Review Article

Effectiveness of hyperbaric oxygen therapy in irradiated maxillofacial dental implant patients: A systematic review with meta-analysis

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Abstract

The significantly higher implant failure rates in maxillofacial patients, undergoing radiotherapy, might be caused by the long-term effects of reduced vascularization compromising the implantation site. An extensive preclinical animal literature and a multitude of clinical reports suggest the use of hyperbaric oxygen (HBO) therapy as it can improve the tissue vascularity. Hence, it may increase the implant survival rate by enhancing osseointegration process in such patients. The objective of this systematic review was to investigate the effectiveness of HBO therapy on dental implant survival rate in irradiated maxillofacial patients who require prosthodontic rehabilitation. An electronic search without time restrictions was undertaken in April 2016 using databases: PubMed, Google Scholar, and the Cochrane Oral Health Group Trials Register. We also tried to contact the manufacturers and researchers in the field for necessary details. Clinical human studies, on irradiated maxillofacial dental implant patients, including randomized controlled trials (RCTs), prospective controlled trials, retrospective studies, and preliminary reports were included in the study. Data collection was carried out by two of the authors' independently. The titles and abstracts of all reports were screened for the study design and type of reported intervention; all the duplicates were removed. The data search yielded 62 titles, out of which 14 articles were selected for the study by the article filtration criteria: Title/abstract/full text. Data which were extracted by two authors with any disagreement were resolved by the third author, and a meta-analysis was done using binary random-effect model. The results show decreased implant failure rate in HBO group (9.21%) compared to non-HBO group (22.44%). The potential limitations of this study are amount of radiation doses used, period lasting from radiotherapy to the placement of the implants, and follow-up period which varies for every subject of the included study, which can affect the treatment outcome. Although there are many sensitive articles published about HBO, including a number of review papers, RCTs are still lacking. According to the statistical analysis, it can be concluded that preventive HBO therapy can reduce the risk of implant failures in irradiated patients by 1.21 (relative risk) with 95% confidence interval ($P < 0.001$). Hence, HBO can be the effective treatment protocol for the implant treatment in irradiated maxillofacial patients.

Key Words: Dental implants, dental implant failures, hyperbaric oxygen, implants, irradiation, osseointegrated, radiotherapy, randomized controlled trials

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INTRODUCTION

Description of the condition

Thorough knowledge and wide field of understanding of the etiologic and risk factors of the implant failure are necessary to decrease the implant failure rates. From the last few years, implants are more commonly used in maxillofacial oral cancer patients, so whether these irradiated patient in the head and neck region are more at risk of losing dental implants or not is still unclear. Reduced tissue healing capacity leads to osteoradionecrosis, necrotic bone exposure, and pathological fracture in response to tissue trauma; thus, with reduced healing ability and osteoradionecrosis in response to injury, the implant survival rate may be reduced for the maxillofacial oral cancer patients who have undergone radiotherapy treatment.[1-6]

Description of the intervention

Hyperbaric oxygen (HBO) therapy and its effectiveness is still a controversial topic.[7] There are numerous studies reported for the usefulness of HBO for the treatment of osteoradionecrosis of different bone tissues. In addition to its usefulness in treating osteoradionecrosis, it may also prevent this condition. A randomized/prospective clinical trial using HBO and penicillin was carried out by Marx *et al*.[8] This trial demonstrated that HBO reduced the development of osteoradionecrosis after tooth removal and this reduction was statistically significant.[9]

HBO therapy can be performed in multiplace or monoplace chambers. Patient is kept in a pure 100% oxygen chamber under pressure of 1.5–3 atmosphere absolute.[10]

How the intervention might work?

HBO therapy increases the oxygen pressure, collagen production, and fibroblastic activity and creates a matrix for neovascularizations.[11] According to Johnsson, it also counteracts the negative effect of irradiation, stimulates the osseointegration, and improves the implant survival rate.[12]

Need to do this systematic review

This systematic review helps maxillofacial surgeon and prosthodontist to understand the evidence, to integrate the valid information, and to provide rational decision-making on the use of the HBO therapy for their patients. It will also help them in improving the dental implant survival rate and quality of life of such patients by providing long-term successful rehabilitation.

OBJECTIVE

The objective of the present review was to compare the implant failure rates for patients being irradiated or previously irradiated in the head and neck region and receiving HBO therapy versus irradiated patients and not receiving such therapy having follow up period of 1-2 years to 26 years.

MATERIALS AND METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs), prospective clinical trials, and retrospective studies.

Types of participants

Maxillofacial patients who have had radiotherapy and treated with dental implants for oral rehabilitation.

Types of intervention

HBO therapy compared with no HBO therapy.

Type of comparison

HBO group versus non-HBO group.

Types of outcome measures

Implant failure rates.

