Patient Preference and Adherence

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REVIEW

Evaluation of Treatment Modalities for Radiation Therapy-Induced Trismus, Considering the Timing and Adherence to Progress in Mouth Opening and Oral Health–Related Quality of Life: A Systematic Review

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Purpose: To assess the effectiveness of treatment modalities for radiation-induced trismus in improving mouth opening (MO) and oral health–related quality of life (OHRQoL), with considering of treatment timing and patient adherence.

Methods: Electronic databases (PubMed, Google Scholar, Scopus, EBSCOhost, and ScienceDirect) were searched for studies published between 2015 and 2025 using relevant Medical Subject Headings (MeSH) combined with Boolean operators, including "Treatment OR therapy AND trismus OR limited mouth opening AND radiation therapy OR radiotherapy AND head and neck neoplasm OR head and neck cancer" and "Timing OR starting time AND treatment OR exercise AND trismus OR limited mouth opening OR restricted mouth opening." After duplicate removal, titles, abstracts, and full texts were screened for eligibility.

Results: The initial search identified 472,480 articles, of which 18 met the inclusion criteria after screening titles, abstracts, and full texts. Kruskal–Wallis analysis demonstrated significantly greater improvement in mouth opening when trismus treatment was initiated during or after radiotherapy compared to before radiotherapy ($p = 0.020$). The greatest improvement was observed with combined laser therapy and Therabite exercises, initiated concurrently with radiotherapy for 3 months with high adherence, resulting in a mean increase of 26.95 mm in MO and an improvement in OHRQoL. The second most effective modality was threaded tapered screw appliance (TTSA) therapy combined with low-level laser therapy (LLLT) administered post-radiotherapy for 6 weeks, yielding a 15 mm improvement with high adherence.

Conclusion: The effectiveness of treatment for radiation-induced trismus is influenced by the therapeutic modality, timing of therapy initiation, and patient adherence, all of which contribute to improvements in MO and OHRQoL. Combination therapy modalities, particularly laser therapy combined with jaw movement devices, initiated during or after radiotherapy and supported by high patient adherence, optimize mouth opening and enhance OHR-QoL.

Keywords: adherence, mouth opening, oral health–related quality of life, radiation therapy, treatment modalities, trismus

Introduction

Trismus is characterized by a reduction in maximal interincisal opening (MIO). Individuals with trismus exhibit a mouth opening of less than 35 mm, measured measured as the interincisal distance between the maxillary and mandibular anterior incisors, or less than 40 mm, measured from the interalveolar ridge distance.[1,2] Trismus is classified as mild (25

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to 35 mm), moderate (16 to 25 mm), or severe (15mm or less interincisally).[3] Limited mouth opening may result from various factors, including complications following wisdom tooth extraction, physical trauma or post-accident injuries, tetanus infections, malignancies, and temporomandibular-joint disorders that cause inflammation and structural damage.[4] Additionally, trismus may develop in head and neck cancer (HNC) patients due to tumor proximity to the masticatory apparatus or as a consequence of radiation therapy (RT) with or without concurrent chemotherapy (ChT) or surgery in the head and neck region.[5]

Radiation-induced inflammation results from endothelial injury, hypoxia, and fibrosis. Radiation-induced cell damage in irradiated tissues results from double-strand DNA damage and the generation of reactive oxygen species. Enzymes released during tissue injury further increase oxidative stress, leading to tissue ischemia and vascular thrombosis. These processes intensify local tissue damage and stimulate the production of inflammatory cytokines and chemokines. The resulting inflammatory response typically leads to hypoxia and irreversible radiation-induced fibrosis of the masticatory apparatus, ultimately resulting in radiation-induced trismus (RIT).[6]

The incidence of post-radiation trismus in HNC patients averages 69%. Trismus typically occurs 3–4 months after radiation therapy and peaks at six months. Patients with trismus not only experience limited mouth opening but also reduced jaw movement, pain, and stiffness or tension in the masticatory muscles.[6–8] These limitations adversely affect chewing, phonation, jaw function, and overall oral health-related quality of life (OHRQoL). Oral health-related quality of life has a substantial impact on daily functional activities as well as the psychosocial well-being of patients. The severity of functional limitations is subjectively perceived, and the associated psychosocial impact largely depends on individual patient perception.[1,9,10]

Many therapies have been carried out to overcome post-radiation trismus with or without chemotherapy or surgery in head and neck cancer patients, including mouth-opening exercises and jaw range-of-motion exercises.[11–13] However, few syntheses provide a detailed overview of this topic.[14,15] To address this gap, this review study aims to investigate and synthesize studies on whether mouth opening therapy is effective in terms of modality of treatment, the initial time of trismus therapy, adherence, and its effect on improving mouth opening related to the patient's oral health-related quality of life.

