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Derleme / Review

Dental Implant Treatment in Patients with Oral Cancer: Literature Review

Ağız Kanseri Geçirmiş Hastalarda Dental İmplant Tedavisi: Literatür Derlemesi

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Abstract: The aim of this review is to evaluate the timing of dental implants placement and long-term survival rates in patients who have had prosthetic rehabilitation with dental implants after ablative surgery and radiotherapy (RT), and have had head and neck cancer (HNC). For this purpose; implant survival (IS) rates placed as primary/secondary or placed in bones with/without RT were evaluated. The literature published between 2000 - 2020 has been reviewed for the evaluation of dental implant treatment in patients with HNC. The search terms used in PubMed scans were "head and neck cancer", "oral cancer", "dental implant" and "radiotherapy". 134 related articles have been defined in PubMed database searches and 16 were included in the final analysis. Dental implant applications have gained importance in the prosthetic treatment of patients with oral cancer. In cases where conventional prosthetic treatments are insufficient, dental implants provide retention and stability to dentures. However, before starting treatment, whether the patient is receiving chemotherapy, RT and the use of bisphosphonate should be taken into consideration and the timing of the surgical procedures should be adjusted correctly. In addition, these patients should be followed up regularly for a long time.

Keywords: Dental implants; Head and neck cancer; Oral cancer; Radiotherapy

Özet: Bu derlemenin amacı, ablatif cerrahi ve radyoterapi sonrasında dental implantlar ile protetik rehabilitasyonu yapılan, baş-boyun kanseri geçiren hastalarda dental implantların yerleştirilme zamanlaması ve uzun süreli sağ kalım oranlarını değerlendirmektir. Bu amaçla; implantların primer/sekonder yerleştirilmesi, radyoterapi almış/almamış çene kemiklerinde implant sağ kalım oranları değerlendirilmiştir. 2000 - 2020 yılları arasında yayınlanan literatürler, baş-boyun kanseri geçirmiş hastalarda dental implant tedavisinin değerlendirilmesi amacıyla gözden geçirilmiştir. PubMed taramalarında kullanılan arama terimleri ‟baş boyun kanseri”, ‟oral kanser”, ‟dental implant”, ‟radyoterapi” idi. Yapılan PubMed taramasında 134 ilgili makale bulunmuş ve 16 makale derlemeye dahil edilmiştir. Ağız kanseri hastalarının tedavisinde protetik tedavi amaçlı dental implant uygulamaları günümüzde önem kazanmıştır. Konvansiyonel protetik tedavilerin yetersiz kaldığı durumlarda, dental implantlar protezlere retansiyon ve stabilite sağlamaktalardır. Ancak uygulamadan önce hastanın kemoterapi, radyoterapi alıp almadığı ve bifosfanat kullanım durumu dikkate alınmalı, yapılacak cerrahi işlemlerin zamanlaması doğru ayarlanmalıdır. Ayrıca bu hastalar düzenli olarak uzun süre takip edilmelidir.

Anahtar Kelimeler: Dental implant; Baş boyun kanseri; Oral kanser; Radyoterapi

Abbreviations: CP: Conventional prosthesis, HNC: Head and neck cancer, IS: Implant survival; ISP: Implant supported prostheses, ORN: Osteoradionecrosis, RT: Radiotherapy, QoL: Quality of life

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1. Introduction

The term head and neck cancer (HNC) describes malignancies occurring in the oral cavity, paranasal sinuses, salivary glands, pharynx and larynx (1, 2). According to World Health Organization reports, it is the eleventh most common cancer in the world (3). HNC results in more than 650,000 cases and 330,000 deaths each year worldwide (1). The average age of patients diagnosed ranges from 55 to 65, and men are twice as affected by women (4). Poor oral hygiene, Human papilloma virus, diet, chewing tobacco, alcohol and smoking are among the most common causes of oral cancer (2, 5, 6).