SEARCH STRATEGIES

An electronic search without time restrictions was undertaken in April 2016 for clinical studies comparing the implant failure rates (O), in irradiated maxillofacial patients (P), undergoing dental implant treatment either with additional HBO therapy (I) or without HBO therapy (C), using following databases: PubMed, Google Scholar, and the Cochrane Oral Health Group Trials Register. The search strategy used a combination of controlled vocabulary and free text terms.

Following keywords were used in the search box of all three databases either alone or in combination with two or more keywords (i.e., #1, #2, #3, or #1, #2, #3, #5) in an attempt not to miss any related trial, eligible to get included in the study.

1. Dental implants or oral implants or endosseous implants or osseointegrated implants
2. Radiation therapy or radiotherapy or irradiation or irradiated tissues
3. Hyperbaric oxygen or hyperbaric oxygen therapy or HBO therapy or hyperbaric oxygenation
4. Dental implant failures and/or randomized controlled trials
5. HBO therapy and experimental trials
6. Irradiation, dental implants, HBO therapy, randomized controlled trials, experimental trials (Word variations had been used, i.e., radiotherapy for irradiation).

A manual search of dental implant-related journals, reference list of the identified studies, and relevant reviews on the subject was also scanned for possible additional studies. Moreover, online databases providing information about clinical trials in progress were also checked (clinicaltrials.gov; www.centerwatch.com/clinicaltrials; www.clinicalconnection.com; www.cochranelibrary.com).

Data collection and analysis

Selection of studies

The review process consisted of two phases. In the first phase, titles and abstracts of the search were initially screened by two authors for relevance and the full text of relevant abstract was obtained and accessed. Any disagreement was solved by discussion and with the third author's suggestion. The hand search of selected journals as well as search of reference of the selected studies was also done. The articles were obtained after first step of the review process using the following inclusion and exclusion criteria and were screened in the second phase, and relevant and suitable articles were isolated for further processing and data extraction. Duplicates and articles with insufficient necessary data were excluded.

Inclusion criteria's

Clinical human studies, on irradiated maxillofacial dental implant patients, including:

- RCTs
- Prospective study
- Retrospective study
- Preliminary reports.

Exclusion criteria's

- Case reports
- Technical reports
- Animal studies
- *In vitro* studies
- Review articles
- <5 patients treated.

In general, RCTs constitute the highest level of evidence. Although developing recommendations based on the highest level of evidence is desirable, adequate number of RCTs is not always available. Hence, we included some prospective and retrospective clinical studies with a preliminary report (Ali *et al*., 1997). The purpose of the report was to provide some preliminary data collected from a long-term, prospective investigation on the effects of HBO therapy on implant integration in the irradiated jaw. Data on the effects of various doses of irradiation to the perioral region were collected by regular clinical, radiologic, and histologic examinations.

Data extraction and management

Three review authors independently extracted data from the studies using standardized selection criteria, developed for this review. We tried to contact the authors of primary studies to request further information when data were missing or incomplete. Review authors resolved all differences by discussion. Data were excluded until further clarification became available if agreement could not be reached.

For each trial, the following data were recorded.

- Year of publication and country of origin
- Details of the participants including demographic characteristics and criteria for inclusion
- Details of the type of intervention
- Details of the outcomes reported including method of assessment and time intervals.

Assessment of "risk of bias" in the included study

The assessment of the risk bias was conducted using the recommended approach by Cochrane reviews [Table 1 and Graph 1] and was completed independently and in duplicate by two review authors as a part of the data extraction process.

Table 1: Assessment of "risk of bias" in the trials included in the meta-analysis

Number	Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
1	Franzén *et al*., 1995[13]	Unclear	High	High	High	Low	High
2	Barber *et al*., 1995[14]	Low	High	High	Low	Low	Unclear
3	Esser and Wagner, 1997[15]	High	High	High	Low	Unclear	Unclear
4	Ali *et al*., 1997[16]	High	High	High	Unclear	High	Unclear
5	Niimi *et al*., 1997[17]	Unclear	High	High	Low	Low	Unclear
6	Jisander *et al*., 1997[18]	High	High	High	Low	Low	Unclear
7	Niimi *et al*., 1998[19]	High	High	High	Low	Low	Unclear
8	Andersson *et al*., 1998[20]	High	High	High	Low	Low	High
9	Granström *et al*., 1999[21]	High	Unclear	High	High	Low	Low
10	Granström *et al*., 2003[22]	Low	High	High	High	Unclear	Unclear
11	Shaw *et al*., 2005[23]	High	High	Unclear	High	Low	High
12	Granström, 2006[24]	High	Unclear	High	Low	Low	Unclear
13	Schoen *et al*., 2007[25]	Low	High	High	Unclear	Low	Unclear
14	Barrowman *et al*., 2011[26]	Low	Unclear	High	Low	High	High

Results of the search for data collection

The database search yielded 62 titles, out of which 22 titles were discarded by title evaluation. Abstracts evaluation was done for the remaining 40 articles, and 6 articles were discarded on the basis of inclusion and exclusion criteria. Full-text data were obtained for the remaining 34 articles, among which 8 articles were discarded due to insufficient data and 12 articles did not match the criteria of the study. Hence, finally, 14 articles were selected for the study [Flowchart 1].