Materials and Methods

Data Sources and Electronic Search

We used five electronic databases to identify studies (PubMed (United States National Library of Medicine), Google Scholar, Scopus, EbscoHost, and ScienceDirect) from January 2015 to December 2025. Several Medical Subject Headings combined into Boolean MeSH into search strategies are "Treatment or therapy and Trismus or limited mouth opening and Radiation therapy or Radiotherapy or Head and neck neoplasm or head and neck cancer" and "Timing or starting time and treatment or exercise and trismus or limited mouth opening or restricted mouth opening." As a guide for the search strategy, the following Population, Intervention, Comparison/Control, and Outcomes (PICO) criteria were addressed. Population: individuals with head and neck cancer currently or already undergoing radiation with/without chemo and/or surgery therapy; Intervention: trismus treatment; Comparison/Control: No trismus treatment/usual care/no structured treatment; Outcomes: improving mouth opening related to the patient's oral health-related quality of life.

Data Collection and Selection Techniques

Initially, all authors selected titles and abstracts that could potentially meet the inclusion criteria. The inclusion criteria included published academic articles; publications from 2015 to 2025; cross-sectional, randomized controlled, and prospective study designs; and studies involving radiation therapy in the head and neck region, with or without chemotherapy and/or surgical treatment. The exclusion criteria included non-open-access articles, non-English publications, studies focusing on single surgical or chemotherapy interventions, post-radiation therapy complications other than trismus, studies without instruments for measuring quality of life, and animals or plant studies.

Statistical Analysis

The statistical test used in this study was descriptive statistics, followed by the Shapiro–Wilk normality test. Then, the Kruskal–Wallis test was used to determine differences in mouth-opening progress between studies at the initial time point (before, during, and after radiation therapy).

A descriptive ranking was conducted to identify the most effective therapy modality for achieving optimal mouth opening across studies.

Results

Study Selection

After removing duplicate articles, excluding those that did not meet the inclusion criteria, selecting the abstracts, and reading the entire contents, the articles were filtered. A total of 472,480 titles were found by electronic searches of the databases (PubMed, Google Scholar, Scopus, Ebsco Host, and Science Direct). Following the removal of articles that did not meet the inclusion criteria and had the same title, 106 relevant articles were found through a rapid title-based search. A total of 64 publications were retrieved following a brief abstract-based search. Furthermore, continuing the search using the full-text articles, 18 articles met the criteria and were approved by all reviewers. The process of selecting studies is displayed in Figure 1.

Table 1 summarizes the extracted study characteristics, including study design, sample size, age, sex, and cancer treatment. The included studies comprised three randomized controlled trials (RCTs); one randomized, open-label, controlled, three-centre feasibility study; eight prospective studies; one pilot randomized controlled experimental study; one single-arm clinical trial; one prospective single-arm cohort feasibility study; one prospective RCT; one randomized, controlled, double-blind, three-arm, parallel-group prevention clinical trial; and one quasi-experimental study.

The total sample size across the included studies was 1,088 participants aged 18 years or older, comprising 676 males and 412 females. Tumor sites included the oral cavity, pharynx, oropharynx, nasopharynx, floor of mouth, hypopharynx, tonsil, tongue, buccal mucosa, mandible, maxilla, and salivary glands. Cancer treatments included radiotherapy (RT), delivered using conventional techniques, intensity-modulated radiation therapy (IMRT), or volumetric modulated arc therapy (VMAT), with or without chemotherapy (ChT) and/or surgical intervention.

The overall risk of bias assessment included seven randomized controlled trials (RCTs) evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool (Table 2) and eleven non-randomized studies assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool (Table 3). The RoB 2 assessment indicated that five studies had some concerns, while two studies were judged to have a low risk of bias. In contrast, the ROBINS-I assessment showed that all eleven non-randomized studies were at serious risk of bias.

Table 4 displays the extracted data, including the initial time of treatment for trismus, duration, modalities, progress on MIO, level of adherence, and oral health-related quality of life. The treatment of trismus consists of active jaw movement, passive jaw movement (using a device), and a combination of active and passive jaw movement.

Active jaw movement interventions included myofascial release (MFR; n = 1), Matrix Rhythm Therapy (MaRhyThe®; n = 1), and oral exercises (n = 2). Passive jaw movement interventions included the TheraBite® jaw motion rehabilitation system or Engström device (n = 2), TheraBite® jaw motion rehabilitation system (n = 5), wooden spatulas or wooden tongue depressors (n = 2), threaded tapered screw appliance therapy (TTSA; n = 1), low-level laser therapy (LLLT; n = 1), photobiomodulation therapy (PBMT; n = 1), RestoraBite™ (n = 2), laser therapy (n = 1), and the Dynasplint Trismus System (DTS; n = 1).

