



# Evidence-based Practical Recommendations for Prevention and Management of Radiation-induced Trismus

Efsun SOMAY,<sup>1</sup> Erkan TOPKAN,<sup>2</sup> Nilüfer KILIÇ DURANKUŞ,<sup>3</sup> Şükran ŞENYÜREK,<sup>3</sup>  
 Sibel BAŞÇIL,<sup>4</sup> Uğur SELEK<sup>3</sup>

<sup>1</sup>Department of Oral and Maxillofacial Surgery, Başkent University Faculty of Dentistry, Ankara-Türkiye

<sup>2</sup>Department of Radiation Oncology, Başkent University Faculty of Medicine, Adana-Türkiye

<sup>3</sup>Department of Radiation Oncology, Koç University Faculty of Medicine, Istanbul-Türkiye

<sup>4</sup>Department of Periodontology, Başkent University Faculty of Dentistry, Ankara-Türkiye

## SUMMARY

Head and neck cancer (HNC) patients undergoing radiation therapy (RT) commonly experience radiation-induced trismus (RIT), a significant complication that profoundly impacts their quality of life and functional outcomes. Hence, a comprehensive understanding and management of this condition are imperative for radiation oncologists. RIT, characterized by a limited ability to open the mouth, can severely impact essential functions such as speaking, eating, and maintaining oral hygiene. These malfunctions can lead to nutritional deficiencies, weight loss, and an increased risk of oral infections. The pathophysiology involves radiation-induced fibrosis and damage to the masticatory muscles and temporomandibular joint, often exacerbated by concurrent chemotherapy. Identifying at-risk patients and implementing preventive measures against RIT is crucial. These measures may include using advanced radiation techniques such as intensity-modulated RT or proton therapy and early physical therapy. Additionally, personalized treatment planning and multidisciplinary care involving radiation and medical oncologists, dental specialists, and physical therapists can help reduce the onset and severity of RIT. Given the significant impact of RIT on the functionality and quality of life of patients with HNC and the relatively low level of interest in oncological communities, the purpose of this review is to provide an evidence-based summary of effective preventive and management strategies for RIT in HNC patients, which hopefully will serve as a valuable guide for physicians in related disciplines.

**Keywords:** Chemoradiotherapy; head and neck cancer; late toxicity; radiation-induced trismus; radiotherapy.  
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## INTRODUCTION

Radiation-induced trismus (RIT) is a serious complication of radiotherapy (RT), chemo-RT (S-CRT), or concurrent chemoradiotherapy (C-CRT) in individuals diagnosed with head and neck cancers (HNC). Frequently reported symptoms associated with RIT and their consequential impact include pain, jaw stiffness, impaired eating and chewing, speech impediments, halitosis, alterations in facial appearance,

depression, social isolation, and diminished quality of life (QoL) metrics.[1] The prevalence of RIT among HNC patients ranges widely, from 5% to 69%. This variability is contingent upon several factors, including the tumor's anatomical site, its extent of infiltration into adjacent tissues, the stage of malignancy, the extent of surgical intervention, the dosage of RT received by the masticatory apparatus, and the concurrent or sequential (neoadjuvant or adjuvant) administration of chemotherapy.[2]

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Dr. Efsun SOMAY  
Başkent Üniversitesi Diş Hekimliği Fakültesi,  
Ağız, Diş ve Çene Cerrahisi Anabilim Dalı,  
Ankara-Türkiye  
E-mail: efsuner@gmail.com



RIT typically manifests within 3 to 48 months after RT or C-CRT.[2] Unfortunately, there is no consensus on the best method for measuring maximum mouth opening (MMO) and, consequently, for determining restricted inter-incisal opening and RIT status. However, an MMO of 35 mm or less represents the most widely recognized criterion for an RIT diagnosis in HNC patients.[3] This diagnostic threshold, established by Dijkstra et al.[3] is applied uniformly to all HNC patients, irrespective of their initial MMO measures and the subsequent relative changes following RT or C-CRT. Although determining the normal MMO range is crucial to achieving a comprehensive diagnosis of RIT, the data on this pivotal issue are conflicting. For instance, Carlsson and Svardstrom conducted a survey involving 299 individuals, revealing that the mean MMO for men was  $44.8 \pm 9.4$  mm, while for women, it was  $39.2 \pm 10.8$  mm.[4] In contrast, Agerberg reported that the normal MMO range was 44 to 77 mm in males and 42 to 75 mm in females.[5] Therefore, diagnosing RIT is problematic as there is no consensus on the normal mouth opening range. As a consequence of this difficulty, the exact rates of RIT are often overlooked, and the impact of RIT on affected patients' functionality and QoL measures is obscured.