Description of the included studies

The data obtained after the search strategy were tabulated and statistically analyzed. The results were as follows:

- Table 2 shows the required details, regarding the 14 selected studies, included in this systematic review
- Table 3 shows the evidence level of the selected articles according to the study design
- Table 4 shows the characteristics of the each included study.

Description of the excluded studies (with the reason for being excluded)

Table 5 shows the characteristics of the excluded studies.

Risk of bias assessment

Table 1 shows the assessment of the risk of bias of the included studies.

Graph 1 shows the assessment of the risk of bias of the included studies.

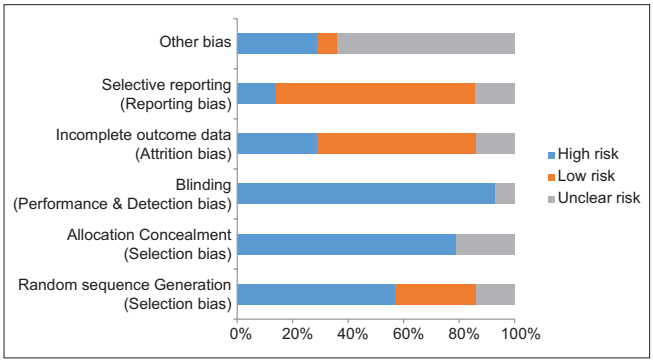
Effects of intervention and statistical analysis

Effect of intervention was studied for all 14 selected studies, and the implant survival rate for each group was statistically calculated [Tables 2 and 4].

Results of the study

Experimental studies

Table 6 shows estimated values for implant failures in HBO(+) group for an experimental study when the *P* value is set at $P < 0.05$, with the confidence interval (CI) of 95%.



Graph 1: The assessment of the risk of bias of the included studies

Table 7 shows estimated values for implant failures in non-HBO(+) group for an experimental study when the *P* value is set at $P < 0.05$, with the CI of 95%.

Forest Plot 1 shows implant failures in HBO and non-HBO group for experimental studies.

Prospective studies

Table 8 shows estimated values for implant failures in HBO(−) group for three prospective studies when the same *P* value is set at $P < 0.05$, with the same CI of 95%.

Table 9 shows estimated values for implant failures in non-HBO(−) group for 3 prospective studies when the *P* value is set at $P < 0.05$, with the same CI of 95%.

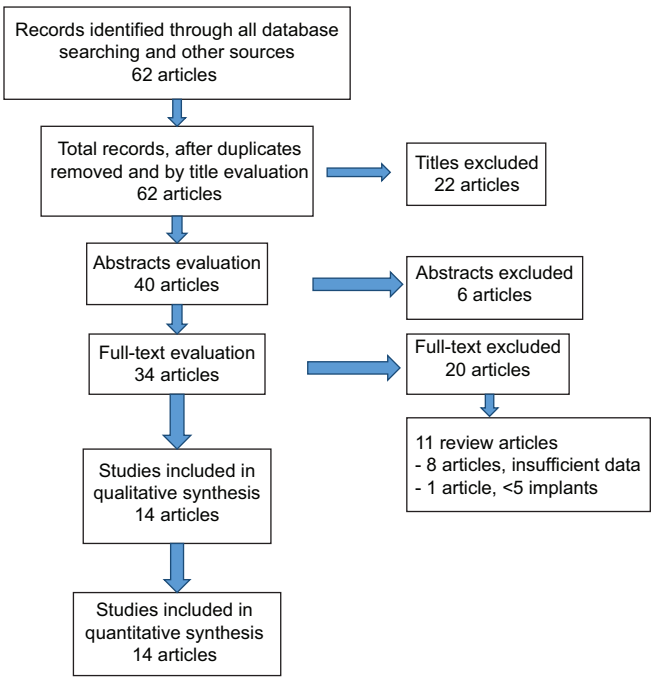
Forest Plot 2 shows implant failures in HBO and non-HBO group for prospective studies.

Retrospective studies

Table 10 shows estimated values for implant failures in HBO(−) group for four retrospective studies when the same *P* value is set at $P < 0.05$, with the same CI of 95%.

Table 11 shows estimated values for implant failures in non-HBO(−) group for seven retrospective studies when the same *P* value is set at $P < 0.05$, with the same CI of 95%.