The combination exercise included passive and active jaw exercises with a Jaw Trainer© (n=2); a combination of active and passive exercise using theraBite (n=1); combination of physical therapy using transcutaneous electrical nerve stimulation (TENS), hot pack dan manual stretching (n=1), combined of TTSA and LLLT (n=1), combination of laser therapy and theraBite exercises (n=1).

The timing of trismus therapy varied, with interventions initiated before radiotherapy (n = 3), during radiotherapy (n = 8), and after radiotherapy (n = 7). The duration of treatment ranged from 3 to 24 weeks. Compliance levels varied from high (n = 12) to moderate (n = 5) and low (n = 1). Regarding changes in mouth opening following treatment, an increase was reported in 21 studies, whereas a decrease was observed in 5 studies.

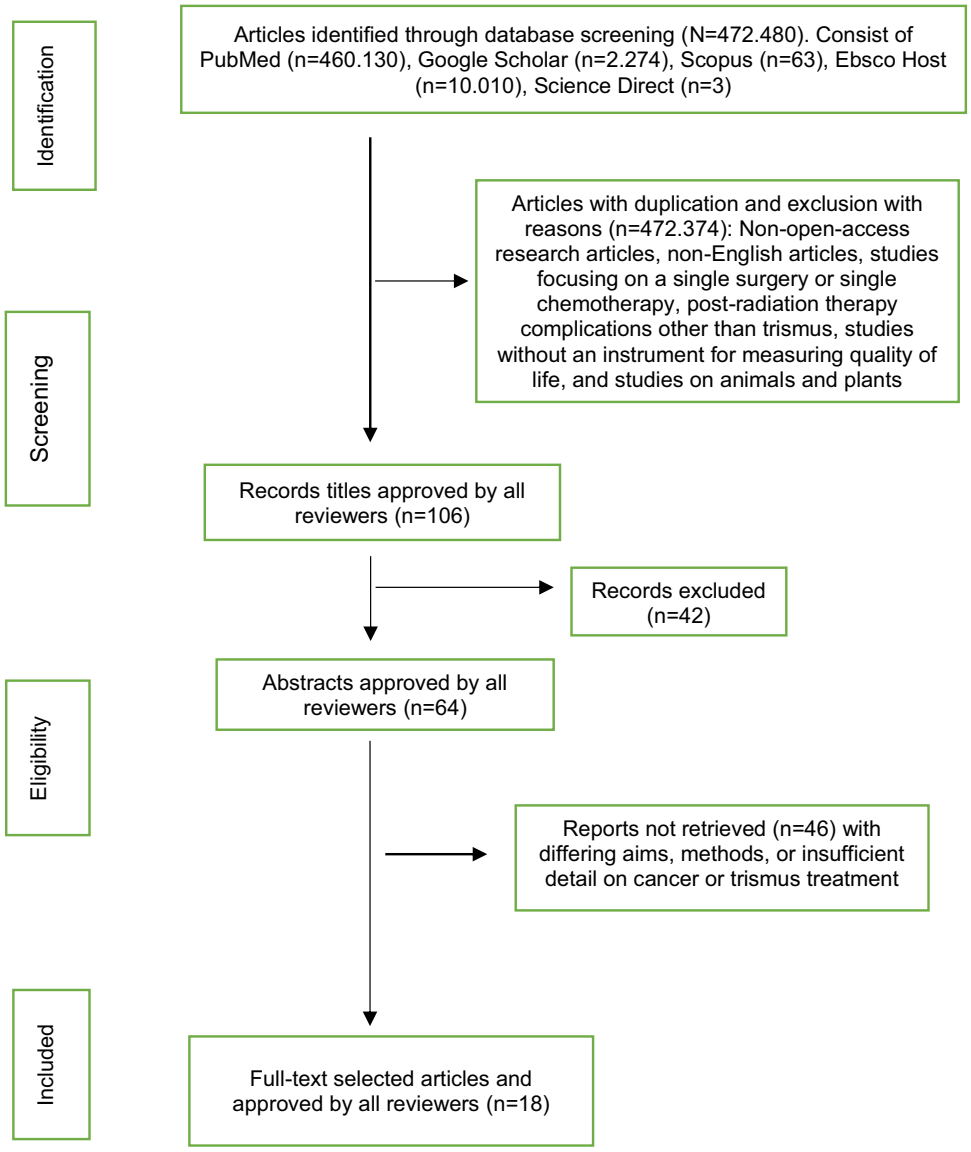

Figure 1 The process of selecting studies.

