaire has strong psychometric qualities. This questionnaire has 21 items, 13 of which are grouped into three domains: jaw-related issues (six items), feeding limits (four items), and muscle stress (three items). The GTQ has a 1-week recall time for each of the three domains. The domains and single items are scored from 0 to 100, with 100 representing the highest number of symptoms and 0 signifying no symptoms. In research by Pauli et al. (22) using the GTQ, it was discovered that patients with trismus had greater problems than patients without trismus with their ability to work and engage in leisure, social, and family activities in terms of jaw-related issues and eating limitations. Additionally, it was demonstrated in this study that individuals with trismus reported worse health-related QoL deficits in the domains of mouth opening ($p<0.001$), jaw-related issues ($p>0.05$), eating restrictions ($p>0.05$), and muscle tension ($p>0.001$) (19). These findings were consistent with those of other research and with the prevalence of trismus (8, 19, 30). The GTQ has been suggested as a screening tool for jaw-related problems ($p<0.05$), eating limitations ($p<0.05$), and muscular tension

($p<0.001$) (19). The GTQ has also been proposed as a means of assessing outcomes in studies of jaw physical therapy and rehabilitation (22).

Several general QoL questionnaires are also used to measure the impact of trismus in HNC patients. One of these is the PSS (51), which has three subscales: eating in public, dietary normality, and patient speech clarity. Each subscale is scored from 0 to 100, with higher scores indicating better performance (51,54). The European Organization for Research and Treatment of Cancer QoL Questionnaire (EORTC QLQ C30) is a cancer-specific general questionnaire. The EORTC QLQ-H&N35 module for the head and neck is used to subjectively quantify mouth-opening among the six scales that evaluate HRQoL in cancer patients (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial problems) (55,56). The surveys include five function scales (physical, role, emotional, cognitive, and social functioning), a global QoL scale, three symptom scales, and six single items, totaling 30 questions on the patients' symptoms and functional level over the previous week. A supplemental 35-item module, the EORTC QLQ-H&N35, can be used to examine additional symptoms linked to HNC and its therapy (55). Scale scores are calculated from 0 to 100. A score of 100 implies optimum functionality on the functioning scales and global QoL scales, but a score of 100 indicates the worst possible symptoms on the symptom scales and single items. Pain, swallowing, senses, speech, social eating, social interactions, and sexuality are among the multi-item scales, while teeth, mouth-opening, dry mouth, sticky saliva, coughing, feeling unwell, pain relievers, nutritional supplements, feeding tube, weight loss, and weight gain are among the single items (50). A change of more than 10 points in scores over time might be considered clinically significant. These questions have been re-evaluated on a regular basis and have been shown to be sensitive and accurate (56,57). According to one study, individuals with trismus who completed the HRQoL test reported more problems with bodily functioning, pain, and a clinically significant decrease in appetite 12 months after

treatment than patients without trismus (56). Similarly, after 12-month follow-up in patients completing the EORTC QLQ-H&N35 test, the trismus group reported more issues with mouth-opening and clinically significant more problems with pain, social eating, and sexuality than the non-trismus group (22).

Although the University of Washington QoL questionnaire (UWQOL) v4 has been validated for patients with head and neck cancer, it is not as broadly used as the EORTC questionnaire (23). The UWQOL v4 evaluates pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood, and anxiety status. The chewing, saliva, mood, and anxiety domains were included in the questionnaire to determine the influence of limited mouth-opening on these domains, which are measured on a Likert scale from 0 (worst) to 100 (best). However, no explicit mention of a score method for defining trismus using the UWQOL was available (23).

The Functional Assessment of Cancer Therapy (FACT)-Head and Neck (HN) Scale (FACT-HN) is a self-reported questionnaire that consists of 28 generals plus 11 head and neck-specific items rated from 0 to 4 on a Likert-type scale (58). FACT domains describe functionality in six categories: physical well-being, social and family well-being, doctor-patient relationship, emotional well-being, functional well-being, and head-and-neck related symptoms (HNS) (58, 59). The FACT-HN module additionally includes domains that question the potential problems related to the patient's oral comfort, breathing, voice, eating, appearance, tobacco smoking, alcohol use, and social communication features (59).