Forest Plot 3 shows implant failures in HBO and non-HBO group for retrospective studies.



Flowchart 1: Results of the search through various sources

Table 2: Summarized data

Serial number	Author name and year	Number of irradiated patients	Number of implants placed	Location of the implants maxilla		Radiation dose (Gy)	Number of implants treated with HBO (+)	Number of HBO sessions			Number of implants treated without HBO(−)	Follow-up period (years)	Number of implants failed in HBO(+) group	Number of implants failed in non-HBO(−) group	Implant survival rate (%)	Implant survival rate (%)
				Maxilla	Mandible			Preoperative time (min)	Postoperative time (min)	Atmospheric pressure					HBO(+) group	Non-HBO(−) group
1	Franzén *et al.*, 1995[13]	5	20	0	20	25-64	0	-	-	-	20	3-6	-	1	-	95
2	Barber *et al.*, 1995[14]	5	20	0	20	50	20	20 (90)	10 (90)	2.4	0	1-2	0	-	100	-
3	Esser and Wagner, 1997[15]	64	249	28	221	35-60	0	-	-	-	249	10	-	38	-	84.73
4	Ali *et al.*, 1997[16]	10	42	10	32	25-57	0	-	-	-	42	-	-	6	-	85.71
5	Niimi *et al.*, 1997[17]	24	110	39	71	25-66	34	20 (90)	10 (90)	2.4	84	4-5	4	8	88.23	90.47
6	Jisander *et al.*, 1997[18]	17	103	38	65	50	42	-	-	-	61	2	2	3	95.23	95.08
7	Niimi *et al.*, 1998[19]	44	228	59	169	26-65	161	20 (90)	10 (90)	2.4	67	4-5	4	16	97.51	76.11
8	Andersson *et al.*, 1998[20]	15	90	12	78	44-68	0	-	-	-	90	8	-	2	-	97.8
9	Granström *et al.*, 1999[21]	32	246	-	-	25-145	99	20 (90)	10 (90)	2.5	147	1-15	8	79	91.91	46.26
10	Granström, 2003[22]	45	206	109	97	48-120	133	-	-	-	73	2-22	5	17	96.24	76.71
11	Shaw *et al.*, 2005[23]	34	172	-	-	50	77	20 (90)	10 (90)	2.4	95	14	15	17	80.51	82.1
12	Granström, 2006[24]	107	631	-	-	-	340	-	-	-	291		29	117	91.47	59.8
13	Schoen *et al.*, 2007[25]	26	103	-	-	46-116	54	20 (80)	10 (80)	2.5	49	1-2	8	3	85.18	93.87
14	Barrowman *et al.*, 2011[26]	12	30	8	22	??	30	20 (60)	10 (60)	2-2.5	0	15	5	-	89.5	-

HBO: Hyperbaric oxygen

Table 12 represents "Pearson's Chi-square test" which shows the total number of implants placed, failed, and survived in both the groups, with $P < 0.001$, which shows that significant difference exists between both the group regarding the number of implants failed and survived.

Table 3: Evidence level of selected articles

Number	Author's name	Study design	Evidence level
1	Niimi *et al*., 1998	Survey	3
2	Niimi Atsushi, 1997	Survey	3
3	Andersson, 1998	Retrospective, *in vivo*	2
4	Barrowman, 2011	Retrospective, *in vivo*	2
5	Franzen, 1995	Prospective, *in vivo*	2
6	Schoen, 2007	RCT, *in vivo*	2
7	Granstrom, 1999	Case controlled study, *in vivo*	2
8	Granstrom, 2006	Retrospective, *in vivo*	2
9	Granstrom, 2003	Retrospective, *in vivo*	2
10	Shaw, 2005	Retrospective, *in vivo*	2
11	Jisander, 1997	Prospective, *in vivo*	2
12	Elmar Esser, 1997	Retrospective, *in vivo*	2
13	Arshad Ali, 1997	Preliminary reports	2
14	Barber, 1995	Prospective, *in vivo*	2

RCT: Randomized controlled trial

Graph 2 shows the significant difference regarding the implant failure rate in both the groups:

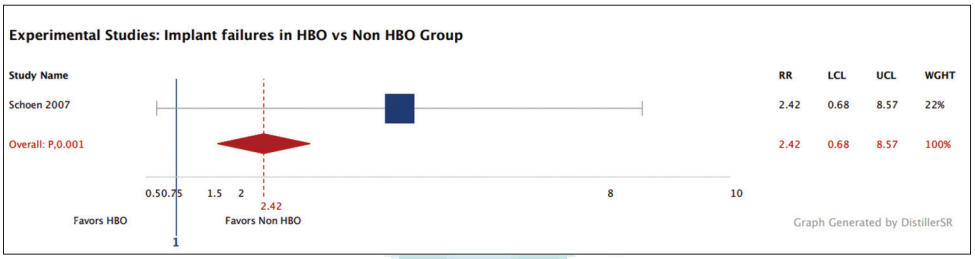
- Implant failure rate (%) in HBO(+) group: 9.21%
- Implant failure rate (%) in non-HBO(−) group: 22.44%