In the diagnosis, treatment and rehabilitation stages of these patients, cooperation of experts from different fields is required (7-9). Good communication between surgeons, radiation oncologists, medical oncologists and maxillofacial prostodontist should be ensured for good treatment (10, 11). Treatment planning varies depending on factors such as the location of the primary tumor, the stage of cancer, age and the general health of the patient. However, oncology patients are usually treated with ablative surgery, radiotherapy (RT), chemotherapy or a combination of these (10, 12-15). Surgical treatment of HNC causes deformity and changes in the anatomy of the region. Resection of the maxilla, mandible or part of the teeth limits speech, chewing and swallowing. As a result, nutrition is also adversely affected. Loss of ear, eyes or nose creates aesthetic changes in the patient. Functional and aesthetic problems occur negatively affect the psychology and quality of life (QoL) of patients (11, 16, 17).

Another stage of cancer treatment is to restore the function and aesthetics that the patient has lost (10). Dental and prosthetic rehabilitation can significantly improve patients' QoL after HNC treatment (18-20). However, treatment of oncological patients; becomes difficult due to trismus, radiation fibrosis, xerostomia, changing intraoral anatomy, soft tissues lost or scarring, changing muscle connections, impaired tongue functions, and insufficient resilience of soft tissues (2, 21). In order to make a correct dental prosthetic treatment, the remaining teeth, hard and soft tissues should be examined in detail and correct planning should be done (22, 23). The aim of prosthetic therapy is to restore the patient's chewing, swallowing and speaking functions. After the therapeutic phase, patients can receive dental or implant supported prosthetic treatments. It is difficult to obtain a functional conventional prosthesis (CP) in cases where the integrity of the bone and mucosa is impaired, there is not enough support area for the prosthesis, tongue functions are impaired, decreased orofacial motor functions and xerostomia are observed after resective and reconstructive surgical procedures. In some cases, a maxillary prosthesis is prepared for patients to meet their aesthetic needs only, or treatment is often neglected (2, 17, 24-28).

When RT is applied after ablative surgery, saliva secretions decrease. Oral functions such as chewing and swallowing are adversely affected due to trismus originating from RT. Due to the changes in the mouth anatomy after surgical treatment, the neutral zone area is frequently affected in patients. This can cause retention problems in prostheses, as they limit the support area of CP. It is difficult and sometimes even impossible to produce a functional CP, especially in the mandible. Segmental resections also allow the construction of a removable partial denture, which makes little contribution to chewing performance (28-31). CP do not meet the patients' function, phonation, aesthetic expectations and affect their QoL negatively. Therefore, implant supported treatment of patients is becoming an alternative treatment option. It is thought that the risk of necrosis will be prevented by eliminating the risks that cause mucous irritation with implant supported prostheses (ISP) (32).

The use of dental implants for prosthetic rehabilitation has increased significantly over the past three decades thanks to advances in material science, creation of specific clinical protocols and surgical techniques (33, 34). Dental implants were originally used in the treatment of patients with no cancer and teeth

deficiency. Later, the use of implants for dental or cosmetic rehabilitation became widespread in patients with HNC (35).

Dental implants play an important role in the oral rehabilitation of patients affected by malignancies in the HNC region and treated with RT (36). In order to obtain a positive prognosis from ISP in patients who have received RT; many risk factors should be taken into consideration such as age, gender, total radiation dose received, type of RT applied, the time between RT and implant surgery. Technical aspects such as the surgeon's experience, bone quality and topography in the region where the implant will be placed, implant length, diameter, and primary stability also play an important role in implant success (15, 18, 37). Dental implants can be placed in the mandible, maxilla or free bone flaps. Craniofacial implants are placed in the orbital edge, anterior nasal apertura and temporal bone, increasing the prosthesis connection (35). Dental implant treatment can result in more effective oral rehabilitation in terms of chewing, aesthetics and speech function (19, 38, 39). Xerostomy and sensitive mucosa that occur after RT make the use of CP difficult. In this case, ISP are seen as a suitable option (40). The aim of implant treatment is to increase retention of removable dentures and to reduce the load on sensitive soft tissues. This is to improve the QoL of patients (41).

