The Influence of Radiation Therapy on Dental Implantation in Head and Neck Cancer Patients

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Abstract: Radiotherapy is used to treat patients with head and neck cancers as a primary therapy or as an adjuvant to surgery or chemotherapy. Irradiation results in several complications that can be very overwhelming to the patient. Frequently there is loss of function due to tooth loss, compromised aesthetics, pain and discomfort from xerostomia and mucositis, it also significantly impacts the quality of life.

A major advance in dentistry is the successful rehabilitation and replacement of lost teeth by osseointegrated implants. However, the risk of osteoradionecrosis and failure of osseointegration are barriers to implant therapy for those irradiated patients.

The aim of this review article is to primarily find out whether the radiotherapy used in the treatment of head and neck cancer patients can affect the success and survival of dental implants according to different studies, and also, to highlight some other pertinent factors that may concurrently influence these implantation.

The primary outcome measure shows implants survival in irradiated patients. Most of the studies reported that dental implants can osseointegrate and remain functionally stable in irradiated patients following oral cancer surgery. Accordingly, rehabilitation using dental implants is a viable option for head and neck cancer patients receiving radiotherapy. However, all studies included indicated that survival was significantly higher in non-irradiated patients.

Factors such as the mode of radiation therapy delivery, gender, age, implant site and radiation dose at the implant site can affect the survival of dental implant.

More research and randomized controlled trails are needed for more accurate judgment.

Keywords: Dental implants, Head and neck cancer, Radiation therapy, Irradiated patients, Implant survival, Osteoradionecrosis, Oral rehabilitation.

INTRODUCTION

Head and neck cancer is surprisingly very common, as a matter of fact head and neck cancer is the seventh most common cancer in the world [1-2]. It accounts for approximately 900,000 cases and over 400,000 deaths annually worldwide [3].

According to Cancer.Net Editorial Board, 02/2022, Head and neck cancer accounts for about 4% of all cancers in the United States, They estimated that in the year 2022, about 66,470 people (48,520 men and 17,950 women) are to be diagnosed with head and neck cancer. In the year 2020 an estimated 562,328 people were diagnosed with head and neck cancer worldwide and an estimated 277,597 people worldwide died from it.

According to the American Cancer Society, the incidence of oral and pharyngeal cancers is over 54,000 cases per year in the U.S., resulting in over 11,000 annual deaths. Over 20% of the cases occur in people under the age of 55.

Head and neck cancers are more than twice as common among men as they are among women [4-5]. These cancers include a diverse group of tumors affecting the upper aerodigestive tract.

Many different forms and histologies exist, however the most common is squamous cell carcinoma [2]. Risk factors include the use of tobacco, alcohol abuse, and oncogenic viruses like human papillomavirus and Epstein-Barr virus.

Alcohol and tobacco consumption (including secondhand smoke and smokeless tobacco, also known as “chewing tobacco” or “snuff”) are, as a matter of fact, the two most important risk factors for head and neck cancers, especially cancers of the oral cavity, hypopharynx, and voice box [6].

Over 70% of squamous cell carcinoma of the head and neck are found to be avoidable by some lifestyle changes, specifically the effective reduction of exposure to risk factors such as tobacco consumption and alcohol drinking [7].

Although smoking and alcohol consumption are traditional risk factors for head and neck cancer, they are declining in many countries; however, there is a

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steady increase in diagnoses of human papillomavirus (HPV) related cancers, frequently affecting the oropharynx [8].

Vaccination against HPV has been recently reported to reduce prevalent oral HPV infection [9].

Mortality rates of head and neck cancers have started to increase within the last ten years, reflecting a rise in the incidence and static survival rates [1].

Treatment methods include a combination of surgery, radiotherapy and systemic therapy.

Radiotherapy can be a very overwhelming and a devastating experience for patients. It causes irreversible damage to hard and soft tissues, it also hinders wound healing and creates a risk for osteoradionecrosis.

In addition to the loss of function resulting from tooth loss, pain and discomfort from mucositis, hypogeusia, dysgeusia, dentinal hypersensitivy, xerostomia, dental caries, and trismus occur, plus the significant psycho-social impact [10].

Osseointegrated implants are considered by many to be an effective mean of rehabilitation; the use of dental implants has actually improved the quality of life of patients who have recovered from head and neck cancer by allowing reconstruction of tumor defects and replacement of missing structures by a variety of prostheses.

However, irradiation results in a set of challenges that can affect the outcome of treatment.

The aim of this paper is to evaluate whether radiotherapy treatment in head and neck cancer patients could affect the longevity, success, and survival of dental implants.