SUMMARY

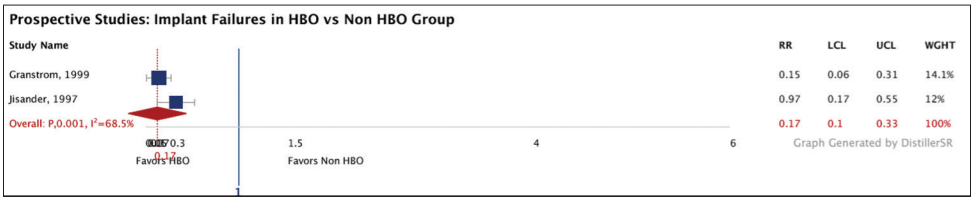
The present systematic review was undertaken to compare the implant failure rates for patients being irradiated in the head and neck region and receiving HBO therapy versus non-HBO therapy. There are many scientific papers[27] written about this subject including a number of review articles, but only one RCT (Schoen *et al*. 2007) including a limited number of participants was found for this review.

CONCLUSION

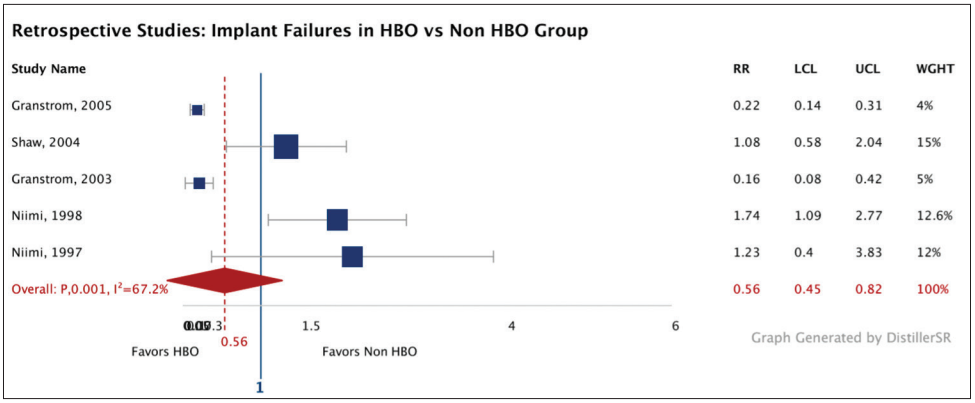
According to above statistical analysis, results show that preventive HBO therapy can reduce the risk of implant failures in irradiated patients, may be due to improved vascularity which leads to reduced risk of radiation-induced



Forest Plot 1: Experimental studies: Implant failures in hyperbaric oxygen versus nonhyperbaric oxygen group



Forest Plot 2: Prospective studies: Implant failures in hyperbaric oxygen versus nonhyperbaric oxygen group



Forest Plot 3: Retrospective studies: Implant failures in hyperbaric oxygen versus nonhyperbaric oxygen group