Implant treatment is also difficult in oral cancer patients. Because the bone where the implants will be placed is in either RT or graft area. As a result of the decrease in the amount of bone after surgery, it is difficult to place the implants in an ideal position. Therefore, angled abutments and telescopic parts are required in the prosthetic stage (11, 30). Failure rate increases when implants are placed on irradiated bone. Progressive fibrosis of the vascular and soft tissue, which are among the side effects of RT, may cause a decrease in the capacity to heal. In addition, radiation reduces bone vascularity, clinically this condition occurs as osteoradionecrosis (ORN). ORN prevents the osseointegration of implants. Ionizing radiation damages bone, periosteum, connective tissue and vascular endothelium and causes loss of resistance in tissues. This situation causes hypoxia, hypovascularity and decrease in cell number in the future. However, resistance to trauma and infection decreases (26, 30, 42).

The timing of implant placement in patients with RT is also controversial (43). The time between RT and implant surgery can affect implant success. Some authors recommend placing implants during ablative surgery (19, 20, 39, 43, 44).

Advantages of implant placement during ablative surgery (19, 20, 43, 45, 46):

- Since the osseointegration process takes place before irradiation, the risk of late complications such as the development of ORN is reduced.
- There is no need for auxiliary prophylaxis such as long-term antibiotic use and hyperbaric oxygen therapy.
- Oral rehabilitation starts earlier, as a result of which the QoL improves.

Risks of implant placement during ablative surgery (39, 46):

- It causes delay in oncological treatment including RT.
- Ablative surgery can lead to improper implant positioning when causes large changes in the relevant region anatomy and/or intermaxillary relationship.
- There is a risk of developing complications after treatment due to implants placed during ablative surgery.
- There is a possibility that implants cannot be used due to early tumor recurrence.
- Especially in patients with large defects, difficulties occur in obtaining adequate keratinized mucosa around the implants.

Studies have reported that there is no significant difference in the effect of implant placement on implant loss before or after RT; however, most studies report on implants placed after RT (39, 45). There are a limited number of studies in the literature regarding

the success of implants placed primarily during surgery. Therefore, the general aim of the literature review is; to review published literature on dental implant treatment results of patients with HNC. For this purpose; implant placement timing and implant success were evaluated.

Authors, year, study design, number of patients/implants inserted, location, time of implant placement, radiation dose applied to the implant site, follow-up duration, and conclusion are summarized in Table 1.

Table 1. A summary of the current literature of dental implants survival in irradiated jaws