MATERIAL AND METHODS

An extensive search in the electronic databases of PubMed and National Library of Medicine was performed. No language or time restrictions were applied.

The review was performed for studies and clinical trials that included the insertion of dental implants for Head and Neck cancer patients receiving Radiation Therapy as their oncologic treatment, with the assessment of the success and survival rates.

DISCUSSION

Radiotherapy is used as a method of treatment to eradicate cancer in head and neck cancer patients, along with resection of the tumor and tissue grafting procedures.

These treatment methods result in drastic reduction of bone-healing capacity, atrophied and erythematous mucosa, xerostomia, a disturbed myodynamic, unfavorable interocclusal relations, compromised aesthetics and an overall changed postoperative anatomy [7-10].

Dental and prosthetic rehabilitation can significantly improve the quality of life of patients recovering from head and neck cancer, however, the poor condition of the bones of the jaw makes the placement of removable prosthesis a quite challenging and difficult procedure; Accordingly failure to restore satisfactory aesthetics and mastication adds to the overall morbidity of cancer therapy and results in reduced quality of life of head and neck cancer patients.

And hence dental implants could be the choice; the use of osseointegrated implants would be a better option to improve the quality of life of recovered head and neck cancer patients by allowing reconstruction of tumor defects with a variety of prostheses.

However, since most patients with head and neck cancer receive radiotherapy before implant placement, a clinical concern arises. Does implant osseointegration become affected by presurgical irradiation? Complications such as the risk of implant failure and osteoradionecrosis must be evaluated when implants are placed in patients who have had radiation therapy.

The severity of complications resulting from radiotherapy depends on various factors, including the total dose of radiation delivered, the time span of delivery and which parts of the head and neck received the radiation [11].

The optimal radiation dose for treating head and neck cancers depends mainly on the size and location of the primary tumors and the neck lymph nodes [12]. However, generally speaking, the protocol for therapeutic radiation for head and neck tumors commonly consists of 50 to 70 gray units (Gy) over 4 to 7 weeks, 1 Gy is equal to 100 rad and to 100 cGy.

Side effects could be divided into early and late. Early side effects occur during the course of treatment,

while receiving radiotherapy and during the immediate post therapy period. Late effects can occur any time, from weeks to years later [13].

Patients are usually worried by the early effects of Radiotherapy, even though these will eventually resolve by time. On the other hand, late effects are the real concern; Late side effects include permanent loss of saliva (Xerostomi); osteoradionecrosis; pharyngoesophageal stenosis; radiation induced dental caries; necrosis of the oral cavity; fibrosis of blood vessels, soft tissues and muscles; radiation recall myositis, impaired wound healing; decreased proliferation of bone marrow; impaired collagen production; skin changes and skin cancer; lymphedema; hypothyroidism, hyperparathyroidism, lightheadedness, dizziness and headaches; secondary cancer; and neurological and neck structures damage.

The bone marrow in patients treated by radiotherapy becomes hypocellular, hypovascular and shows signs of marked fibrosis and fatty degeneration. The irradiated tissue is also hypocellular, hypovascular and hypoxic [11-13], all leading to compromised bone and soft tissue healing capacity; therefore it's believed that this is the main cause of failures in dental implant osseointegration. As a matter of fact, dental implants rehabilitation was actually considered a contraindication for irradiated patients in the past [14].

Still dental implants are favored for rehabilitation over the conventional tissue-borne prosthesis, for its improved retention, mastication, and patient acceptance. Dental implants in combination with prosthesis would be a better option to restore function, aesthetics and quality of life [15].

However to achieve a satisfactory result in irradiated patients with head and neck cancer, many factors should be considered such as: age, gender, site of implant, total radiation dose, time span between the end of radiotherapy and implant surgery, type of radiation therapy, and the use of hyperbaric oxygen (HBO) therapy.

The objective of this paper is to evaluate the effect of radiotherapy on dental implant survival in head and neck cancer patients with consideration to multiple factors according to different studies.

According to one study [16] that was held by the department of Oral and Maxillofacial Surgery, University Hospital La Princesa (Madrid, Spain), where they evaluated 225 implants placed in 30 patients who had been treated by radiation therapy as their oncologic treatment. Radiation doses ranged between about 50 and 70 Gy.

39 implants were placed for patients after receiving a combination treatment of both radiotherapy and chemotherapy. Data denoted tumor type and reconstruction, presence of osteoradionecrosis, site of implant installation and type of prostheses. Survival rates were calculated using cumulative Kaplan-Meier survival curves and comparison between different groups was done with a log-rank test.