Table 4: Characteristics of included studies

Trial	Franzén *et al.,* 1995[13]
Methods	An observational, retrospective study, regarding oral implant rehabilitation of irradiated maxillofacial patients
Participants	5 maxillofacial patients treated by surgery and radiotherapy, undergoing implant treatment
Intervention	20 Branemark implants placed in the irradiated tissues, without HBO therapy
Outcome measures	Age, sex, smoking habit of patients Type of tumor and its recurrence Type of surgical modalities used for implant placement Radiation dosage, estimated dose Implant success rate
Trial	Barber *et al.,* 1995[14]
Methods	A pilot study on evaluation of implant osseointegration in irradiated mandible
Participants	5 head and neck cancer patient, treated with mandibular resection and radiotherapy
Intervention	20 implants placed in irradiated mandibles, with vascularized fibula flap reconstruction and adjunctive HBO therapy
Outcome measures	Evaluation of implant osseointegration and implant survival rate
Trial	Esser and Wagner, 1997[15]
Methods	A retrospective study, regarding dental implant treatment in irradiated maxillofacial patients
Participants	64 maxillofacial patients, undergoing implant therapy, between 1985 and 1995.
Intervention	249 implants (maxilla - 28, mandible - 221) placed in irradiated jaws without using HBO therapy
Outcome measures	Implant success rate after cancer surgery and radiotherapy Survival analysis of IMZ and Branemark implants Event of recurrence Implants without initial osseointegration Implants with secondary loss of osseointegration Incidence of osteoradionecrosis
Trial	Ali *et al.,* 1997[16]
Methods	A preliminary report, following 64 months of prospective investigation, regarding implant rehabilitation of irradiated jaws
Participants	10 irradiated maxillofacial patients (7 males, 3 females), undergoing implant treatment
Intervention	42 Branemark titanium implants (maxilla - 10, mandible - 32) placed in irradiated jaws without HBO therapy and provided implant supported overdenture or fixed prosthesis
Outcome measures	Implant survival rate for maxilla and mandible, factors accounting for implant failure
Trial	Niimi *et al.,* 1997[17]
Methods	A multicenter study of osseointegrated implants in irradiated jaws in nine Japanese centers
Participants	24 maxillofacial patients, treated with bone anchored prosthesis using Branemark system implants (118), following malignant tumor surgery and radiotherapy
Intervention	34 implants treated with HBO therapy Control group: 84 implants (non-HBO)
Outcome measures	Implants buried Implants removed Implant survival rate for HBO and non-HBO group Implant survival rate, regarding radiation dose and location of the implants, implant failure related to time from placement to abutment connection Implant failure, regarding type of prosthesis
Trial	Jisander *et al.,* 1997[18]
Methods	A prospective study on dental implant survival in the irradiated jaws
Participants	17 oral cancer patients (15 males, 2 females) with a mean age of 67 years (range: 47-78), treated with external radiation of the jaws, 18-228 months (mean: 88) before implant placement
Intervention	The patients received 98 Nobel Biocare (Göteborg, Sweden) and 5 Astra (Astra Tech AB, Mölndal, Sweden) dental implants. Thirty-eight implants were placed in 8 maxillae and 65 implants in 14 mandibles. Eight patients (36 implants) were given more than 50 Gy of radiation (Subgroup A), and nine patients (67 implants) were given less than 50 Gy (Subgroup B) at future implant sites. Before implant placement, 6 patients (7 implants) in Subgroup A and 1 patient (2 implants) in Subgroup B received HBO treatment.
Outcome measures	Effects of radiation dose to the perioral region
Trial	Niimi *et al.,* 1998[19]
Methods	A survey on osseointegrated implants in irradiated jaws in nine Japanese centers and two US centers
Participants	44 maxillofacial patients, treated with bone anchored prosthesis using Branemark system implants (228), following malignant tumor surgery and radiotherapy
Intervention	161 implants treated with HBO therapy Control group: 67 implants (non-HBO)
Outcome measures	Implants buried Implants removed Implant survival rate for HBO and non-HBO group Implant survival rate, regarding radiation dose and location of the implants, implant failure related to time from placement to abutment connection Implant failure, regarding type of prosthesis

Contd...

Table 4: Contd...

Trial	Andersson *et al.,* 1998[20]
Methods	A retrospective study, regarding oral implant rehabilitation in irradiated patients without adjunctive HBO therapy with a follow-up period of 8 years
Participants	15 irradiated maxillofacial patients (11 males, 4 females), undergoing implant treatment
Intervention	90 Branemark implants placed in irradiated alveolar bone without adjunctive HBO therapy
Outcome measures	Total implant loss Success rate for implant stability and prosthesis stability
Trial	Granström *et al.,* 1999[21]
Methods	A case-controlled study, on osseointegration of implants in irradiated cancer patients
Participants	78 maxillofacial patients undergoing implant treatment
Intervention	Group A (irradiated): 147 implants Group B (nonirradiated): 89 implants Group C (Irradiation+HBO): 99 implants
Outcome measures	Implant survival rate in all the groups
Trial	Granström, 2003[22]
Methods	A retrospective study, regarding radiotherapy, osseointegration and HBO therapy
Participants	45 irradiated maxillofacial patients, treated with dental Implants, following malignant tumor surgery and radiotherapy
Intervention	133 implants out of 206, treated with HBO therapy Control group: 73 implants (non-HBO)
Outcome measures	Implant survival rate for HBO and non-HBO group Implant survival rate, regarding radiation dose and location of the implants Implant failures in native bone and grafted bone
Trial	Shaw *et al.,* 2005[23]
Methods	A retrospective cohort study (1987-2002) for irradiated patients, undergoing oral surgery and oropharyngeal resections in a regional head and neck oncology unit
Participants	81 irradiated patients (49 males, 32 females) with a median age of 58 years at the time of implant placement, treated for squamous cell carcinoma
Intervention	77 out of 172 implants treated with HBO therapy Control group: 95 implants (non-HBO)
Outcome measures	Data were collected retrospectively, for etiology of implant and prosthesis failure, Effect of radiotherapy on loss of implants Implants unloaded (Sleepers) Implants removed Prosthesis design versus outcome Implant survival rate for HBO and non-HBO group Implant failure rates comparing both the groups
Trial	Granström, 2006[24]
Methods	A retrospective study, on evaluation of implant osseointegration in irradiated cancer patients over a 25 year period
Participants	107 maxillofacial patients, treated with implants, following malignant tumor surgery and radiotherapy
Intervention	340 implants out of 631, treated with HBO therapy Control group: 291 implants (non-HBO)
Outcome measures	Implant survival rate for HBO and non-HBO group Implant failure rate regarding type of cancer, radiotherapy protocols, and implant-related elements were analyzed
Trial	Schoen, 2007[25]
Methods	An RCT, comparing the effects of HBO therapy on implant osseointegration
Participants	26 maxillofacial patients, treated with implants, following malignant tumor surgery and radiotherapy, between 1990 and 2000
Intervention	54 implants out of 103, treated with HBO therapy Control group: 49 implants (non-HBO), with antibiotic prophylaxis
Outcome measures	Prosthesis and implant failures marginal bone level changes on radiographs, postimplantation complications, plaque index, calculus, bleeding index, gingival index, probing pocket depths, width of the attached gingiva, periotest, functional assessment and quality of life, denture satisfaction, subjective chewing ability. Outcomes were assessed preoperatively when feasible, and 6 weeks and 1 year after placement of the prostheses
Trial	Barrowman *et al.,* 2011[26]
Methods	A retrospective study, regarding oral rehabilitation with dental implants after cancer treatment
Participants	31 maxillofacial patients, with a mean age of 50.7 years (range: 20-76 years), undergoing implant therapy as a part of oral rehabilitation between 1992 and 2007
Intervention	48 out of 115 Branemark dental implants placed in irradiated tissue and treated with additional HBO therapy
Outcome measures	Demographic data and factors including implant survival, type of prosthesis provided, radiotherapy and HBO therapy, were analyzed