Disabling RIT presents challenges in terms of prevention and treatment. The economic burden, coupled with its adverse effects on patients' functionality and quality of life, further complicates the management of this condition. Considerably, a patient may face occupational repercussions, potentially leading to job loss, mainly if speaking is integral to their professional responsibilities. Thus, the financial support necessary for cancer treatment and daily sustenance may be compromised. Additionally, the looming threat of unemployment can inflict profound psychological distress, potentially precipitating melancholic states. The treatment of HNC is both time-consuming and expensive. Efforts to address RIT and its associated consequences may increase the overall cost of care, potentially making it unaffordable for patients with relatively low incomes. For example, the cost of RIT therapy devices can vary immensely, and most devices also require customization for each patient, further driving up treatment costs. Similarly, the rental of continuous passive motion devices, daily or weekly, can cost several hundred dollars each week. It is essential to strive towards developing more affordable yet effective technologies that are accessible to all RIT patients. Therefore, it is important to identify RIT, assess its symptoms, and take the necessary precautions.[6]

The primary objective of this review is to elucidate the concept of RIT as applied in routine dental and radiation oncology practices, expound upon the assessment criteria, recognize associated symptoms, and ultimately contribute to refining the evaluation and management of affected patients.

## MATERIALS AND METHODS

The current review thoroughly analyzed systematic reviews, original articles, meta-analyses, cohort studies, case reports, and abstracts published in English between 1971 and 2024. A PubMed search was performed using the terms "trismus," "RIT," "radiation-induced fibrosis," "restricted mouth opening," "masticatory muscles," and "masticatory apparatus" to find relevant papers. This literature review excluded studies with a sample size of less than 50 patients.

## RESULTS

A PubMed search yielded 70 articles. However, 38 of them were excluded from the review process because they were case reports ( $n=10$ ), case series with fewer than 50 patients ( $n=12$ ), or duplicate studies ( $n=16$ ). Subsequently, 32 original (retrospective or prospective) and review studies that met the specified selection criteria were thoroughly analyzed to formulate the recommendations presented within this review.

## DISCUSSION

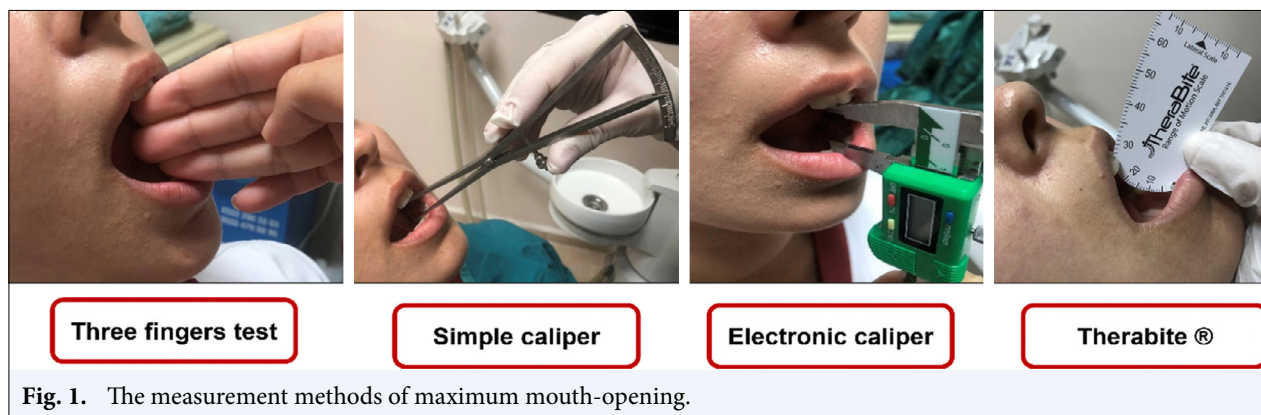
Head and neck cancers (HNCs) constitute approximately 10–15% of all malignancies globally.[7] Curative radiotherapy (RT) and concurrent chemoradiotherapy (C-CRT), with or without surgical intervention, serve as the backbone treatment modalities for these patients, contingent upon the stage of the disease.[8] Nonetheless, these therapeutic approaches can give rise to radiation-induced injury affecting the masticatory muscles and the temporomandibular joint, provoking exacerbated local and systemic inflammation and hypoxia. These repercussions may culminate in the fibrosis of these anatomical structures, ultimately leading to a complication recognized as radiation-induced trismus (RIT).[9–11] Radiation-induced injury in these anatomical structures may lead to RIT due to muscle atrophy, which is triggered by chronic, severe tissue inflammation, hypoxia, and fibrosis.[11]