Another 152 implants were placed for patients who presented previous reconstruction procedure. Osteoradionecrosis was developed as a complication for five patients due to the radiotherapy treatment, once the osteoradionecrosis recovered, 41 implants were installed for those patients.

The results of this study showed a substantial survival difference of implants placed in patients with (92.6%) and without (96.5%) irradiation, the overall 5 year survival rate in patients who got exposed to radiation for treatment was 92.6%. Irradiated patients had a marginally significantly higher implant loss compared to non-irradiated patients. ($p = 0.063$). The 5 year survival rate in the group with osteoradionecrosis was of 48.3% and in the non-osteoradionecrosis group 92.3%, with a statistically significant difference between both groups. ($p = 0.002$). Implants failed in patients with irradiation occurred mainly due to peri-implant infection, asymptomatic peri-implant bone loss and consecutive integration loss. On the other hand, implants failed in patients without irradiation occurred at the beginning of the follow-up period owing to failure of primary osseointegration.

Another recent study [17] was held at University Medical Centre Ljubljana, Slovenia. The study included 20 irradiated head and neck cancer patients who received a removable implant-supported denture. To assess the implant survival and success rate, Kaplan-Meier survival analysis, Cox proportional hazard models and logistic regression were used.

100 implants were inserted for 20 patients, after 1 year the estimated implant survival rate was 96% and 87% after 5 years. Failures were mostly observed before loading (91.2%). Implants inserted in the transplanted bone were significantly more likely to fail. Out of 89 implants supporting the dentures, 79 implants (88.7%) were successful, meaning that they were

functionally loaded and showed no signs of pain, radiolucency or progressive bone loss. However in case of older patients Prosthetic treatment was significantly less successful. It was found that the attachment system and the number of implants inserted did not have a statistically drastic significance on the success rate.

Another study [18] was made to analyze the long-term success and factors that might potentially influence the success of dental implants placed in irradiated patients with a minimum total dose of 50 Gy during the years 1995 to 2010. The study included Thirty-five patients (169 dental implants). Data on demographic characteristics, tumor type, radiation therapy, implant sites, implant dimensions, and hyperbaric oxygen therapy (HBOT) were collected and analyzed. And like previous studies, Implant survival was estimated using Kaplan–Meier survival curves.

They inserted 79 dental implants in the maxilla and 90 in the mandible. The mean follow-up after implants were installed was 7.4 years (range 0.3–14.7 years). The overall 5-year survival rate for all inserted implants was 92.9%. Gender ($P < 0.001$) and the mode of radiation therapy delivery ($P = 0.005$) had a statistically significant influence on the survival of implants.

However; age, time of implantation after irradiation, implant brand and dimensions, and HBOT (Hyperbaric Oxygen Therapy) had no significant influence on the survival of implants.

Another observational study [19] was made to review implant survival and quality of life provided by implant-based prosthetic rehabilitation of head and neck cancer patients. This prospective study presented preliminary results of 29 edentulous head and neck cancer patients (20 patients after undergoing radiotherapy) with 165 OsseoSpeed implants. Implant success was then evaluated after 1-year of follow-up using the Albrektsson criteria. Quality of life was analyzed with the EORTC QLQ-C30, QLQ-H&N35, and OHIP 14 questionnaires.

The overall implant survival rate after 1 year was 95.2% (157/165). Implant success measured by the Albrektsson criteria provided less success rate of 86.7% (143/165), mostly due to peri-implant marginal bone loss with a mean of 0.8 mm after 1 year. Xerostomia ($p = 0.008$), implant insertion within the radiation target volume ($p = 0.09$), implantation in transplanted bone ($p = 0.05$), and smoking ($p = 0.041$) were mainly accountable for the failure of implant, followed by D4 bone quality, maxillary implant site, and insufficient primary stability. Quality of life had considerably improved 1 year after denture placement compared to before treatment.

This study concluded that it is acceptable and possible to use Implant-based prosthesis for rehabilitation of head and neck cancer patients as it can significantly improve patients' quality of life, however, at a calculable risk.

A risk factor analysis [20] was done to evaluate dental implant outcomes in irradiated patients who had previously received radiotherapy as a treatment for head and neck cancer. Ninety dental implants were investigated in 27 patients who received radiotherapy for head and neck cancer and received dental implants afterwards. The cumulative implant survival rate (CISR) was then calculated. The implant quality was also assessed using "Health Scale for Dental Implants.

The cumulative implant survival rate CISR after 3 years was 79.6%. The mean radiation dose at the implant site (D_{mean}) was identified as an independent prognostic factor for the survival of dental implant. Implant didn't fail if D_{mean} was less than 38 Gy. As for implant quality, dental implants in grafted bone and D_{mean} were identified as independent risk factors. As a result it was found that dental implants can be considered and accepted when Dmean is less than 38 Gy.

