



Survival of Dental Implants in Oncology Patients versus Non-Oncology Patients: A 5-Year Retrospective Study

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Patients with a history of cancer are increasingly common in the dental office. Treating cancer patients requires a multidisciplinary team, which should include the dentist, in order to control the complications that occur in the oral cavity and also to recover the patient undergoing treatment in any of its types: surgical, medical, radiotherapeutic, or its possible combinations. Dental implants can be a safe and predictable treatment option for prosthetic rehabilitation. The aim of this paper is to describe in retrospect the success rate of osseointegrated implants in oncology and non-oncology patients placed by the Master of Dentistry in Oncology and Immunocompromised Patients, as well as the Master of Medicine, Surgery and Oral Implantology of the University of Barcelona Dental Hospital, between July 2011 and March 2016. 466 patients were reviewed, with a total of 1405 implants placed, considering the oncological history of the patients and the implant success rate. The total success rate in the concerned period was 96.65%. When comparing cancer patients with healthy ones, the success rate has been 93.02% in the first case, and 97.16% in the latter. According to the literature review, our results encourage implant placement in cancer patients, it is important to recognize that this is an analysis of a complex care pathway with a large number of confounding variables. However, the findings should not be considered as generalizable.

Key Words: oral cancer, dental implants, cancer, implant survival.

Introduction

According to the World Health Organization, cancer is the between first or second leading cause of death worldwide (1,2). In 2018, there were about 18 million new cases and 9.6 million related deaths (2). The body can be affected by more than one hundred different types of cancer. The number of new cases is expected to increase by approximately 70% over the next 20 years. The most frequently diagnosed types of cancer in men are those of the prostate, lung, colon and rectum, stomach and liver; in women, breast, lung, colon and rectum, cervix and stomach (1).

The use of tobacco is the most relevant and controllable risk factor; it is the cause of more than 20% of cancer-related deaths in general and 70% in the case of lung cancer, according to the World Cancer Report in 2014. The development of cancer related to tobacco use depends on the susceptibility of different tissues and organs. Therefore, in the oral cavity, tobacco produces a direct harmful action, while the effect on other organs (such as the lung, for example) is related to the participation of active metabolites. The risk of smoking patients having oral cancer is 5 to 20 times higher than non-smoking one (1,3,4).

Head and neck cancer has a series of features that

makes its vision established as a whole, thus when we talk about this anatomical area we include: paranasal sinuses, nasopharynx, oropharynx (tonsil, soft palate, base of tongue), hypopharynx, larynx, oral cavity (oral mucosa, floor of mouth, salivary glands, gum, hard palate, tongue and lip; it represents 5% of all tumors) (3).

The mortality rate of head and neck cancer (as well as any other type of cancer) is higher in developing countries, both in men and women. The female population, either white or black, has the same incidence of tumor involvement oral cavity. Black men, on the other hand, have 30% more oral cavity/pharyngeal tumors; black men and women have twice as many tumors as white people in laryngeal involvement. In India, high rates of oral cavity cancer are reported. Hispanics have a lower rate of oral cavity/pharyngeal cancer and Asians, a lower rate of larynx cancer. The average age of disease onset to diagnosis is around 60 years old, although the incidence of cancer in adults under 50 years old is increasing, mainly in relation to the Human Papillomavirus (HPV) (3,4).

The different forms of tobacco consumption (inhaling, chewing), along with its different combinations depending on geographical locations, as well as the substantial ingestion of alcohol, constitute the main risk factors

of oral cavity cancer (3,5). Poor oral hygiene is another factor to consider. Viruses, such as HPV and Epstein-Barr (EBV) are associated with oral/nasopharyngeal carcinomas and Burkitt lymphoma, typical of sub-Saharan Africa, respectively. It has also been linked to poor nutrition, and specific deficiencies of vitamins A, E and iron, in many cases associated with chronic alcohol consumption (3).

