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Dental Implants

Immediate implant placement in edentulous oral cancer patients: a long-term retrospective analysis of 207 patients

J. G. H. Wetzels[1,2], G. J. Meijer[1], A. F. J. de Haan[3], M. A. W. Merkx[1,4], C. M. Speksnijder[1,2,5]

[1]Department of Oral and Maxillofacial Surgery, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Department of Oral and Maxillofacial Surgery and Special Dental Care, University Medical Center Utrecht, The Netherlands; [3]Department for Health Evidence, Section Biostatistics, Radboud University Medical Center, Nijmegen, The Netherlands; [4]Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands; [5]Julius Center Sciences, University Medical Center Utrecht, Utrecht, The Netherlands

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Abstract. Although the functional benefits of implants in the rehabilitation of edentulous cancer patients are well-known, most studies report on postponed implant placement. The outcome of immediate implant placement regarding successful rehabilitation, implant loading and survival is unclear. Two hundred and seven edentulous oral cancer patients that received implants during ablative surgery at the Radboud University Medical Centre between 2000 and 2011 were included. Data regarding the oncological treatment, implant placement, follow-up and prosthodontic rehabilitation were recorded retrospectively with a follow-up period of 5–17 years. Functioning implant-retained dentures were made in 73.9% of the patients. Of the surviving patients, 81.9% had functioning dentures after 2 years and 86.3% after 10 years. Patients with ASA score 1 and younger patients were rehabilitated more frequently. The median time of functioning denture placement was 336 days after surgery, with a negative influence of postoperative radiotherapy. Implant survival was 90.7%, and was lower when the implant was placed in a jaw involved in the tumour. Immediate implant placement during oral cancer surgery led to a high number of edentulous patients rehabilitated with implant-retained dentures, which are placed at an early time.

Key words: dental implants; edentulous mouth; mouth neoplasms; prosthodontics; radiotherapy.

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Patients treated for oral cancer often suffer from permanent functional impairments after surgery, especially when postoperative radiotherapy is administered. Important functions at risk include chewing, speech and swallowing, and their deterioration negatively influences quality of life[1–3]. Oral cancer patients who are edentulous, or become edentulous during tumour surgery, are even more at risk of losing oral functions, because fabrication of conventional full dentures is often difficult or impossible. Especially in the lower jaw, ablative surgery may reduce the area of support for the dentures, while radiotherapy-induced xerostomia and atrophy of the mucosa underlying the dentures may hinder denture tolerance even

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more. Because satisfying conventional dentures can only be made in 30–50% of this patient group, a large number of edentulous patients will receive no dentures or wear solely an upper denture for aesthetics or speech[4,5]. Patients without functioning dentures have markedly decreased masticatory performance, which may restrict them to soft foods or fluids permanently[6,7].

When full dentures are retained by implants, they increase the dentures' stability and retention, which has been widely documented in healthy edentulous patients[8,9]. In patients treated for oral cancer, prosthodontic rehabilitation using implants leads to more functioning dentures, improved patient chewing ability and denture satisfaction compared with conventional dentures[5,10–12]. To date, the timing of implant placement in oral cancer patients remains a matter for discussion.

Most head and neck oncology centres place implants after a disease-free period of at least 6–12 months following oncological treatment, on the condition that conventional dentures could not be made or when patients report significant functional problems with their dentures. This protocol of postponed implant placement is reported to have a high rate of successful rehabilitation and high implant survival, ranging between 93% and 96%[13–15]. Even higher implant survival is reported when implants are placed in the mandible versus the maxilla, or in native bone versus autologous bone grafts[16,17]. Although past studies suggested a significant difference in implant survival between irradiated and non-irradiated patients with oral cancer, recent studies that include modern radiation techniques report more similar implant survival[18]. The main disadvantage of the postponed protocol is that, in the end, many patients will not receive implants, because they are unwilling or incapable of undergoing an extra surgical and prosthodontic procedure. Furthermore, in patients that received high-dose radiotherapy in the interforaminal area, the risk of developing osteoradionecrosis either makes implant placement impossible or necessitates additional hyperbaric oxygen therapy[19].