Typical signs and symptoms characterize the clinical presentation of RIT. Specifically, the primary manifestation of RIT is restricted mouth opening, which demonstrates a progressive nature in the absence of promptly initiated treatment measures. It is regrettable that, owing to its progressive fibrotic characteristics, timely intervention may only decelerate rather than arrest its advancement in severely affected patients. Due to pain in the jaw muscles, temporomandibular joint (TMJ), or surrounding areas, the patient has difficulty, particularly when trying to open the mouth, chew, or speak.[1] Frequent jaw locking may cause tension or stiffness in the muscles around the jaw region, which may worsen over time. Difficulty chewing is a common problem in RIT patients, mainly when eating certain foods requiring a wide mouth opening. In such cases, softer or liquid-based ingredients may be preferred. Patients may also experience difficulties with intelligible speech and articulation due to restricted and painful jaw movements.[10] Various degrees of deformations in facial appearance may occur if not treated on time, and, in severe cases, significant asymmetry or changes in the facial structure may result from persistent involuntary and painful muscle contractures, stiffness, and atrophy. In some cases, the affected individual may struggle to deal with the problem, leading to depression and social withdrawal, which may require psychiatric assistance. When confronted with severely restricted mouth opening, challenges relating to oral hygiene maintenance, halitosis, and elevated susceptibility to periodontal and dental issues may manifest commensurate with the severity of the condition. Severe instances may experience TMJ clicking, popping, or locking, culminating in discomfort and constrained jaw mobility. These complications may further worsen the afflicted individual's psychological well-being and intimate relationships.[1,12] Therefore, prompt assistance from oral and maxillofacial surgeons, general dentists, periodontologists, dietitians, and psychiatrists would be highly beneficial in nearly all cases of RIT, given its harmful impact on all aspects of quality of life (QoL) measures.

RIT may affect up to 38% to 42% of HNC patients undergoing oncological treatment; hence, its diagnosis must be made timely and correctly for appropriate management, considering its detrimental effects on patients' life quality.[3,13] However, defining RIT with a universally accepted maximum mouth opening (MMO) cutoff value remains challenging due to the diverse methods and threshold values RIT researchers utilize. The same remark also applies to the grading of RIT.[14]

The measurement methods initially used by some researchers involved using calipers—one for individuals with some or partial teeth using a prosthesis and another for edentulous individuals not using a prosthesis. Ensuring all patients maintain a stable and neutral head position during such measurement is essential. Then, patients are instructed to open their mouths to their maximum extent while minimizing discomfort.[15] The “three-finger test” is a simple diagnostic procedure for trismus, where the patient is asked to insert three fingers into their mouth. A normal mouth opening is determined by the ability to fit all three fingers between the incisors. If fewer than three fingers can be inserted, trismus is likely present.[16] An alternative modern approach involves using the Therabite® range of motion scale (Atos Medical AB, Hörby, Sweden). This method allows for convenient and rapid assessments and, because it is disposable, minimizes the risk of infection.[17,18] Patients are instructed to fully extend their mouths using the Therabite® range of motion scale to measure the gap between the upper edge of one of the lower central incisors and the lower edge of the corresponding upper central incisor. It is imperative to consistently assess the MMO in patients at risk of restricted mouth opening, irrespective of the chosen assessment method. It is recommended that these assessments be conducted before treatment initiation and subsequently at 3, 6, 9, and 12-month intervals, followed by biannual assessments during the follow-up period. Regular monitoring is of utmost importance in promptly identifying restricted mouth opening, progression to RIT, and the advancement of RIT to more severe grades (Fig. 1).