20% of the patients who survive head and neck cancer will have another primary neoplasm in the same location (5). Almost all neoplasms of the oral cavity and pharynx are squamous cell carcinomas, about 95%, with different degrees of variation. Most primary neoplasms spread to adjacent tissues and produce metastasis on local lymph nodes. Cancer treatment may require surgery, radiotherapy, chemotherapy or some of these combined, always depending on the study carried out by the cancer committee (5).

Surgery is the most used method to treat cancer. The surgical treatment of cancer may require the removal of the tumor mass with a safety margin and, depending on its extension, the emptying of the cervical ganglionic chain (4). It is an option if the cancer is limited to a specific area, if it is possible to preserve all vital structures that guarantee proper functionality and also keep the aesthetics of the patient. In addition to the surgical procedure, methods used are radiotherapy and chemotherapy (4). In cases of more extensive proportions, induction chemotherapy may be indicated before surgery (3,5).

In head and neck radiotherapy, which is local in action, generates several immediate side effects (oral mucositis, dysgeusia, trismus and hyposalivation) and late side effects (osteoradionecrosis and radiation caries) (6). The salivary glands usually receive a high dose of radiation, causing a progressive and, from certain doses on, irreversible decrease of salivary secretion, among other effects. Furthermore, changes in the composition of the saliva have been observed, reducing its moisturizing capacity (7). The absence of salivary flow may increase tooth decay and decrease the retention of prostheses. The modification of the oral mucosa and the underlying bone also causes a worse adaptation of conventional prostheses (8).

Chemotherapy, on the other hand, is an antineoplastic treatment with systemic action, in which the main cells affected are of greater metabolic activity (characteristic of cancer cells). Chemotherapeutic agents act on the tumor and on healthy tissue, generating side effects in the mouth such as oral mucositis, dry mouth and dysgeusia (9). In addition to that, hypersensitivity, nausea and vomiting as reactions and other possible complications: alopecia, diarrhea, constipation, changes in nutritional status and neurotoxicity (8).

The functional and aesthetic rehabilitation of cancer

patients undergoing large resections constitute one of the biggest challenges for the multidisciplinary team (dentists, oncologists, surgeons) (7). The ability to achieve total rehabilitation of all oral functions is, however, dependent on tumor factors. Tumor factors include the site and stage of disease while patient factors include age, lifestyle habits, oral hygiene, status of dentition, status of the available bone, and soft tissues following treatment in the oral cavity and overall prognosis of the patient. Treatment related factors include the impact of surgery and radiation with or without chemotherapy on all oral cavity structures, including the mandible, soft tissues and mucosa of the oral cavity as well as function of salivary glands (10).

In the patient with oral cancer, rehabilitation with removable prosthesis can often be difficult, if not impossible in some patients following surgical management (10,11). The use of osseointegrated dental implants has allowed improved retention of removable prostheses, reduced loading on vulnerable tissues and with this resulted in a reported improvement in the quality of life for patients (11,12).

Treatment with osseointegrated implants has evolved very quickly in different fields since its inception. The use of new biomaterials, surfaces and techniques that improve the biological aspects at the bone/implant interface is under constant evolution (13). However, after surgery for oral cancer, several aspects can have an impact on the osseointegration of the implants: the remaining bone, the bone topography, the origin of the bone in case of graft (fibula, iliac crest, cap), stain and radiation dose therapy. In addition, poor health, poor oral hygiene, previous smoking and alcohol abuse reduce the survival of the implant (14).

With the increasing use of dental implants in the oral rehabilitation of head and neck cancer patients, an improved evidence base is required to help inform clinical decision- making (11).

The aim of this paper is to retrospectively review the survival of dental implants in oncology patients versus non oncology patients. The implants were placed at the Master of Dentistry in Oncology and Immunocompromised Patients and the Master of Medicine, Surgery and Oral Implantology of the University of Barcelona Dental Hospital between July 2011 and March 2016. Specific objectives were set: a) to describe the success rate of all implants placed in both masters within the period referred; b) to present the relationship between implant survival depending on the profile of patient (oncology/non-oncology) and c) to evaluate the implant survival placed in head and neck cancer patients and to compare it with patients that have cancer in other organs; as secondary objectives, to report the type of cancer more associated with failure, and also the dose of radiotherapy received in the head and neck

area, as well as the failure rate.