The Karnofsky Performance Status Scale (KPS) was originally developed to assess patient activity and medical care requirements. KPS is a widely used general measure of patient independence, with a scoring range of 0 (dead) to 100 (completely independent). The KPS can also be used to compare the efficacy of different therapies and predict individual patient prognosis; the lower the Karnofsky score, the lower the chance of survival for most

serious illnesses. Pauli et al. (22) used the Karnofsky Performance Status Scale (KPS) to examine the prevalence of trismus and its long-term effects on health-related QoL in patients with HNCs (60). They reported in their study that KPS was lower in the trismus group. However, highlighting the importance of using multi-dimensional assessment tools, it was recently revealed that KPS is a one-dimensional measure of health status that does not fully reflect all domains of a comprehensive QoL assessment (60).

A correlation between objective mouth-opening measurements and subjective measures using the UWQOL questionnaire was attempted (23). The authors found a significant relationship between mouth opening and UWQOL chewing domain ($rs = 0.45$, $p<0.0001$) and UWQOL overall QoL ($rs = 0.25$, $p = 0.01$). There were some exceptions, however, as ten patients who were not clinically shown to have trismus complained subjectively of problems opening their mouths, while 16 patients with objective trismus denied having problems opening their mouths (23). Despite these exceptional instances, there was generally a high correlation between subjective and objective measurements. The difference in mean MFIQ scores between patients with and without trismus at a cut-off point of 35 mm was significant, which is the common denominator of these measures. The minimum MFIQ score for trismus was 8.3, which corresponds to a mouth opening of 35 mm (18).

Although several objective and subjective techniques have been put forth to evaluate the effect of trismus on the QoL measures of the affected patients, the majority of the data that is readily available comes from trismus induced by other causes rather than from patients who underwent RT or CCRT. Similarly, the majority of surveys ask multiple questions related with various health -related issues at the same time, instead of focusing specifically on RIT and its negative consequences. It should be noted that cancer patients who present with RIT may react differently than other trismus patients because they are psychologically more

vulnerable to the devastating effects of treatment-related toxicities. In stark contrast, such patients may also prefer to deny RIT and its adverse consequences, as the desire to survive may outweigh the discomfort of RIT. As a result, such concerns stress the critical need for the development of RIT-specific surveys that can better assess the physical, psychological, and social status of RIT patients (Figure 3).

Discussion and Future Perspectives

Trismus in HNC patients can be caused by tumor invasion or growth around the masticatory muscles, oral cavity, or TMJ. It is directly connected to radiation-induced fibrosis, which is comprehended to be a persistent issue that renders HNC patients disabled and can arise as a late effect of RT or C-CRT (16, 61-63). Trismus is also linked to other symptoms, such as the dry mouth and dental issues after oncologic treatment, which can significantly impair patients' nutritional status and health-related QoL (46). But regrettably, there has been little research on trismus and related QoL in HNC patients, and the studies that have been conducted are typically small, retrospective, single-institutional studies (64).

Even though the incidence of HNC has been rising steadily, thanks to significant advancements in cancer therapies, an increasing number of patients can be anticipated to live for years. On the other hand, such an increase in survival times may also provide an opportunity for the manifestation of treatment-related late side effects, resulting in a greater necessity for preventive and rehabilitative efforts to improve functional impairments and associated QoL measures in these patients, including RIT sufferers. Compared to HNC patients without trismus, patients with trismus reported more QoL issues such as general and social eating, dry mouth, swallowing problems, appetite loss, pain, and jaw-related problems (22). Oral health problems, more specifically difficulty opening the mouth, have been identified as predictors of survival in HNC patients, irrespective of the underlying cause (65). Malnutrition is more likely in HNC patients whose oral health has deteriorated and whose

mouth opening has become limited, resulting in impaired recovery, a longer rehabilitation period, and a shorter life span, presumably as a result of the unavoidable development of fatal cachexia (66,67). Furthermore, deterioration in eating function caused by trismus will cause patients to abstain from social eating and be involved in the social environment, resulting in loneliness, social isolation, and psychological disorders (64). Halitosis is another negative effect of trismus on QoL that is frequently overlooked. Halitosis also has an impact on patients' social isolation, relationships with their social partners, and sexual performance. Reduced sexual performance may harm the family structure, lead to the end of relationships, and serve as another factor in the person's loneliness and depression (17,22,34-37).