Further examination of the current literature is warranted to address the prevailing disparities in RIT definitions, grading systems, and their practical applications in clinical contexts. Previous investigations have introduced varied MMO cutoff values for RIT, contingent upon the dental condition of the subjects. Notably, the study by Louise Kent et al.[19] established an MMO threshold of 35 mm for patients with teeth and 40 mm for edentulous patients. In contrast, Lindblom et al.[20] utilized a 35 mm cutoff value for RIT. Nevertheless, the authors underscored the necessity for a standard RIT cutoff value by illustrating that applying a 20 mm cutoff would encompass only 8% of their patient cohort in the RIT classification. These findings underscore the imperative for a universally acknowledged RIT cutoff and emphasize the critical requirement to define a standard cutoff value that can be widely applied to cancer patients undergoing RT or C-CRT. Steiner et al.[21] established



**Fig. 1.** The measurement methods of maximum mouth-opening.

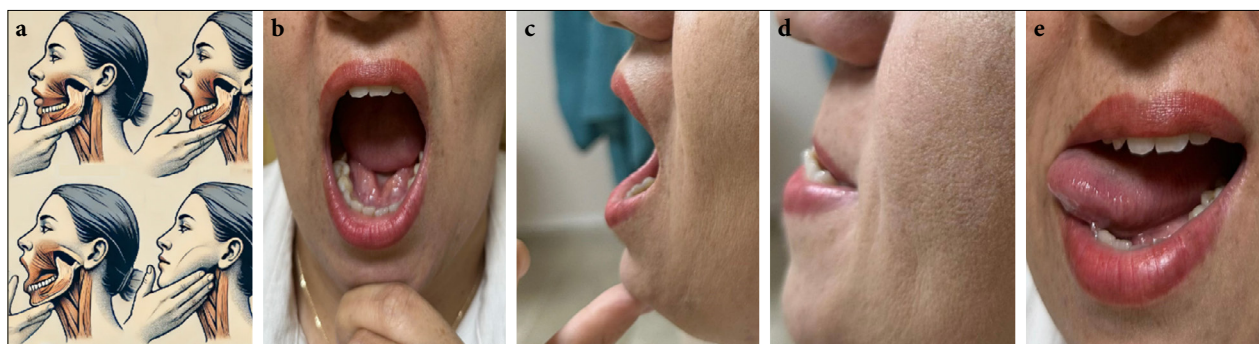
a cutoff value of 35 mm for RIT and classified MMO measurements of less than 25 mm as indicative of severe trismus. Additionally, they employed grading systems to assess trismus severity, with grades 2, 3, and 4 assigned to MMOs of 10–20 mm, 5–10 mm, and less than 5 mm, respectively.[22] However, the utilization of diverse MMO cutoff values in defining RIT in previous studies lacks a systematic approach.[23,24] This is primarily due to the absence of objective and reliable metric assessments comparing MMO measurements before and after RT. The application of variable RIT cutoff values complicates the analysis of risk factors and the evaluation of different therapeutic interventions for RIT. Nevertheless, efforts have been made by Dijkstra et al.[3] to standardize the definition of trismus in HNC patients by establishing a generally accepted MMO cutoff value of 35 mm or less. However, Dijkstra et al.[3] widely accepted RIT definition fails to consider the relative changes between the pre-RT and post-RT measurements, as it applies identical criteria to every patient with HNC.