Material and Methods

The medical records of the patients submitted to the placement of dental implants performed by the Master in Dentistry in Oncology and Immunocompromised Patients and the Master in Medicine, Surgery and Oral Implantology of the University of Barcelona Dental Hospital between July 2011 to March 2016 were reviewed, considering as research variables: history of head and neck cancer, history of cancer in other parts of the body, the type of treatment given (surgery, radiotherapy, chemotherapy or a combination of them), and data related to implant survival in case of loss, depending on the time in which it occurred.

The data collected were analyzed in an anonymized using the spreadsheet program Excel® (Microsoft, Redmond, WA, USA). Data included gender, age, oncological diagnosis and TNM classification and staging; the number of implants used and the sites of the implants placed; the date of the last follow-up was recorded or where appropriate the date of death. For the purpose of this service evaluation, implant survival was defined as an implant fixture still in situ and implant failure defined as implant fixture not in situ which had been lost or removed for whatever reason. Implant survival time was defined as the time interval from the date of implant placement to the date of implant failure or the last follow-up date, whichever occurred first.

All analyses were performed using the version 11 of SPSS® package (SPSS Inc, Chicago, IL, USA); in order to perform the tests, it was used Student's t-distribution, and also chi-square distribution and logistic regression to obtain absolute and relative figures (percentages), as well as measures of central tendency (means) and dispersion (standard deviation), with a degree of confidence of 95%. The study was approved by the Ethics Committee of the University of Barcelona Dental Hospital, No 38/2016.

Results

During the research period, 1,405 implants were placed in 466 patients. The study population comprised of 248

women (53%) and 218 men (47%) with a mean age of 54.2 years (range 20–79 years). Of the 466 patients, 414 healthy (1,233 implants) and 52 oncology ones (172 implants). The group of oncology patients was split into two: "cancer in other location" and "head and neck cancer".

A variety of implant systems were used which included 493 Avinent® (Avinent Implant System, Santpedor, Spain) implants, 373 Microdent® (Implant Microdent System, Barcelona, Spain) implants, 176 Mozo Grau® (Mozo Grau, Valladolid, Spain) implants, 141 Neodent® (JJ GC Indústria e Comércio de Materiais Dentários S.A. Neodent®, Curitiba, PR, Brazil) implants, 139 MegaGen® (MegaGen CO., Ltd, Daegu, Korea) implants, 16 BioHorizons® (Biohorizons Implant Systems, Birmingham, AL, USA) implants, 15 Mis® (Dentsply Implants, Mannheim, Germany) implants, 13 Nobel Biocare® (Nobel Biocare, Zurich, Switzerland) implants, 11 Phibo® (Phibo Dental Solutions, Barcelona, Spain) implants, 9 Galimplant® (Galimplant Dental Implant System, Lugo, Spain) implants, 5 Zimmer® (Zimmer Holdings®, Indiana, United States) implants, 4 Brånemark® (Nobel Biocare, Zurich, Switzerland) implants, 4 Brånemark Zygoma® (Nobel Biocare), 3 Straumann® (Institut Straumann, Basel, Switzerland) implants, 2 Klockner® (Klockner Implant System, Barcelona, Spain) implants and one Astra Tech® (Dentsply Implants, Mannheim, Germany) implant.

The analysis which compared the success versus failure of implants placed in all kinds of patients (1405 implants) during the referred period shows that the success rate was 96.65% (Table 1).

Comparing the success and the failure rates of implants placed in healthy patients versus oncology patients, a 97.16% success rate in healthy patients was verified, while the success rate in oncology patients reached 93.02% ($p=0.16$). In healthy patients, 1,233 implants were placed, of which 35 were lost. In oncology patients, 172 implants were placed, of which 12 were lost (Tables 2 and 3). Of the 12 failures implants, 2 were lost in the group "cancer in the other location" and 10 were lost in the group "head and neck cancer".