A retrospective study [21] was conducted at the Department of Oral and Maxillofacial Science, Sapienza University of Rome. The aim was to evaluate the survival of dental implants inserted after undergoing ablative surgery, in both non-irradiated and irradiated patients that was treated for oral cancer.

Data for 34 patients was collected (22 females, 12 males; mean age: 51 ± 19) with oral cancer who had undergone ablative surgery and orally rehabilitated using dental implants between 2007 and 2012. Twelve patients received radiation therapy (less than 50 Gy) postoperatively before implant placement. In both irradiated and non-irradiated bone there was a total of 144 titanium implants inserted, at a minimum interval of 12 months.

The results stated that dental implant loss was mainly dependent on the position and location of the implants ($P = 0.05–0.1$). Furthermore, implant survival was mainly dependent on whether the patient was

irradiated or non-irradiated. This result was statistically significant ($P < 0.01$). Another highly significant ($P < 0.01$) factor determining survival was whether the implant was loaded. A significantly better outcome was noticed when the implant was not loaded for at least 6 months after being placed.

The study concluded that a delayed loading will give the best chance of implant osseointegration, stability and, ultimately, effective dental rehabilitation.

Another study [22] was conducted by The Department of Oral and Maxillofacial Surgery and Maxillofacial Prosthetics, University of Groningen. This study aimed to assess functioning, satisfaction, condition of peri-implant tissues, and the survival of dental implants 14 years after they have been inserted in patients with oral cancer who had their mandibular overdentures placed over primary implants. Endosseous dental implants were inserted in the interforaminal region of the mandible during removal of the tumour in 164/180 patients suffering from oral neoplasms. All 58 patients were evaluated during a final assessment in 2012. Mandibular overdentures that were retained using implants got inserted, prosthetic rehabilitation and oral functioning were not related to primary site or stage of the tumour, number or type of implants inserted, or the type of reconstruction.

The peri-implant mucosa was mostly free of inflammation. However, more implants were lost in irradiated patients (27/318, 8.5%) than in those not so treated (1/206, 0.5%). Patients who had been treated by radiation therapy had more problems in oral functioning and less satisfaction compared to those who had not. Patients who got an implant-retained mandibular overdenture had fewer problems in oral functioning compare to patients without an overdenture.

The study concluded that primary insertion of an implant should be added in the surgical planning for patients with oral cancer, because oral functioning in patients wearing mandibular overdentures improved significantly and peri-implant health was reasonable.

One more study [23] was held at The Royal Melbourne Hospital, Parkville, Victoria. The study aimed to evaluate dental implants placed in patients after removal of oral cancer over a 15-year period. This included the insertion of dental implants in irradiated tissues, and the use of hyperbaric oxygen treatment (HBOT).

Dental implants were placed for 31 patients as part of their oral rehabilitation between 1992 and 2007. Demographic data and factors such as implant survival, type of prosthesis provided, radiotherapy and the hyperbaric oxygen therapy (HBOT) were analyzed.

The results of this study indicated that there was a retention rate of 110 implants from a total of 115 implants placed. A high rate of implant retention was found, with only 5 failed implants from a total of 115 implants inserted. It was found that the 5 failed implants occurred in free flap bone that had been exposed to radiation.

CONCLUSION

Osseointegrated implants can be used successfully in the oral rehabilitation of most irradiated patients. It is even an acceptable option for patients who had suffered from osteoradionecrosis. Totally implant supported prostheses are recommended after irradiation as they provide satisfactory function, stability, aesthetics and a better quality of life.

It was revealed that some influencing factors can affect the longevity of dental implant in irradiated patients; For instance delayed loading was proved to help with improving implant osseointegration, the mean radiation dose at the implant site (Dmean) is pivotal and should be less than 38 Gy, there may be a higher risk of implant failure in free flap bone that has been exposed to radiation, gender is also believed to play a role as the 5-year success rate was 98.9% for irradiated male patients and 81.6% for irradiated female patients ($P < 0.001$), and patients receiving IMRT had better implant success rates than those receiving conventional conformal radiotherapy.

Long-term data on dental implants inserted to irradiated head and neck cancer patients are to some extent difficult to obtain because of the relatively poor prognosis of these patients:

More Prospective cohort studies and randomized controlled trails are still in need to draw more evidence based conclusions.

Even though dental implants for irradiated head and neck cancer patients are encouraged for a better quality of life, their success and survival in non-irradiated patients remains way ahead.

CONFLICTS OF INTEREST

The author declares no conflict of interest.

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