The frequently cited risk factors associated with the development of RIT encompass age, sex, genetic predisposition, nutritional status, smoking, presence of chronic inflammatory disorders, TMJ disorders, arthropathies, history of prior trauma, fibrotic disorders, tumor characteristics (such as location, size, and stage), the involvement and location of neck nodes, prior surgical interventions and their extent, the proximity of the RT field to the masticatory muscles and TMJ, RT modality and technique, as well as the inclusion of chemotherapy in conjunction with RT and their administration sequence.[25] Intensity-modulated radiotherapy (IMRT) has improved the distribution of radiation doses to the tumor, neck, and high-risk regions compared to previous methods, reducing radiation doses to at-risk organs.[26] Consequently, individuals who undergo IMRT treatment are anticipated to have a reduced occurrence

of RIT in comparison to those treated with conventional methods. As an example, Chen et al.[27] documented an RIT prevalence of only 5.7% in patients with nasopharyngeal cancer who had treatment with IMRT. Moreover, proton therapy appears to result in the lowest RIT rates, according to its exceptional tissue-sparing capabilities. While there is insufficient long-term evidence on the rates of RIT, particularly for proton treatment, preliminary studies indicate that the occurrence of RIT may be reduced compared to IMRT, perhaps less than 5%. Traditional RT modalities have been shown to have higher incidences of RIT, ranging from 25% to 40%. On the other hand, IMRT has lower rates of trismus, ranging from 5% to 15%. Proton therapy, however, has the lowest rates of trismus, less than 5%. This comparison emphasizes the benefits of IMRT and proton therapy in minimizing the likelihood of RIT in patients receiving RT for HNC. Nevertheless, the availability of advanced technologies such as IMRT and proton therapy might provide an obstacle for countries with limited funds, a drawback of these technologies.[28]

CCRT poses a higher risk for RIT development than RT alone. Borges et al.[29] recently addressed this issue in a meta-analysis of eight articles and 2332 patients: chemoradiotherapy (n=1474) and RT alone (n=858). The results of this meta-analysis demonstrated that the addition of chemotherapy to RT increases the RIT prevalence by a factor of 2.55 (p=0.0003). Therefore, the risk of RIT must be assessed on a per-patient basis by considering the significant variabilities among numerous factors predisposing to RIT in HNC patients, which may be beneficial in the early arrangement of preventive measures for high-risk patients.

RIT is more likely to occur when the radiation doses to the masticatory muscles, namely the masseter, pterygoid, and temporalis muscles, or the TMJ, surpass 60 Gy.[30] Although a prescription dose of >60 Gy is