47 of 1405 implants failed. Comparing the time of each implant failure, there were more late losses than early ones (before or after implant loading): 36 implants were lost lately, and 11 implants were lost prematurely ($p=0.15$). (Tables 4– 6 and Fig. 1).

When the success rate in oncology patients is analyzed and the patients with head and neck cancer and cancer in

Table 1. Success x failure of implants – all patients

Total amount of implants	Success [amount (%)]	Failure [amount (%)]
1,405	1,358 (96.65%)	47 (3.35%)

Table 2. Implant success x failure in healthy patients

Total amount of implants	Success [amount (%)]	Failure [amount (%)]
1,233	1,198 (97.16%)	35 (2.84%)

Table 3. Implant success x failure in oncology patients

Total amount of implants	Success [amount (%)]	Failure [amount (%)]
172	160 (93.02%)	12 (6.98%)

other location are compared, there is a slight decrease in the success rate of the first group. The following graphic makes a comparison between the cited oncology patients vs. healthy patients (p=0.19). (Table 7, Fig. 2).

Of 52 oncology patients, 13 (25%) patients received some form of radiotherapy and 7 received radiotherapy in the head and neck (13%) region. When comparing the success rate of implants in irradiated patients vs. non-irradiated ones, 97.12% of the implants placed in non-irradiated patients were successful. Nonetheless, when regarded only patients that underwent radiotherapy, there is a lower success rate within the group who have undergone radiotherapy in the head-neck area, compared to patients which underwent radiotherapy in another location (p=0.17). (Table 8, Fig. 3).

Discussion

As shown by Laverty et al. (11), the use of dental implants as part of the oral and dental rehabilitation in head and neck oncology patients has become highly popular. This paper presents the implant survival rates in a large head and neck cancer patient cohort at a regional treatment center. The results obtained demonstrate that implant survival is high and reliable in this challenging patient group. In comparison with other studies, our findings are consistent with the literature, which reports implant survival ranging from 75 to 97.1% with average follow-up ranging from 30.9 months to 5.4 years (8,15,16).

For Tanaka et al. (17), implant therapy in irradiated patients is not less favorable than in non-irradiated patients, since they identified survival rates of 74.4% - 98.9%, with

the majority below 84% (20, 22). The success rate verified in this study was 97.12% in non-irradiated patients and 93.75% in patients who were irradiated in other parts of the body, except head and neck. When comparing irradiated patients in the head-neck area, the success rate drops to 80.56%. However, the follow-up period of both studies must be considered, since it may influence the percentage difference (17).

A meta-analysis that incorporated studies published from 2007 to 2013 compared implant placement in irradiated and non-irradiated patients in the head-neck area (18). The result showed no significant difference and concludes that implants are a truly accurate option of treatment to irradiated patients. Esposito et al. also conclude in their meta-analysis that radiation itself is not a contraindication to implants.

A study with irradiated patients had a success rate of 97.9% of all implants over 5 years of follow up (19). They came to the conclusion that radiotherapy had no significant impact on osseointegration or loss of osseointegration. In addition, according to the authors, the placement of dental implants leads to an improvement in food intake, speech and balance of the lower third of the face in cancer patients, therefore, implant placement has a strong and positive impact on their quality of life.

After 10 years of follow-up, Linsen et al. (9) reported a success rate of 84.7% in non-irradiated cancer patients compared to 95.6% in irradiated patients. Although the difference is apparently significant, these authors connect such difference within the non-irradiated group to the death of a patient due to a tumor. Excluded the non-irradiated deceased patient, they consider that the differences between the two groups are not statistically significant.