Although many questionnaires have been used to assess the effects of trismus, very few are specifically designed for HNC patients with trismus. As a result, despite being a severely disabling complication that needs attention in this patient group, the precise impact of trismus and related symptoms on a patient's quality of life has not yet been identified. Therefore, it is necessary to develop novel questionnaires specifically for HNC patients that include objective domains such as the type of cancer, the dose and duration of the prescribed RT, TMJ, and oral evaluation before treatment, as well as subjective domains such as the patients' social, sexual, and psychological status.

Conclusion

Trismus is usually neglected as a side effect of RT or C-CRT in HNC patients in radiation oncology and dentistry textbooks. However, this physically, socially, and emotionally debilitating complication, which affects roughly one-third of HNC patients treated with RT, must be appreciated as needed and assessed objectively as well as subjectively. Defining the individual effects of trismus on patients' QoL will help HNC survivors in their daily life functions after oncologic treatment by assisting in the planning of treatments and preventive methods specific to patient complaints and needs.

REFERENCES

1. Akkas EA, Yucel B, Kilickap S, Altuntas EE. Evaluation of quality of life in Turkish patients with head and neck cancer. *Asian Pac J Cancer Prev*.2013;14:4805-4809
2. Citak E, Tulek Z. Longitudinal quality of life in Turkish patients with head and neck cancer undergoing radiotherapy. *Support Care Cancer*.2013;21:2171-2183.
3. Hashemipour MA, Pooyafard A, Navabi N, Kakoie S, Rahbanian N. Quality of life in Iranian patients with head-and-neck cancer. *J Educ Health Promot*. 2020 ;29;9:358.
4. Strojan P, Hutcheson KA, Eisbruch A, et al. Treatment of late sequelae after radiotherapy for head and neck cancer. *Cancer Treat Rev*. 2017;59:79-92.
5. Krogman WM. Illustrated Dictionary of Dentistry. By S. Jablonski. Philadelphia: W.B. Saunders. 1982:xvii+919.
6. Rapidis AD, Dijkstra PU, Roodenburg JL, et al. Trismus in patients with head and neck cancer: etiopathogenesis, diagnosis and management. *Clin Otolaryngol*. 2015;40(6):516-26.
7. Sakai S., Kubo T., Mori N.et al. A study of the late effects of radiotherapy and operation on patients with maxillary cancer. A survey more than 10 years after initial treatment. *Cancer*.1988; 62, 2114–2117.
8. Chen A.M., Bucci M.K., Singer M.I. et al. (2007) Intraoperative radiation therapy for recurrent head-and-neck cancer: the UCSF experience. *Int. J. Radiat. Oncol. Biol. Phys*.2007; 67, 122–129.
9. Ozsaran Z., Yalman D., Baltalarli B. et al. Radiotherapy in maxillary sinus carcinomas: evaluation of 79 cases. *Rhinology*.2003; 41, 44–48.
10. Thomas F., Ozanne F., Mamelle G. et al. Radiotherapy alone for oropharyngeal carcinomas: the role of fraction size (2 Gy vs 2.5 Gy) on local control and early and late complications. *Int. J. Radiat. Oncol. Biol. Phys*.1988; 15, 1097–1102.