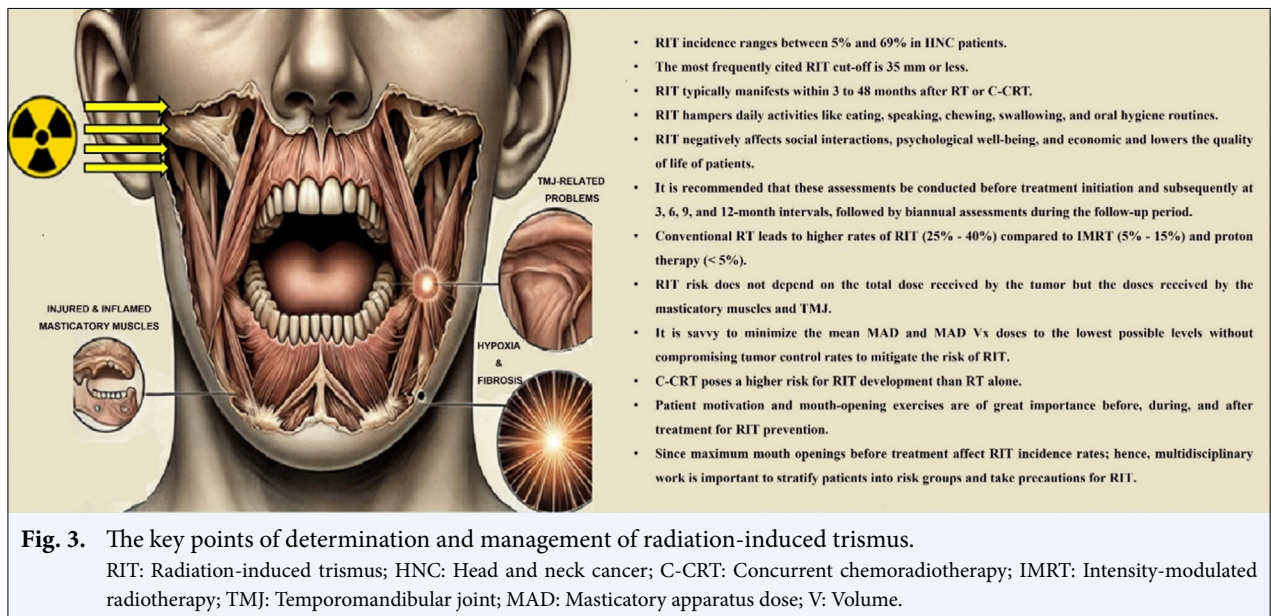


**Fig. 2.** Jaw opening and stretching exercises applied to patients in our clinic: (a) Exercises that assist in opening the mouth. (b) Perform self-mouth opening exercises, also known as mouth-open-wide exercises: a. Maintain the position for a duration of 7–10 seconds; b. Repeat the exercise 10 times, with 2 repetitions for each set. (c) Jaw resistance (Using one hand, gently grasp the chin with the index finger and thumb; apply pressure by closing your mouth while providing gentle downward force on the chin): a. Maintain for 7–10 seconds; b. Repeat 10 times, with 2 sets; (d) Forward jaw displacement: Move the upper jaw forward so that the lower teeth are positioned in front of the upper teeth: a. Hold for 7–10 seconds; b. Repeat 10 times, with 2 sets); (e) Perform lateral jaw movement by moving the jaw from side to side with a slightly open mouth: a. Maintain this position for 7–10 seconds. b. Repeat this action 10 times, with two sets of repetitions.

often reported as the threshold dose for RIT development, the fundamental determinant of the RIT risk is not the total dose received by the tumor but the doses received by the masticatory muscles and TMJ.[10] This is because the doses delivered to the masticatory apparatus may be significantly lower or higher than the prescribed doses to the tumor, depending on factors such as the size of the irradiated volume, its proximity to these structures, the location of the hot spot doses, the radiation modality, and the technique used. [10] For instance, Somay et al.[31] administered 70.0, 59.4, and 54.0 Gy for high-risk, intermediate-risk, and low-risk planning target volumes (PTVs) using the simultaneous integrated boost IMRT technique in 230 locally advanced nasopharynx (LA-NPC) patients who underwent C-CRT. However, the authors found that a mean masticatory apparatus dose (MAD) of  $>37.2$  Gy ( $p < 0.05$ ) and the MAD  $V_{53.2}$  Gy  $> 38.6\%$  ( $p < 0.05$ ) were the threshold values associated with a significantly increased risk of RIT development, even though these values are much lower than the prescribed doses to the PTVs. Consequently, the mean and Vx (percentage receiving X Gy or higher) doses of MAD emerge as more reliable indicators of the extent of injury to the masticatory apparatus and, hence, the risk of RIT in HNC patients undergoing RT or C-CRT. This assertion accords well with the anatomical structure and functional characteristics of the masticatory apparatus, which operates as a parallel organ when irradiated.[31] Despite the lack of reliable outcomes from well-structured large-scale studies providing adequate data to formu-

late definitive recommendations for threshold doses in routine RT planning, it is savvy to minimize the mean MAD and MAD Vx doses without compromising tumor control rates to mitigate the risk of RIT.[32]