Table 4. Implant loss in healthy patients according to the time spent: late failures x early failures

Early failures		Late failures	
Failure rate	% of implants (total)	Failure rate	% of implants (total)
11	0.78%	36	2.56%

Table 5. Early failures x late failures of implants in healthy patients

Early failures		Late failures	
Failure rate	% of implants (total)	Failure rate	% of implants (total)
9	0.73%	26	2.11%

Table 6. Early failures x late failures of implants in oncology patients

Early failures		Late failures	
Failure rate	% of implants (total)	Failure rate	% of implants (total)
2	1.16%	10	5.81%

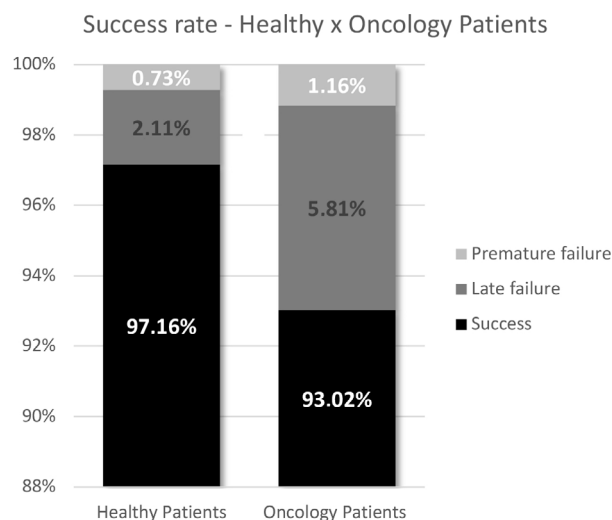


Figure 1. Healthy patients x Oncology patients.

A prospective study (16) evaluated the outcome and the satisfaction of cancer patients who have been rehabilitated with implant-supported or implant-retained mandibular prostheses up to 5 years after treatment. All the implants were placed during tumor resection surgery. 62%, i.e., 31 patients, received post-surgery radiotherapy (dose > 40 Gy in the implant area). During the study, 14 out of 76 implants failed, 13 in irradiated bone (89.4% survival rate) and 1 in non-irradiated bone (98.6% survival rate). They have figured out that cancer patients can benefit from the setting up of implants during tumor resection, with a high implant survival rate. Patients are highly satisfied with the rehabilitation treatment (16). The success rate in prosthetic rehabilitation of oncology patients is high and the adverse effects are low. Some authors conclude that the use of implants in cancer and irradiated patients is considered a good treatment option (15).

However, there are other authors who did find significant differences in their researches and stated that the implant success rate in irradiated patients is significantly lower when

compared to the success rate in non-irradiated patients. Some others researchers even report that radiotherapy is a contraindication for implant placement (20).

For Pompa et al. (14), the results accomplished in their study indicate that implant survival is directly related to the use or not of radiotherapy. Yerit et al. (15) achieved 72% success rate in irradiated patients versus 95% in non-irradiated ones during 8 years of follow-up. These results are consistent with those of other studies: Andersson et al. (21) achieved a success rate of 97.8% at 8 years and Kovács et al. (21) obtained 83.5% at 6 years. All of these authors attribute the lower incidence of success to reduced bone maturation, osseointegration, the dose of radiation to which the patients are subjected and the resection performed during the surgical act itself (9,15,20,21).

Ilde et al. (22) state that there is a significant difference and that the risk of implant failure is 2 to 3 times higher in irradiated than in non-irradiated bone.

A meta-analysis established that there were significant differences between the two types of treatment, but it also included articles published from 1979-2004, therefore, it did not cover the technical developments introduced in recent years, such as: three-dimensional planning, guided surgery and changes in the surface of the implant (18).

During a 13-year time span, Yerit et al. (15) analyzed

I. F. V. Silva et al. Table 7. Success of implants in healthy patients versus patients with head and neck cancer and patients with cancer in other locations

Healthy patients	Oncology patients	
	Other locations (n=109)	Head and neck
Total: 1,233	Total: 109	Total: 63
Success: 1,198	Success: 107	Success: 53
Success rate 97.16%	Success rate 98.17%	Success rate 84.13%

Table 8. Success rate in irradiated versus non-irradiated patients

	Non-irradiated	Radiation (other location)	Head and neck radiation
Success rate	97.12%	93.75%	80.56%