11. Eisen M.D., Weinstein G.S., Chalian A. et al. Morbidity after midline mandibulotomy and radiation therapy. *Am. J. Otolaryngol*. 2000;21, 312–317.
12. Wolden S.L., Zelefsky M.J., Hunt M.A. et alFailure of a 3D conformal boost to improve radiotherapy for nasopharyngeal carcinoma. *Int. J. Radiat. Oncol. Biol. Phys.*2001; 49, 1229–1234.
13. Yeh S.A., Tang Y., Lui C.C. et al. Treatment outcomes and late complications of 849 patients with nasopharyngeal carcinoma treated with radiotherapy alone. *Int. J. Radiat. Oncol. Biol. Phys.*2005; 62, 672–679.
14. Lee LY, Chen SC, Chen WC, Huang BS, Lin CY. Postradiation trismus and its impact on quality of life in patients with head and neck cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;119(2):187-195.
15. Jia Z, Li J, Harrison C, Pawlowicz E, Clump DA 2nd, Wasserman-Wincko T, Moore K, Johnson JT, Nilsen ML. Association of Trismus With Quality of Life and Swallowing in Survivors of Head and Neck Cancer. *Otolaryngol Head Neck Surg*. 2022;166(4):676-683.
16. Dijkstra PU, Kalk WW, Roodenburg JL. Trismus in head and neck oncology: a systematic review. *Oral Oncol*.2004; 40:879–889.
17. Kent ML, Brennan MT, Noll JL, et al. Radiation-induced trismus in head and neck cancer patients. *Support Care Cancer*. 2008;16:305–309.
18. Dijkstra PU, Huisman PM, Roodenburg JL. Criteria for trismus in head and neck oncology. *Int J Oral Maxillofac Surg*.2006; 35:337–342.
19. Bensadoun RJ, Riesenbeck D, Lockhart PB, Elting LS, Spijkervet FK, Brennan MT, Trismus Section, Oral Care Study Group, Multinational Association for Supportive Care in Cancer (MASCC)/International Society of Oral Oncology (ISOO). A systematic review of trismus induced by cancer therapies in head and neck cancer patients. *Support Care Cancer*. 2010;18(8):1033-1038.

20. Hsiung CY, Huang EY, Ting HM, Huang HY. Intensity modulated radiotherapy for nasopharyngeal carcinoma: the reduction of radiation-induced trismus. *Br J Radiol*. 2008; 81:809–814.
21. Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol*. 2011;12(5):489-495.
22. Pauli N, Johnson J, Finizia C, Andréll P. The incidence of trismus and long-term impact on health-related quality of life in patients with head and neck cancer. *Acta Oncol*. 2013;52(6):1137-1145.
23. Scott B, Butterworth C, Lowe D, Rogers SN. Factors associated with restricted mouth opening and its relationship to health-related quality of life in patients attending a Maxillofacial Oncology clinic. *Oral Oncol*. 2008;44: 430–438.
24. Johnson J, van As-Brooks CJ, Fagerberg-Mohlin B, Finizia C. Trismus in head and neck cancer patients in Sweden: incidence and risk factors. *Med Sci Monit*. 2010; 16:CR278–282.
25. Eisbruch A, Schwartz M, Rasch C, et al: Dysphagia and aspiration after chemoradiotherapy for head-and-neck cancer: Which anatomic structures are affected and can they be spared by IMRT? *Int J Radiat Oncol Biol Phys*.2004; 60:1425-1439.
26. Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, et. al. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. *J Clin Oncol*. 2008 ;1;26(22):3770-3776.
27. de Jong PR, de Heer-Groen T, Schröder CH, Jansen NJ. Generalized tetanus in a 4-year old boy presenting with dysphagia and trismus: a case report. *Cases J*. 2009; 29;2:7003.
28. Peterson DE, Doerr W, Hovan A, et al. Osteoradionecrosis in cancer patients: the evidence base for treatment-dependent frequency, current management strategies, and future studies. Support Care *Cancer*. 2010;18(8):1089-1098.