Several instruments used in the included studies assessed oral health–related quality of life (OHRQoL), either directly or indirectly. These instruments included the Visual Analogue Scale (VAS), Numerical Rating Scale (NRS) for pain, Composite Pain Index (CPI), Gothenburg Trismus Questionnaire (GTQ), European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), EORTC Quality of Life Questionnaire–Head and Neck 35 (EORTC QLQ-H&N35), Temporomandibular Joint Disability Index (TDI), Functional Intraoral Glasgow Scale (FIGS), Functional Assessment of Cancer Therapy–Head and Neck (FACT-H&N), Global Quality of Life (GQL), Mandibular Function Impairment Questionnaire (MFIQ), and University of Washington Quality of Life questionnaire (UW-QOL). The scores obtained from these instruments indicated improvement (n = 11), no significant change (n = 1), worsening (n = 5), and borderline outcomes (n = 1).

To evaluate changes in mouth opening according to the timing of trismus therapy, descriptive statistical analyses were performed (Table 5), followed by the Shapiro–Wilk normality test. Descriptive statistics showed that the mean change in mouth opening during radiotherapy (M = 7.61 ± SD 8.04) and after radiotherapy–based trismus therapy (M = 7.71 ± SD 3.38) was greater than that observed in pre-radiotherapy trismus therapy (M = −3.28 ± SD 0.64). The Shapiro–Wilk test indicated that changes in mouth opening across the three treatment time points (before, during, and after radiotherapy) were normally distributed ($p > 0.05$).

Table 1 Characteristics of the Included Studies (N= 18)

Authors	Type of Study	Number of Samples/Study Population	Age	Male (M)/ Female (F)	Type of Cancer/Region	Cancer Treatment
Aboelez et al[16]	RCTs	36	50-65	20/16	HNC	RT
Lee et al[17]	Randomised, open-label, controlled, three-centre feasibility study	71	>18	49/22	Oral & oropharyngeal cancer	RT (IMRT) ± ChT-surgery therapy
Deepak et al[18]	Pilot randomized control trial-experimental	30	18-65	28/2	HNC	RT ± ChT- surgery therapy)
Petersson et al[19]	RCTs	89	42-83	68/21	HNC at tonsil, base of tongue, hypopharynx, and larynx.	RT ± ChT
Borges et al[20]	Single-arm Clinical Trial.	16	53 - 70	10/6	HNC	RT ± ChT
Pauli et al[21]	Prospective Study	100	55-61	62/38	HNC at the oropharynx, the tumor colli, the oral cavity, the nasopharynx	RT ± ChT
Karlsson et al[22]	Prospective Study	100	29-80	62/38	HNC (the oropharynx, tumor colli, the oral cavity, the nasopharynx)	RT± ChT / surgery therapy
Charters et al[12]	Prospective single-arm cohort feasibility study	9	44 - 75	6/3	HNC	RT using VMAT
Charters et al[13]	Prospective Study	110	22–90	41/69	SCC, Adenoid cystic carcinoma, Osteosarcoma, other at the Oral cavity, Oropharynx, Carotid	RT± ChT /surgery therapy
Yang et al[23]	Prospective RCTs	72	M (Mean): 57	45/27	HNC (Oral cancer, Buccal mucosa, Base of tongue, Floor of mouth, Soft palate, Gingiva)	RT post-surgery
Mohammed et al[24]	Prospective Study	60	40 - 60	30/30	HNC	RT post-surgery
Şahan et al[25]	Prospective study	50	M: 56	28/22	HNC	RT post-surgery.
Kamstra et al[26]	Prospective Study	18	M: 62	9/9	HNC	RT± ChT /surgery therapy
Montalvo et al[27]	Prospective Study	15	30-75	4/11	HNC	RT± surgery
Bragante et a[28]	Randomized, controlled, double-blind, 3-arm, parallel-group, prevention clinical trial	90	54	76/14	HNC (neoplasms of the oral cavity, oropharynx, nasopharynx, salivary glands, and nasal fossae)	RT± ChT
Wang et al[29]	Quasi-experimental study	69	M: 50.2	66/3	Oral Cancer	RT± surgery
Diracoglu et al[30]	Prospective Study	95	M: 35	33/62	Tumor in the maxillary or nasopharyngeal region	Rt
Saghafi et al[31]	RCTs	58	>18	39/19	SCC of the head and neck (oropharynx, hypopharynx, larynx)	Rt using VMAT ± ChT

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Table 2 Overall Risk of Bias Assessment for Randomized Controlled Trials (RoB 2; n = 7)

Authors	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result.	Overall RoB
Aboelez et al[16]	Some Concerns	Some Concerns	Low risk	Low risk	Some Concerns	Some Concerns
Lee et al[17]	Some Concerns	Some Concerns	High risk	Some Concerns	Low risk	High risk
Deepak et al[18]	High risk	High risk	High risk	Some Concerns / High risk	Some Concerns	High risk
Petersson et al[19]	Some Concerns	Some Concerns	Some Concerns	Low risk	Some Concerns	Some Concerns
Yang et al[23]	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Bragante et a[28]	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Saghafi et al[31]	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns

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Table 3 Overall Risk of Bias Assessment for Non-Randomized Studies (ROBINS-I; n = 11)

Authors	Bias Due to Confounding	Bias in the Selection of Participants into the Study	Bias in the Classification of Interventions	Bias Due to Deviations from Intended Interventions	Bias Due to Missing Data	Bias in the Measurement of Outcomes	Bias in the Selection of the Reported Result	Overall
Borges et al[20]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Pauli et al[21]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Karlsson et al[22]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Charters et al[12]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Charters et al[13]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Mohammed et al[24]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Şahan et al[25]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Kamstra et al[26]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Montalvo et al[27]	Serious risk	Moderate risk	Low risk	Serious risk	Moderate risk	Serious risk	Moderate risk	Serious risk
Wang et al[29]	Serious risk	Serious risk	Low risk	Serious risk	Moderate risk	Serious risk	Some concern	Serious risk
Diracoglu et al[30]	Serious risk	Moderate risk	Low risk	Moderate risk	Moderate risk	Serious risk	Moderate risk	Serious risk

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Table 4 Characteristics of the Trismus Treatments

Author	Initial Time	Duration	Modalities	Progress MIO (mm)	Level of Adherence	OHR-QoL
Petersson et al[19]	1-2 weeks before RT	Before & during RT	Passive and active jaw exercises with a Jaw Trainer©	Intervention group: -4.0 Control Group: −7.0	Moderate	EORTC QLQ-H&N35 showed a significant worsening of several HNC-related symptoms in both groups.
Yang et al[23]	G1: Before RT G2: At the start of RT	To the end of RT	Combination of active and passive exercise (using TheraBite)	G1: −3.027 G2: −1.917 (control) p < 0.001	Attrition rate: 5.26%	Both groups showed significant worsening in VAS and UW-QOL scores (p < 0.001).
Saghafi et al[31]	Before RT	During RT, and up to 1 month post-treatment	Combination of active and passive exercise (Jaw Trainer™)	6 months follow-up: Intervention group: -2.8 Control group: - 8.2	Moderate	After 6 months: NRS: control group reported a greater increase in pain intensity compared with the intervention group (p = 0.015). CPI: results were close but not significant between the groups (p=0.061)
Borges et al[20]	During RT	During RT	PBMT (Photobiomodulation therapy)	7.19 ± 4.84 (p < 0.001).	High	VAS scores improved significantly (p < 0.05)
Bragante et al[28]	During RT	During RT	G1: Exercise + theraBite G2: Exercise Only CG: No exercise or therabite	G1: 0.1 (95% CI: 0.1, 2.5 to 2.7) G2: −0.7 (95% CI: -0.7, 3.6 to 2.2) CG: −3.7 (95% CI: -3.7, 6.1 to 1.4)	Moderate	VAS scores significantly worsened (p <0.001) G1: 95% CI: 2.6(1.3 to 3.9) G2: 95% CI: 1.5(0.1 to 2.8) CG: 95% CI: 0.4(0.6 to 1.6)

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Deepak et al[18]	During RT	3 weeks	1. MFR (Myofascial release) 2. MaRhyThe© (Matrix rhythm therapy)	MaRhyThe©: 8.31 (p=0.0001) MFR: 4.74 (p=0.0001)	High	MaRhyThe©: 1.VAS: 2.53 ± 0.92 (p=0.0086) 2. GTQ: 27.87±10.33 (p=0.001) 3./TDI: 32.60±11.31 (p=0.001) 4.FIGS: −2.00±1.25 (p=0.001) MFC: 1. VAS: 2.93 ± 1.44 (p= 0.0128) 2. GTQ: 31.53 ± 9.16 (p=0.001) 3. TDI: 37.33 ± 11.02 (p=0.001) 4. FIGS: −2.87 ±1.19 (p=0.001)
Charters et al[12]	During RT	10 weeks	RestoraBite™	7.8 (p=0.03)	High	GTQ significantly improved at 10 weeks and 6 months (p=0.04; 95% CI: −9.2 to 11.2)
Charters et al[13]	During RT	10 weeks	RestoraBite™	10.4 (95% CI 9.2 to 11.6, p < 0.001).	High	GTQ: Improved significantly (p <0.005)
Mohammed et al[24]	During RT	3 months	G1: Laser treatment G2: TheraBite exercises G3: Combined of Laser treatment and TheraBite exercises	G1: 13.65 (p=0.0001) G2: 13.05 (p=0.0001) G3: 26.95 (p=0.0001) Highly significant increase in all studies	100% adherence	MFIQ and VAS increase significantly in all groups (p= 0.0001). Best improved in G3 MFIQ: Highly significant Decrease G1: 24.9000 (p=0.0001) G2: 25.4000 (p=0.0001) G3: 28.1500 (p=0.0001) VAS: Highly significant Decrease G1: 6.05000 (p=0.0001) G2: 5.6000 (p=0.0001) G3: 6.46000 (p=0.0001)
Diracoglu et al[30]	Undergone RT	15 session	Physical therapy (TENS, Hot Pack& manual stretching)	Cancer group (G1): 2.3 Non cancer group (G2):9.7	High	VAS: Significant improvements in G1&G2 (p=0.00) Post-treatment patient global self-assessment: Significantly higher in G2 (p= 0.005).
Lee at al[17]	During & after RT	6 months	1.Therabite® jaw motion rehabilitation system (Atos Medical) 2. Wooden spatulas	−2.43 (95% CI −8.15 to 3.29).	The compliance was poor, with a high attrition rate	Worsening in EORTC QLQ-C 30 and EORTC QLQ H&N 35