RCT: Randomized controlled trial, HBO: Hyperbaric oxygen

Table 5: Characteristics of excluded studies

Trial	Reason for exclusion
Goiato MC, 2012	A case report only
Goiato MC, 2009	A literature review only
Harding SA, 2008	Study reported 66 irradiated maxillofacial patients referred for perioperative HBO therapy for debridement of necrotic tissue or prevention of osteoradionecrosis. Not all the patients underwent implant rehabilitation, did not fulfill the inclusion criteria
Adkinson C, 2003	Could not find the full-text data and so all the treatment outcomes
A. N. Kanatas, 2004	Did not match the inclusion criteria of the study
Bodard Anne, 2011	A review only
Zhang F, 1999	A review article only
Harrison JS, 2003	A literature review only
Coppola D, 1999	Could not find the data on treatment measures
August M, 1998	Study mainly compared the implant survival rate in radiated versus nonirradiated patients with only two patients received HBO therapy (very small group)
Granstrom, 1992	A review article only
Michael R, 1997	Only 4 patients involved in the study, matching the exclusion criteria (<5 patients studied), incomplete data
Granstrom, 2006	A review article only
Paul Coulthard, 2002	A review article
Coulthard P, 2002	A review article only
Chambrone, 2013	A review article only
Esposito M, 2013	A systematic review
Bruno Ramos, 2012	A systematic review
Nasser Nooh, 2013	A literature review
Larsen, 1997	A review article

HBO: Hyperbaric oxygen

Table 6: Estimated values for implant failures in hyperbaric oxygen(+) group for an experimental study when the *P* value is set at *P*<0.05, with the confidence interval of 95%

Studies	Estimate	95% CI		Event (implant failure)/treatment (number of implants)
Schoen, 2007	0.148	0.053	0.243	8/54
Over all	0.0148	0.053	0.243	84/54

CI: Confidence interval

Table 7: Estimated values for implant failures in nonhyperbaric oxygen(+) group for an experimental study when the *P* value is set at *P*<0.05, with the confidence interval of 95%

Studies	Estimate	95% CI		Event (implant failure)/treatment (number of implants)
Schoen, 2007	0.061	0.000	0.128	3/49
Over all	0.061	0.000	0.128	3/49

CI: Confidence interval

damages to tissue, and thus, HBO can be the effective treatment protocol, while planning for the implant treatment in irradiated maxillofacial patients. Still, some important factors, other than irradiation, that affect the implant survival rate in irradiated bone were type of implant, surgical procedures used, time interval between radiotherapy and implant placement, and radiation dose,

Table 8: Estimated values for implant failures in hyperbaric oxygen(−) group for prospective studies when the same *P* value is set at *P*<0.05, with the same confidence interval of 95%

Studies	Estimate	95% CI		Event (implant failure)/treatment (number of implants)
Franzen, 1995	NA	NA	NA	NA
Jisander, 1997	0.048	0.000	0.112	2/42
Granstrom, 1999	0.081	0.027	0.134	8/99
Arshad Ali, 1997	NA	NA	NA	NA
Barber, 1995	0.000	0.000	0.000	0/20
Over all	0.062	0.045	0.078	10/161