29. Saintrain MV, de Souza EH. Impact of tooth loss on the quality of life. *Geriodontology*. 2012;29(2):e632-6.
30. Pauli N, Andréll P, Johansson M, Fagerberg-Mohlin B, Finizia C. Treating trismus: A prospective study on effect and compliance to jaw exercise therapy in head and neck cancer. *Head Neck*. 2015;37(12):1738-1744.
31. Satheeshkumar PS, Chamba MS, Balan A, Sreelatha KT, Bhatathiri VN, Bose T. Effectiveness of triclosan in the management of radiation-induced oral mucositis: a randomized clinical trial. *J Cancer Res Ther*. 2010;6(4):466-472.
32. Nordenram G, Davidson T, Gynther G, et al. Qualitative studies of patients' perceptions of loss of teeth, the edentulous state and prosthetic rehabilitation: a systematic review with meta-synthesis. *Acta Odontol Scand*. 2013;71(3-4):937-951.
33. Cella DF, Tulsky DS. Measuring quality of life today: Methodological aspects. *Oncology*. 1990;4:29-38,69-70.
34. Dornan M, Semple C, Moorhead A, McCaughan E. A qualitative systematic review of the social eating and drinking experiences of patients following treatment for head and neck cancer. *Support Care Cancer*. 2021;29(9):4899-4909.
35. Pokharel M, Shrestha I , Dhakal A , Amatya RC . Awareness and Knowledge of Oral Cancer among Medical Students in Kathmandu University School of Medical Sciences. *Kathmandu Univ Med J (KUMJ)*. 2017.;15(57):75-77.
36. Özler, Gül. Does Halitosis Effect Sexual Life in Males?. *Journal of Clinical and Analytical Medicine*. 2012; 6. 10.4328/JCAM.2230.
37. Elias MS, Ferriani MD. Historical and social aspects of halitosis. *Rev Lat Am Enfermagem*. 2006;14(5):821-3.
38. Sanz M, Roldán S, Herrera D. Fundamentals of breath malodour. *J Contemp Dent Pract*. 2001;2(4):1-17

39. Bosy A. Oral malodor: philosophical and practical aspects. *J Can Dent Assoc*. 1997;63(3):196- 201.
40. Sheiham A, Steele JG, Marcenes W, Tsakos G, Finch S, Walls AW. Prevalence of impacts of dental and oral disorders and their effects on eating among older people; a national survey in Great Britain. *Community Dent Oral Epidemiol*. 2001;29(3):195-203
41. Bogdasarian RS. Halitosis. *Otolaryngol Clin North Am*. 1986;19:101-117.
42. Zaitsu T, Ueno M, Shinada K, Wright FA, Kawaguchi Y. Social anxiety disorder in genuine halitosis patients. *Health Qual Life Outcomes*. 2011;9:94
43. Olszewska-Czyz I, Sozkes S, Dudzik A. Clinical trial evaluating quality of life in patients with intra-oral halitosis. *J Clin Med*. 2022;11(2):326.
44. Dhanrajani PJ, Jonaidel O. Trismus: etiology, differential diagnosis and treatment. *Dent Update*.2002; 29:88–92, 94.
45. Dworkin SF, Huggins KH, LeResche L, et al. Epidemiology of signs and symptoms in temporomandibular disorders: clinical signs in cases and controls. *J Am Dent Assoc*.1990; 120:273–281.
46. Weber C, Dommerich S, Pau HW, Kramp B. Limited mouth opening after primary therapy of head and neck cancer. *Oral Maxillofac Surg*.2010; 14:169–173.
47. Lee L-Y, Chen S-C, Chen W-C, Huang B-S, Lin C-Y. Post radiation trismus and its impact on quality of life in patients with head and neck cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol*.2015; 119:187–195.
48. Vissink A, Burlage FR, Spijkervet FKL, Jansma J, Coppes RP. Prevention and treatment of the consequences of head and neck radiotherapy. *Crit Rev Oral Biol Med* .2003;14:213–225.

49. Jager-Wittenaar H, Dijkstra PU, Vissink A, van Oort RP, Roodenburg JLN. Variation in repeated mouth-opening measurements in head and neck cancer patients with and without trismus. *Int J Oral Maxillofac Surg*.2009; 38:26–30.