Acute effects such as inflammation, edema, and muscle spasms may occur during or immediately after RT before RIT manifests. Depending on the dose and fractionation schedule applied, long-term effects such as fibrosis and scarring may also develop.[33] The primary step in managing these effects is to control the disabling pain with analgesic medications, such as non-steroidal anti-inflammatory drugs. Patients should be encouraged to initiate jaw movements and physiotherapy.[34] Alternatively, botulinum toxin has been suggested for pain control. However, injections into the TMJ region are only effective in relieving radiation-induced pain caused by radiation-induced fibrosis syndrome, and additional injections are needed later to relieve recurrent masseter muscle pain. Moreover, no reliable evidence suggests that the administration of botulinum toxin significantly improves the severity of RIT.[35] Although there is no consensus on whether starting exercise before RT or C-CRT will improve mouth opening after treatment, it has been reported that the incidence of RIT is low in patients with high pre-treatment MMO measures.[31] Additionally, jaw exercise therapy before treatment is reported to increase MMO, reduce symptoms associated with radiation-induced trismus, and improve health-related quality of life. Therefore, it is recommended that jaw exercise therapy be initiated early, structured, and continued in the long term, making jaw exercises essential (Fig. 2).[36]



In addition to the non-invasive measures, oral and maxillofacial surgeons can perform various intraoperative interventions to minimize trismus, one of which is the prophylactic excision of the adjacent coronoid process (the insertion site of the temporalis muscle) in cases of cancer in the mandibular ramus area, temples, or zygomatic arch.[37] Surgeons can also perform various intraoperative interventions to minimize RIT incidence or alleviate RIT-related symptoms and functional losses. One of these interventions is the prophylactic excision of the adjacent coronoid process, which is the insertion site of the temporalis muscle, in cases of cancer in the mandibular ramus area, temples, or zygomatic arch.[29] Muscle myotomy is a preferred method to treat myofibrotic contracture of the masticatory muscles that may occur due to RT, surgical scarring, or immobilization. Similarly, coronoidectomy may be considered an alternative in temporalis muscle pathology cases.[38] Surgical excision of scar tissue and fibrotic bands and restoration of tissue defects may improve trismus by alleviating the restriction.[37–39] As the fibrosis in muscle tissue due to surgery increases, there is a risk of further reduction in MMO and the potential for persistent limited mouth opening, which can lead to TMJ ankylosis.[40] It is vital to follow all release-reconstruction operations with rigorous physical therapy regimens and select cooperative and motivated patients for such procedures to increase success rates in managing disabling RIT.

Early diagnosis of RIT is crucial, as it may threaten the patient's life by making it difficult to keep the airway open under emergency conditions. Imaging stud-

ies, such as magnetic resonance imaging and computed tomography scans, are beneficial for assessing structural changes in the TMJ, synovial fluid, and adjacent soft tissues.[41] The aforementioned imaging modalities may further facilitate the evaluation of the severity of secondary complications, including fibrosis, joint abnormalities, and osteoradionecrosis, all of which may exacerbate RIT. Additionally, functional assessments, such as electromyography, can yield a more comprehensive understanding of the neuromuscular aspects of trismus, ultimately contributing to a more thorough diagnostic process.[25,42] The complex nature of RIT and the fact that many aspects of the patient's condition can impact the prognosis and effectiveness of treatment necessitate a multidisciplinary evaluation process in which patients are actively involved. This team typically includes radiation oncologists, medical oncologists, dental oncologists, oral and maxillofacial surgeons, periodontologists, general dentistry specialists, physiotherapists, speech therapists, psychiatrists, and dietitians, emphasizing the need for tailored management of patients requiring special care. Such comprehensive modern approaches will undoubtedly reduce the RIT rates and improve the prophylactic and treatment measures, with resultant advancements in most aspects of QoL scores (Fig. 3).

## CONCLUSION

RIT is a clinically complex and challenging complication of RT and C-CRT that can significantly impact the quality of life of the affected patients. However, early diag-

nosis, preventive measures, and the implementation of comprehensive multidisciplinary treatment and follow-up protocols can help minimize the devastating effects of RIT in these patients. Ongoing research into the underlying mechanisms and management of RIT, coupled with advancements in RT modalities and techniques, offers the potential for further reduction in the occurrence and intensity of this disorder in the coming years. Healthcare practitioners must fully understand RIT and its adverse effects to improve care and long-term functional outcomes for HNC patients receiving RT or C-CRT.

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