(*Continued*)

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Table 4 (Continued).

Author	Initial Time	Duration	Modalities	Progress MIO (mm)	Level of Adherence	OHR-QoL
Sahan et al[25]	Post RT	3 weeks	Cancer patients: 1. TheraBite (G1) 2. Wooden tongue depressor (G2) Non-cancer patients (control): Therabite (G3)	G1: 9.5 G2: 6.5 G3: 9 Significant change ($p < 0.05$) in all groups Insignificant differences ($p > 0.05$) among groups.	High	EORTC QLQ C30 & EORTC QLQ H&N35: improved significantly in all groups ($p < 0.005$)
Aboelez et al[16]	Post RT	6 weeks	Group A: TTSA Group B: LLLT Group C: TTSA + LLLT	Group A: 8,58 (*p* value <0.0001) Group B: 9.59 (*p* value < 0.0001) Group C: 15 (*p* value < 0.0001)	High	1. VAS: Significantly improved compared to the baseline and different between all groups. Group A: 7.50 ± 0.67 to 1.58 ± 0.51 (*p* value < 0.0001) Group B: 7.50 ± 0.52 to 0.58 ± 0.51 (p value < 0.0001) Group C: 7.25 ± 0.62 to 0.00 ± 0.00 (p value < 0.0001) 2. GTQ: improved significantly within each group. The lowest GTQ symptom scores were observed in Group C, followed by Group B and Group A, with a statistically significant difference ($P < 0.0001$).
Pauli et al[21]	3-6 months post RT	10 weeks	TheraBite jaw device or Engstro¨m device	8.3 ($p < 0.001$).	High	GTQ & Global Quality of life (EORTC QLQ C30): improved significantly EORTC QLQ H&N35: not significant
Karlsson et al[22]	3-6 months post RT	10 weeks	TheraBite® jaw device or Engström jaw device	6.4 ($p < 0.001$).	High	GTQ, EORTC QLQ-C30, and EORTC QLQ-H&N35 improved significant ($p < 0.001$)
Kamstra et al[26]	G1: ≤36 months post RT G2: >36 months post RT	16 weeks	DTS	G1: 7.3 ($p = 0.001$) G2: 6.5 ($p = 0.001$)	Moderate	EORTCQLQ H&N35: Borderline significance ($p = 0.086$)
Montalvo et al[27]	6.2 years post Oncologic treatment	10 weeks	Therabite	3.5 (p=0.0002)	High	EORTC QLQ C30, EORTC QLQ-H&N35 & GTQ: significantly improved ($p = 0.007$)
Wang et al[29]	Post RT	6 months	Oral exercise	Intervention: 2 Control: 0.5	High	MFIQ: No significant changes

Table 5 Descriptive Statistics of Maximum Mouth Opening (MMO) (Mm)

Parameter	Before RT	During RT	Post RT
n	3	12	11
Mean	3.28	7.61	7.71
Median	3.03	7.49	8.00
SD	0.64	8.04	3.38

Note: MMO during and post RT is much higher than before RT.

However, because the sample sizes across groups were unbalanced and the data were derived from different studies rather than longitudinal measurements within the same subjects, a nonparametric independent Kruskal–Wallis test was used to compare changes in mouth opening across time points. The results demonstrated a significant difference among the groups before radiotherapy, during radiotherapy, and after radiotherapy ($H = 3.00$, $p = 0.020$).