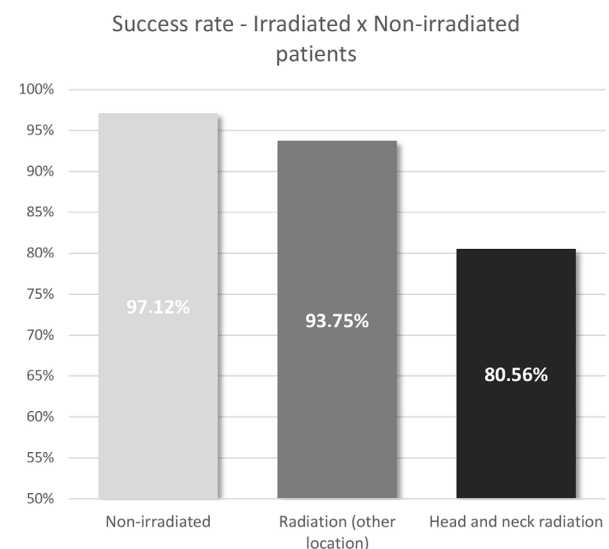
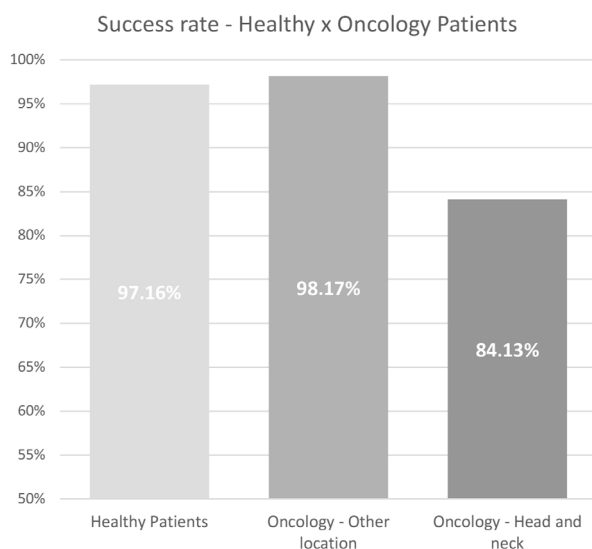


Figure 2. Success rate - Healthy x Oncology patients.

Figure 3. Success rate - Irradiated x Non-irradiated patients.

71 patients treated with post-radiotherapy dental implants with a total dose of 50 Gy. The general survival rates of all implants in two, three, five and eight-year time span were 95%, 94%, 91% and 75%. 44 implants failed in 21 patients during the research period. Implants placed in irradiated bone have presented significantly lower survival rates when compared to non-irradiated bone.

It is known that the radiation dose negatively influences the osseointegration process of the implant. However, there is no consensus on which dose limit patients should receive to ensure that the implant survival rate remains as expected. There are studies that establish that doses higher than 50 Gy modify bone healing, which endangers osseointegration of the implant (23). Verdonck et al. (24) reinforced that the survival rate of the endosseous implants in irradiated bones is lower than in non-irradiated ones, especially when the radiation dose is higher than 50 Gy (24). Other authors (21), state that there is no significant difference regarding the implant survival rate in the group of patients with doses below 60 Gy (90.2%) compared to those who received a dose equal to or greater than 60 Gy (84.3%).

Javed et al. (23) concluded that when patients receive 50–60 Gy, there is no negative influence on the osseointegration process. Ihdé et al. (22), in turn, commented in their literature review that no failure was recorded in the survival rate of the implant under doses below 45 Gy (placed before or after irradiation), regardless of the gap in which the studies were conducted.

Some authors believe that the use of adjuvant therapies such as hyperbaric oxygen therapy (HBOT) may decrease the harmful effect of radiotherapy and, therefore, increase the success rate of implants in irradiated patients. HBOT is a therapy that is being used in many medical conditions, since it raises the levels and diffusion of oxygen in the local tissue by inducing capillary angiogenesis, increasing bone metabolism and stimulating collagen synthesis. In addition, it is believed to increase the body's ability to repair tissues that were damaged by radiotherapy (9,15,17).

Several authors have stated that the use of HBOT is positive, increasing implant success rate when compared with patients not treated by this therapy, so they support its use (19,24). Similar results can be found in the research made by Schoen et al. (12), with success rates of 93.9% in patients that underwent HBOT and 85.2% in patients that did not undergo such therapy.