NA: Not available, CI: Confidence interval

Table 9: Estimated values for implant failures in nonhyperbaric oxygen(−) group for 3 prospective studies when the *P* value is set at *P*<0.05, with the same confidence interval of 95%

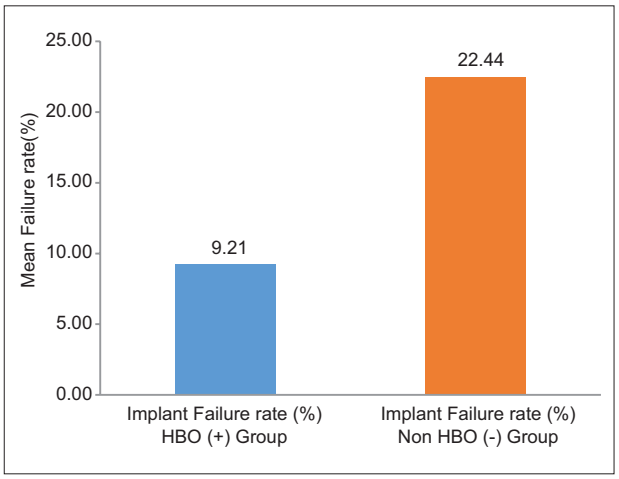
Studies	Estimate	95% CI		Event (implant failure)/treatment (number of implants)
Franzen, 1995	0.050	0.000	0.146	1/20
Jisander, 1997	0.049	0.000	0.103	3/61
Barber, 1995	NA	NA	NA	NA
Granstrom, 1999	0.537	0.457	0.618	79/147
Arshad Ali, 1997	0.143	0.037	0.249	6/42
Over all	0.329	0.265	0.353	89/270

CI: Confidence interval, NA: Not available

Table 10: Estimated values for implant failures in hyperbaric oxygen(−) group for 4 retrospective studies when the same *P* value is set at *P*<0.05, with the same confidence interval of 95%

Studies	Estimate	95% CI		Event (implant failure)/treatment (number of implants)
Niimi *et al*., 1998	0.025	0.001	0.049	4/161
Andersson, 1998	NA	NA	NA	-
Granstrom, 2006	0.085	0.056	0.115	29/340
Shaw, 2005	0.195	0.106	0.283	15/77
Elmar Esser, 1997	NA	NA	NA	-
niimi Atsushi, 1997	0.118	0.009	0.226	4/34
Barrowman, 2011	0.167	0.033	0.300	5/30
Granstrom, 2003	0.038	0.005	0.070	5/133
Over all	0.088	0.071	0.096	57/642

CI: Confidence interval, NA: Not available



Graph 2: The significant difference regarding the implant failure rate in both the groups

Table 11: Estimated values for implant failures in nonhyperbaric oxygen(−) group for 7 retrospective studies when the same *P* value is set at *P*<0.05, with the same confidence interval of 95%

Studies	Estimate	95% CI		Event (implant failure)/treatment (number of implants)
Niimi *et al*., 1998	0.239	0.137	0.341	16/67
Andersson, 1998	0.022	0.000	0.053	2/90
Granstrom, 2006	0.402	0.346	0.458	117/291
Shaw, 2005	0.179	0.102	0.256	17/95
Elmar Esser, 1997	0.153	0.108	0.197	38/249
niimi Atsushi, 1997	0.095	0.032	0.158	8/84
Barrowman, 2011	NA	NA	NA	NA
Granstrom, 2003	0.233	0.136	0.330	17/73
Over all	0.226	0.209	0.241	198/876

CI: Confidence interval, NA: Not available

Table 12: Represents "Pearson's Chi-square test" which shows the total number of implants placed, failed, and survived in both the groups, with *P*<0.001, which shows that significant difference exists between both the groups regarding the number of implants failed and survived

	HBO (+) group	Non-HBO (−) group	Total	*P*
Number of implants failed	80	307	387	<0.001
Number of implants survived	910	961	1871	
Total number of implants placed	990	1268	2258	

HBO: Hyperbaric oxygen

which were not included in the meta-analysis, due to insufficient data.

Hence, further research work has to be done to specify above-mentioned various reasons of failures and various factors affecting the success and failure rates of dental implants in irradiated maxillofacial patients.

There is a definite need for more RCTs to ascertain the effectiveness of HBO in irradiated maxillofacial dental implant patients. These trials ought to be of a high quality and reported as recommended by the consort statement (www.consort-statement.org/). Each clinical center may have limited numbers of patients and it is likely that multicentered trials will be needed. Only with that clinicians will receive the evidence they need for their study and make the best treatment decisions possible.

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Conflicts of interest

There are no conflicts of interest.

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