To identify the therapy modalities associated with the greatest improvements in mouth opening across studies, a descriptive ranking analysis was performed (Table 6). Based on the available data, the combination of laser therapy and TheraBite® exercises, initiated concurrently with radiotherapy for a duration of three months, was associated with the

Table 6 Categories of Treatment Modalities Based on Clinical Effectiveness

Effectiveness Category	Mean Progress in MIO (mm)	Treatment Modalities	Adherence	OH-QoL
Very High	≥ 15	Combined of Laser treatment and TheraBite[24] TTSA + LLLT[16]	High	Significant improved
High	10-15	Laser treatment[24] TheraBite[24]	High	Significant improved
Moderate	5-10	TheraBite[25] LLLT[16] TTSA[16] TheraBite or Engstrom[21,22] PBMT[20] RestoraBiteTM[12,13] MaRhyThe©[18] DTS[26] Wooden tongue depressor[25]	High to moderate	The reported effects ranged from significant improvements to borderline findings
Low	0-5	MFR[18] TheraBite[27] Physical therapy[30] Oral exercise[29] Exercise + Therabite[28]	High to Moderate	Some studies reported improvements, whereas others found no significant effect.
Ineffective	<0	Exercise Only[28] Therabite or wooden spatula[17] Combination of active and passive exercise using TheraBite[23,31] Passive and active jaw exercises with a Jaw Trainer©[19] No-device exercise[28]	Moderate to low	Worsening

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largest improvement in mouth opening (26.95 mm) and improvements in oral health–related quality of life (OHRQoL). The next highest-ranked modality was the combination of threaded tapered screw appliance therapy (TTSA) and low-level laser therapy (LLLT), administered after radiotherapy for six weeks, which resulted in a 15 mm improvement in mouth opening and improvements in OHRQoL.

Discussion

Radiation-induced fibrosis results from the activation and dysregulation of fibroblastic activity, leading to tissue atrophy in the irradiated region. This is referred to as the fibroatrophic theory of radiation damage. This phenomenon involves transforming growth factor beta1 (TGF-β1), a key cytokine that regulates fibroblast proliferation and differentiation. Differentiated fibroblasts synthesize collagen and proteoglycans in the extracellular matrix. Radiation induces over-expression of TGF-β1, likely caused by oxidative stress and an inflammatory response. Elevated serum levels of TGF-β1 correlate with an increased risk of fibrosis in cancer patients. Progressive fibrosis leads to excessive collagen deposition and extracellular matrix accumulation, resulting in tissue stiffness and scar formation in the masticatory muscles and tissues surrounding the temporomandibular joint, thereby contributing to trismus.[32]

Radiation-induced trismus (RIT) significantly impairs daily activities and key oral functions. These include speech, eating, drinking, and oral hygiene. RIT is also linked to psychological distress, malnutrition, and dehydration, which reduce oral health-related quality of life (OHRQoL).[9] Currently, there is no consensus on the best management for trismus related to head and neck cancer (HNC) patients.[33] Studies in this paper used different treatment types, starting times, and durations for trismus. While all aimed to improve mouth-opening and oral health-related quality of life, they produced varied results.

Purkayastha et al,[34] stated that before RIT appears, acute side effects as edema, inflammation, and muscular spasms may occur during or right after RT. Long-term effects, including fibrosis and scarring, may potentially arise, depending on the dose and fractionation schedule used. However, Somay et al,[35] stated that there is no consensus on the appropriate timing for initiating trismus therapy before RT or CRT.

This study found that the increase in mouth opening was greater in the group that underwent trismus therapy during and after radiotherapy. Variation in mouth opening improvement was influenced by treatment modalities and patient compliance. Factors influencing patient compliance include motivation, treatment protocol, acute reaction to radiation, overlapping exercise schedules with radiation therapy, cancer stage affecting systemic health, and the combined effects of chemotherapy and radiation, which can exacerbate trismus.

Reduced mouth opening adversely affects patients' quality of life, as reflected by poor scores on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck Module (EORTC QLQ-H&N35). In this study, preventive exercises did not demonstrate significant effects on mouth opening between the intervention and control groups. These findings are consistent with those of Hogdal N et al,[36] and Saghafi et al,[31] who also reported no significant benefits of early exercise interventions for preventing trismus following radiotherapy for head and neck cancer (HNC) patients when adherence was moderate, and combination therapy was used. Preventive mouth-opening exercises performed before radiotherapy may not demonstrate a significant therapeutic effect on mouth opening because radiation-induced trismus primarily results from progressive fibrosis that develops during and after radiation exposure. Although pre-radiation exercises may improve baseline muscle flexibility, they do not prevent the subsequent fibrotic remodeling of the masticatory muscles, connective tissues, and periarticular structures of the temporomandibular joint induced by radiation. Consequently, the structural and biochemical changes caused by radiotherapy may override any initial functional gains achieved through pre-treatment exercises, resulting in no significant improvement in post-radiation mouth opening.

A recent study showed a significant increase in mouth opening at the initial time during and after radiation therapy, and using a combination of modalities for trismus treatment. This was observed in patients receiving laser therapy combined with TheraBite exercises, and in those treated with TTSA plus LLLT. Their training lasted 6–24 weeks, with a significant increase in the average maximum interincisal opening (MIO) of 26.95 mm and 15 mm. Treatment for trismus began during and after radiation therapy. All participants completed the practice session and showed improved

quality of life, evidenced by higher VAS, MFIQ, and GTQ scores.[16] Factors such as patient motivation and treatment adherence may have contributed to their results, and the patients were not in a state of acute pain.