Authors Year	Study design	Number of patient/ implants inserted	Location	Time of implant placement	Radiation dose applied to the implant site (in Gy)	Follow-up duration	Conclusion
Visch et al, 2002 (47)	prospective	130/446	maxilla mandible	ranged from six months to 22 years	≤50Gy >50Gy	up to 14 year	-A higher IS rate has been reported in mandible and implants placed in areas where RT is applied less than 50 Gy.
Landes e Kovács, 2006 (48)	prospective	30/114	mandible	an average of 21(4–55) months after RT	mean 57 Gy	mean 36 (24-46) months	-More bone loss occurs in patients undergoing RT.
Yerit et al, 2006 (26)	retrospective	71/316	mandible grafted iliac bone	1.41 (± 1.01) years after RT	total dose of 50 Gy	mean 5.42 year	-Lower IS was observed in implants placed in bone treated with RT.
Korfage et al, 2010 (39)	prospective	50/195	mandibula	preradiation	postoperatif > 40 Gy	5 year	- A high success rate has been reported in primary implants.
Sammartino et al, 2011 (34)	prospective	77/172	maxilla mandible	mean 9.4 months after RT	≤50Gy >50Gy	more than 3 years	-Higher success has been achieved in regions where RT is applied at a dose less than 40-50 Gy.
RA Barrowman et al, 2011 (11)	retrospective	31/115	maxilla mandible	-	-	up to 15 years	-The rate of failure of implants placed in free flap bone with RT was increased.
Mizbah et al, 2013 (49)	retrospective	128/314	mandibula	before and after RT	-	5 year	- Prosthetic treatment of patients whose implants were placed as primary was completed in a shorter time.
Mancha de la plata et al, 2012 (30)	retrospective	30/355	maxilla mandible	mean 33 (12-96) months after RT	59.6 Gy (50-70 Gy)	45 (8-96) months	- ISP that did not receive support from the mucosa can be made after RT.
Korfage et al, 2014 (50)	prospective	164/524	mandible	after more than 6 months of waiting	-	3.8 yıl (up to 14 year)	- The patients, where the implants were placed primarily, started to use their prostheses earlier.
Hessling et al, 2015 (51)	retrospective	59/272	maxilla mandible	before and after RT	40 Gy (neoadjuvant group) 61 to 66 Gy (adjuvant group)	30.9 (3-82) months	- Soft tissue management, peri-implantitis, and oral hygiene are important for IS.
Wetzels et al, 2016 (28)	prospective	56/59	mandible	6 weeks before RT	-	5 years	-The bite force and chewing functions of the patients with primary implants were higher than those with delayed loading after 5 years.
Papi et al, 2018 (52)	prospective	32/113	maxilla mandible	12-24 months after RT	43 Gy	25.5±3.4 (24–30) months	-No significant difference was found on crestal bone loss and IS of the different RT techniques applied.
Curi et al, 2018 (15)	retrospective	35/169	maxilla mandible	mean 23.7 (1-92) months after RT	62 Gy (50-70 Gy)	7.41 years (0.3-14.7)	- Dental implants can be successfully used in oral rehabilitation of patients with

							HNC who receive RT. Risk factors such as gender and RT mode can affect the IS.
S. Di Carlo et al, 2019 (53)	retrospective	17/84	maxilla mandible	12, 14, 16 months after RT	<50 Gy	39,5 months	-At least 14 months should be waited for implant surgery after RT.
Ettl, Tobias, et al, 2019 (54)	prospective	52/309	maxilla mandible	mean 45 (12-217) months after RT	61.7 Gy (40-72)	2 years	- In patients undergoing RT, peri-implant bone resorption is a factor for implant failure.
Alberga et al, 2020 (55)	prospective	29/58	mandible	primary immediate implant mandibular placement	primary RT: 32.9 Gy (27–40 Gy) postoperative RT: 41.1 Gy (2.1–64.6 Gy)	mean 18.5 months	- Immediate primary implant placement has been reported to be an appropriate treatment option for HNC patients.

2. Discussion

The period of 8-12 months after tumor carries a high risk of recurrence (56). In a study, 44% of cancer patients undergoing mandibular resection reported recurrence within 13 months after surgery (57). Therefore, it is recommended to wait until the high risk process for oral rehabilitation passes. Although implant placement is usually done at the earliest 6 months after RT, Ganström et al., recommends that implant treatment should be completed 6-18 months after RT (58). Dental implants placed in less than 12 months after RT have been reported to have an increased chance of failure (59). Therefore, it is recommended to wait at least 12 months to obtain the best clinical results (34).

The optimum time to wait between RT and dental implant surgery is controversial. At the same time as ablative tumor surgery, implant placement before RT is called primary placement, and implant placement after RT is called secondary placement. With the primary placement of the implants, it is aimed to achieve osteointegration, reduce the number of surgical procedures and provide early oral rehabilitation before the harmful effects of RT begin (38, 39, 46). It is more preferred to implant secondary placement. In this way, both functional and psychological conditions of the patients can be well considered after surgery. In addition, a more accurate assessment of cancer prognosis is provided (60).

Studies have reported that high success has been achieved with implants placed in primary edentulous patients and patients performed better with a mandibular prosthesis after cancer treatment (28, 49, 61). In their study, Mizbah et al. evaluated primary/secondary implanted patients. They reported that ISP were performed approximately 7 months after the patients who were implanted with primary implants, and that patients who were implanted secondaryly waited more than 27 months (49). As a result of their work, Korfage et al. also recommended that a primary implant be placed. They reported that a good oral function was achieved by implant placement during resection and increased patient satisfaction (50).