50. Ryzek D-F, Mantsopoulos K, Künzel J, et al. Early-stage oropharyngeal carcinomas: comparing quality of life for different treatment modalities. *Biomed Res Int.* 2014:421964.

51. Teguh DN, Levendag PC, Voet P, et.al. Trismus in patients with oropharyngeal cancer: relationship with dose in structures of mastication apparatus. *Head Neck*.2008; 30:622–630.

52. Stegenga B, L. G. M. de Bont, de Leeuw GB R. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain*.1993; 7:183–195.

53. Pace-Balzan A, Cawood JI, Howell R, Butterworth CJ, Lowe D, Rogers SN. The further development and validation of the Liverpool Oral Rehabilitation Questionnaire: a cross-sectional survey of patients attending for oral rehabilitation and general dental practice. *Int J Oral Maxillofac Surg*. 2006; 35:72–78.

54. Hutcheson, Katherine A, Lewin JS. Functional outcomes after chemoradiotherapy of laryngeal and pharyngeal cancers. *Curr Oncol Rep*. 2012; 14:158–165.

55. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85:365–376.

56. Bjordal K, Ahlner-Elmqvist M, Tollesson E, Jensen AB, Razavi D, Maher EJ. Development of a European Organization for Research and Treatment of Cancer (EORTC) questionnaire module to be used in quality of life assessments in head and neck cancer patients. *Acta Oncol* .1994;33:879–885.

57. Steiner F, Evans J, Marsh R, et.al. Mouth opening and trismus in patients undergoing curative treatment for head and neck cancer. *Int J Oral Maxillofac Surg*.2015; 44:292–296.
58. List MA, D'Antonio LL, Cella DF,et.al . The performance status scale for head and neck cancer patients and the functional assessment of cancer therapy-head and neck scale: a study of utility and validity. *Cancer*. 1996;77:2294–2301.
59. Duke RL, Campbell BH, Indresano AT, et.al. Dental status and quality of life in long-term head and neck cancer survivors. *Laryngoscope*. 2005;115:678–683.
60. Connil C,Verger E, Salamero M. Performance status assessment in cancer patients. *Cancer* 1990: 65;1864-1866.
61. Stubblefield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. *PM R*. 2011;3(11):1041-1054.
62. Abendstein H, Nordgren M, Boysen M, et al. Quality of life and head and neck cancer: a 5-year prospective study. *Laryngoscope*. 2005;115(12):2183-2192.
63. Hammerlid E, Taft C. Health-related quality of life in long-term head and neck cancer survivors: a comparison with general population norms. *Br J Cancer*. 2001;84(2):149-156.
64. Cousins N, MacAulay F, Lang H, MacGillivray S, Wells M. A systematic review of interventions for eating and drinking problems following treatment for head and neck cancer suggests a need to look beyond swallowing and trismus. *Oral Oncol*. 2013;49(5):387-400.
65. Osthus AA, Aarstad AK, Olofsson J, Aarstad HJ. Health-related quality of life scores in long-term head and neck cancer survivors predict subsequent survival: a prospective cohort study. *Clin Otolaryngol*. 2011;36(4):361-368.

66. Barrios R, Tsakos G, García-Medina B, Martínez-Lara I, Bravo M. Oral health-related quality of life and malnutrition in patients treated for oral cancer. *Support Care Cancer*. 2014;22(11):2927-2933.

67. Datema FR, Ferrier MB, Baatenburg de Jong RJ. Impact of severe malnutrition on short-term mortality and overall survival in head and neck cancer. *Oral Oncol*. 2011;47(9):910-914.