Combination therapy using laser therapy and a jaw mobilization device was associated with greater improvements than either modality alone. Laser therapy offers several benefits, including biostimulation and analgesia without increasing temperature. It also promotes vasodilation, reduces edema, increases cellular metabolism, changes cell membrane structure to enhance pain threshold, and shortens wound-healing time. In this study, a diode laser with a peak output of 500 mW and a wavelength of 810 nm was used. The application lasted 2 minutes, twice weekly, targeting the pterygoid, masseter, and temporal muscles.[37]

Low-level laser therapy (LLLT) is generally well tolerated and acceptable to patients. It is cost-effective, noninvasive, painless, safe, and well-tolerated. The procedure is rapid and needs minimal dental chair time. Laser supports tissue healing by reducing pain, swelling, and inflammation without side effects. Its effect on soft-tissue trauma pain stems from its indirect reduction of edema, bleeding, neutrophil activity, pro-inflammatory cytokines, and enzyme activity. LLLT minimizes swelling and pain and supports tissue repair by speeding up lymphatic vessel regeneration and limiting vascular permeability.[37]

The patient's strength and motivation influence the applied force.[38] TTSA targets the depressor muscle group. The smaller end is inserted between the premolars. The handle is rotated clockwise two or three times daily. This approach increases maximum mouth opening and restores normal function, likely because both therapies promote vasodilation. The combination of TTSA and LLLT resulted in the most favorable health-related quality-of-life outcomes ($P < 0.0001$).[16] These results match those of Zecha et al,[39] and Geethu et al,[40] who also found LLLT and TTSA highly beneficial after HNC chemotherapy and radiation therapy.

The TheraBite device was employed to facilitate jaw mobilization. It features a mandibular mouthpiece that lowers appropriately when the handle is pressed. Force is distributed to protect the teeth through large mouthpieces equipped with foam cushions. A precision-adjusting screw enables slow opening and accurate positioning. During the stretching procedure, a C-shaped hand aid assists the patient or caregiver in maintaining finger extension. The protocol consisted of 10 consecutive sets of stretches, each lasting 30 seconds, with brief rest intervals between sets. The TheraBite Jaw Motion Rehabilitation System is based on the principle of passive movement and is specifically designed for patients with mandibular hypomobility and restricted mouth opening. The primary objective is to enhance jaw strength and increase the range of motion by restoring mobility and flexibility to the jaw muscles, joints, and connective tissues through repeated passive motion and stretching. Combining low-level laser therapy (LLLT) with TheraBite exercises offers a promising approach for improving mandibular mobility and reducing pain in head and neck cancer patients experiencing trismus.[24]

This study found that the optimal increase in mouth opening was observed in the group with high therapy compliance.[16,24] These findings are consistent with those of Charters et al,[41] who reported that adherence to the exercise program was associated with greater improvement in maximum interincisal opening.

The quality-of-life assessments across these studies found that the group with optimal mouth-opening improvement also had optimal quality-of-life improvement. These results are in line with Montalvo et al,[27] who reported that increased mouth opening is associated with improved quality of life. The greater the improvement in mouth opening, the greater the improvement in quality of life.

In general, the heterogeneity identified across studies includes patients' compliance, oncologic treatment, trismus treatment, and unequal initial treatment time and treatment duration. Motivation, health conditions, cancer staging, treatment protocols, and exercise schedules influence patients' compliance. Attrition rates during the study will affect the significance of the study results.[42,43]

Oncology treatment affects the risk of trismus. Patients treated with combined radiation, chemotherapy, and/or surgery face more limitations in mouth opening than those treated with radiation alone.[44] Furthermore, radiotherapy delivered using intensity-modulated radiotherapy (IMRT) is associated with a lower incidence of trismus compared with conventional techniques.[5,14,45] Differences in modalities, techniques, exercise duration, and intensity across studies lead to substantial heterogeneity in results. Unequal initial treatment time and treatment duration may also affect conclusions regarding the effectiveness or safety of the intervention.

A major limitation of the present study was the high heterogeneity among the included studies. Future research should aim to improve study homogeneity by applying more standardized study designs, intervention protocols, and outcome measures.

Conclusion

The effectiveness of treatment for radiation-induced trismus is influenced by therapeutic modality, timing of therapy initiation, and patient adherence, all of which contribute to improvements in mouth opening and oral health–related quality of life. Combination therapies, particularly laser therapy combined with jaw movement devices initiated during or after radiotherapy and supported by high patient adherence, optimize mouth opening and enhance oral health–related quality of life.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

There are no competing interests to declare.

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