Sammartino et al. compared two groups in their study: implants were placed in the first group in a waiting period of less than 12 months, and implants were placed in the second group after 12 months. The study reports that waiting times of less than 12 months did not result in adequate bone and vascularization directly associated with implant osteointegration. Therefore, the maximum number of complications was seen in the group implanted after waiting less than 12 months after RT (34).

The development of ORN in the jaws after RT is a negative side effect of RT. It is often seen in the mandible. Patients exposed to radiation doses of more than 60 Gy are considered a risk group. ORN can cause excessive bone loss. This affects future prosthetic treatment options (62, 63). It is known that the risk of ORN after RT does not decrease in HNC patients over time, however, it causes progressive and irreversible capillary loss (64). Although dental implant failures are rare

at doses less than 45 Gy, these rates have increased in 65 Gy and above (45, 65). Studies have reported that implant survival rates are higher in patients who have not received RT after tumor surgery (26, 33, 39, 45, 66, 67). In the review of Bassam et al. was reported that high doses of RT, use of bone grafts and the area in the maxilla affected the prognosis negatively (68). As a result of the systematic review by Nobrega et al. dental implants placed in irradiated areas have been reported to have a lower success rate. In addition, they concluded that these patients were at high risk throughout their lifetime in terms of possible complications. They reported that these patients should be followed up for a long time in order to prevent complications and reduce the possibility of failure (69). Alberga et al. reported high IS rates in patients not receiving RT. In addition, oral function, psychological and social conditions of patients who did not receive RT were found to be better than patients who received RT (55). Landes and Kovacs reported an average of 1.4 ± 0.9 mm crestal bone loss after 2 years in patients undergoing RT. These values are quite high compared to non-irradiated patients (0.9 ± 0.4 mm, P <0.01) (48). Ihde et al. reported that implant loss is 12 times more risky in bone treated with RT (67). De La Plata et al. reported that the 5-year survival rate in patients who received RT was 92.6%. However, it has been observed that irradiated patients have higher implant loss than non-irradiated patients (96.5% IS rates have been reported in patients without RT). It has been reported that implant loss in patients undergoing RT generally occurs as a result of peri-implant infection or bone loss (30).

Many retrospective clinical studies have reported that there is no statistical difference in terms of IS between irradiated and non-irradiated bone (70-72). Javed et al. reported that dental implants show up to 100% osseointegration when exposed to radiation doses up to 65 Gy, and radiation doses between 50-65 Gy do not adversely affect osseointegration (73). However, there are studies reporting that a total dose of less than 50 Gy is required to reduce the negative effects of RT (19, 26, 58). Linsen et al. reported IS rates as 96.6%, 96.6% and 86.9%, respectively, in the 1, 5 and 10-year follow-up of patients treated with a combination of surgery and RT (18). Curi et al. reported that osteointegration occurred in patients undergoing implants after 50 to 70 Gy (mean 62 Gy) RT and that they were satisfied with their ISP in terms of function, phonetics, chewing and aesthetics (15).

3. Conclusions

Based on the studies reviewed;

- Considering three-dimensional planning, guided implant surgery, improvements in implant surface features and improvements in treatment concepts in recent years; the use of dental implants for oral rehabilitation of patients undergoing RT in the head and neck area is seen as an appropriate treatment alternative.
- Before starting implant treatment, whether the patient is receiving chemotherapy and RT and the use of bisphosphonate should be taken into consideration and the timing of the surgical procedures should be adjusted correctly.
- It should be remembered that prognosis may be negatively affected in the bone that has been grafted and RT applied.
- In general, a multidisciplinary approach is critical for best treatment outcomes and can significantly improve patient survival.
- The doctor and patient should be aware of the potential risks and complications related to implant treatment in the patient undergoing RT.
- Oncological patients should be called for regular control and a detailed clinical examination should be performed.

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