Figure 1. The impact of radiation-induced trismus on quality of life of patients

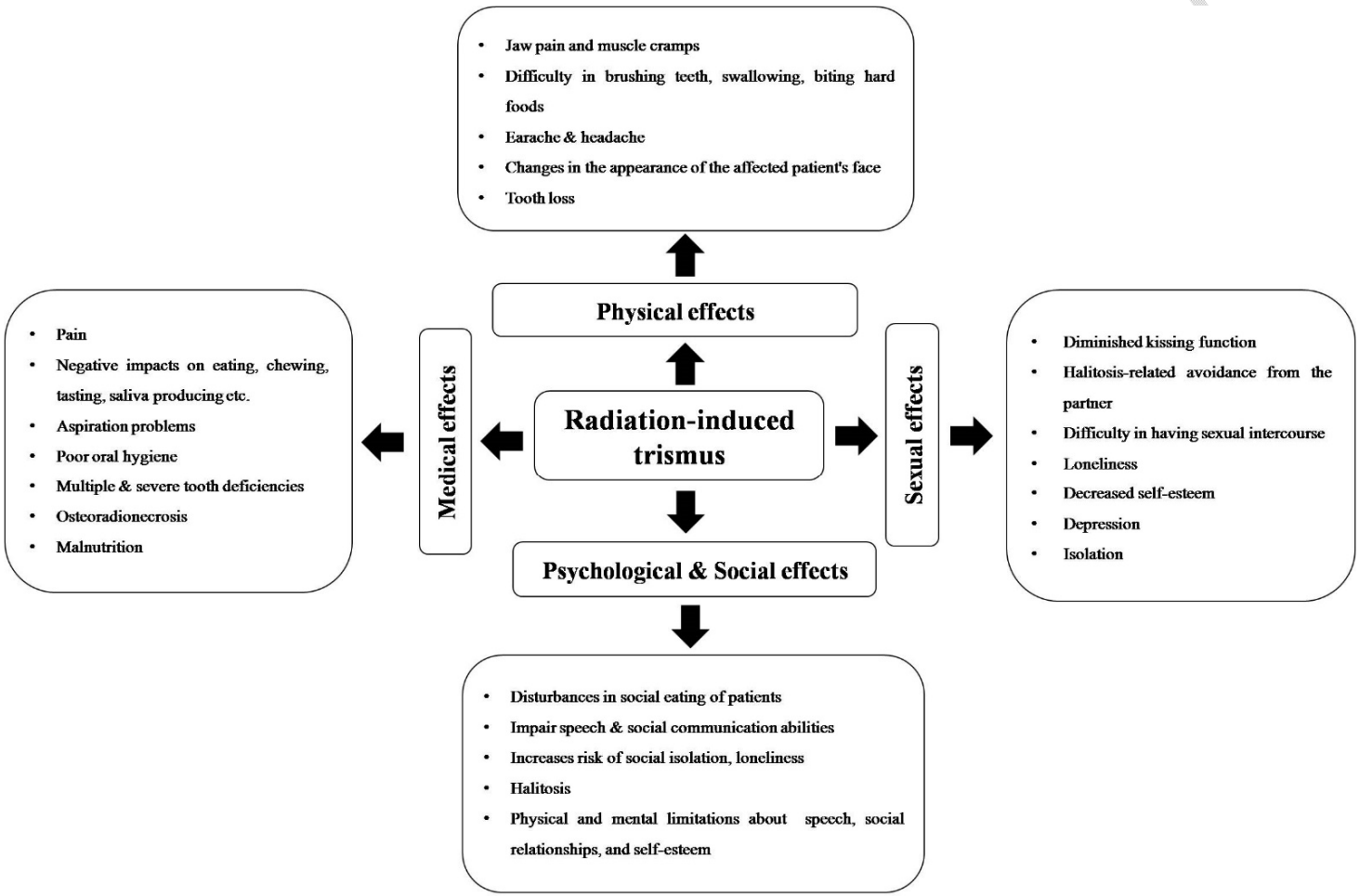

Figure 2. The measurement of mouth opening with Quick tongue- tie assessment tool® (Orofacial Myology Products, USA). A; normal mouth opening, B; trismus.

Figure 3. The most common questionnaires used to determine the effects of on patients' quality of life