Carr et al. (25), in a retrospective study, analyzed 700 medical records from patients of the Master of Periodontology at the Hospital of the Catholic University of Leuven, Belgium, in a period of 2 years and 8 months after implant placement. The results show that radiotherapy has a higher influence on late implant losses in relation to smoking patients or with some systemic alteration. In

this study, the success rate of implants in cancer patients has dropped considerably when the patient has been irradiated and is also a smoker. In irradiated non-smoking patients, there was a success rate of 94.14, versus 58.82% in irradiated smoking patients.

When reviewing the literature on implant survival/failure in oncology patients there is a lack of well-designed prospective studies with long-term follow-up. These studies are hugely variable, to make an effective comparison is difficult and, in some cases, inappropriate.

For Laverty et al. (11), accordingly, there is a clear need for a standardization of reporting implant survival and failure. There is reason- able overall agreement on the criteria for implant survival and failure; however, there is no agreed minimum data set for collection to enable the comparison of studies, and furthermore there is no consensus on the best way to measure outcomes, analyses endpoints and the most appropriate way to statistically analyze the data.

This retrospective study describes the survival rate of implants placed in cancer patients and non-cancer patients. This study reports high implant survival when used as part of the routine oral rehabilitation of oncology patients. Based on our findings, there are differences in the success rates between the two groups, however, they are not significant, and are similar to those found in the literature. The success rate of implants placed in irradiated patients is slightly lower, although not significant, than in implants placed in non-irradiated patients; nevertheless, it decreases in those patients irradiated in the head-neck area, so, it's possible to state that this rate could be related with the irradiated area and probably with the incoming radiation dose. Generally speaking, the loading time of implants in oncology patients may influence their predictability. Based on what has been written, this service evaluation supports the use of dental implants in oral rehabilitation of this complex patient group, but it is important to recognize that this is an analysis of a complex care pathway with a large number of confounding variables. The findings should not be considered as generalizable beyond the specific environment in which this study was conducted.

Resumo

Pacientes com histórico de câncer são cada vez mais comuns no consultório odontológico. O tratamento de pacientes com câncer requer uma equipe multidisciplinar, que deve incluir o dentista, a fim de controlar as complicações que ocorrem na cavidade oral e também para tratar o paciente com qualquer uma das modalidades de tratamento: cirúrgica, médica, radioterápica ou suas possíveis combinações. Os implantes dentários podem ser uma opção de tratamento segura e previsível para reabilitação protética. O objetivo deste artigo é propor um estudo retrospectivo sobre a taxa de sucesso de implantes osseointegrados em pacientes oncológicos e não oncológicos atendidos no Mestrado em Odontologia em Pacientes Oncológicos e Imunodeprimidos, bem como

no Mestrado em Medicina, Cirurgia e Implantodontia Oral do Hospital Odontológico da Universidade de Barcelona, entre julho de 2011 e março de 2016. Foram revisados 466 pacientes, com um total de 1405 implantes instalados, considerando o histórico oncológico dos pacientes e a taxa de sucesso do implante. Resultados: A taxa de sucesso total no período em questão foi de 96,65%. Na comparação entre pacientes com câncer e saudáveis, a taxa de sucesso foi de 93,02% no primeiro caso e 97,16% no segundo. Conclusão: De acordo com a revisão da literatura, nossos resultados encorajam a colocação de implantes em pacientes com câncer, é importante reconhecer que esta é uma análise complexa que requer cuidado devido ao grande número de variáveis. No entanto, os resultados não devem ser considerados de forma generalizada.

Acknowledgements

This is for everyone who had my back throughout these years – I couldn't have done it without you. Thank you! Firstly, I would like to thank to the University of Barcelona for supporting this study and express my thanks to all the group this Master. My very special thanks to Carlos Omaña, Enric Jané and José Lopez. I should like to thank the Ethics Committee of the University of Barcelona Dental Hospital was approved this study No 38/2016.

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Received August 17, 2020
Accepted October 20, 2020