An alternative strategy is immediate placement of implants during the ablative surgery. In this protocol, edentulous patients in whom problems with the prosthodontic rehabilitation are very likely receive implants in the lower jaw or in both jaws, in the same session as the tumour removal. This protocol increases the number of patients rehabilitated with implant-retained dentures and increases the speed of rehabilitation[20]. Because osseointegration takes place before postoperative radiotherapy, implant failure is lower or at least equal to postponed implant placement[21–23]. However, there are also disadvantages to immediate implant placement. Obviously, a number of implants are not utilized due to tumour recurrence, comorbidity, osteoradionecrosis or patient death. Also, the costs of prosthodontic rehabilitation for the total patient group are higher with immediate placement compared with postponed placement, although the individual costs are lower[5]. It is furthermore speculated that immediately placed implants sometimes may not be loaded due to improper placement or soft-tissue problems, and might increase the risk of post-treatment complications such as osteoradionecrosis.

The first aim of this study was to determine implant loss, implant failure, implant loading and denture rehabilitation in edentulous oral cancer patients that received implants during ablative surgery. The second aim was to identify demographic, oncological and treatment-related factors of influence on these outcome measures.

Material and methods

Subjects

All consecutive patients who were treated for oral cancer in the Radboud University Medical Center (Radboud UMC; Nijmegen, The Netherlands) in the years 2000–2011 were examined retrospectively. When patients had a primary malignancy of the oral cavity for which they underwent ablative surgery with a curative intent, their dental records were also screened. Patients were included when they were edentulous in both jaws before surgery or became edentulous during surgery, and received interforaminal implants during ablative surgery. Exclusion criteria were the presence of dental implants prior to oncological treatment and previous or synchronous head and neck malignancies. Patients received postoperative radiotherapy within 6 weeks after surgery based on the histopathologic findings, according to the guidelines of the Dutch Head and Neck Society. The study was conducted in accordance with the World Medical Association Declaration of Helsinki (June 1964) and subsequent amendments, and the rules for reporting observational studies from the STROBE statement.

Implant placement

All oral cancer patients received preoperative dental screening by a multidisciplinary team including a head and neck surgeon, maxillofacial prosthodontist, dentist, and an oral hygienist. Teeth with extensive caries, periodontal disease or periapical periodontitis, were removed during surgery. Teeth were also removed when they had a dubious prognosis and were in a potentially high-dose-radiation area. Prior to oncological treatment, a prosthodontic rehabilitation plan was made for dentate patients with a mutilated dentition, which included the fabrication of partial dentures, crowns and bridges, with or without implant retention. When prosthodontic rehabilitation was not possible due to few remaining teeth or an unfavourable occlusal relationship, patients were made edentulous during surgery.

All edentulous patients, pre-existent or new, were eligible for the placement of two to four implants in the interforaminal region of the mandible. Patients did not receive mandibular implants when insufficient bone height was present, when a segmental resection of the entire interforaminal area was conducted, when there was a lack of motivation for rehabilitation with implant-retained dentures or when there was advanced cognitive impairment. Additionally, implants were placed in the upper jaw in patients who received a maxillectomy and in patients with pre-existing retention problems of the upper denture, provided that sufficient bone volume was present and retention problems with a conventional upper denture could be expected. All implants were Brånemark® Mk II/III (Nobel Biocare AB, Göteborg, Sweden) two-phase implants and were placed in native bone. Implants were loaded after a minimum healing period of 3 months. When patients received postoperative radiotherapy, implants were surgically exposed at least 6 months after radiotherapy.

Data collection

The databases of the hospital and the department of maxillofacial prosthodontics at the Radboud UMC were examined. Hospital data included routine oncology check-ups up to 5 years after treatment, as well as additional appointments regarding implantology, tumour recurrence, or complications with a follow-up period between 5 and 17 years. At the prosthodontics department, data were collected with a follow-up period between 5 and 17 years, regarding both the fabrication and modification of dentures. When dentures were made at an external prosthodontic unit, data from this unit

Table 1. Demographics and tumour details of 207 edentulous oral cancer patients with implants placed during ablative surgery.

Variable		*n*	%
Sex			
	Male	124	60
	Female	83	40
Mean age, years (SD)			
Smoking			
	Yes	128	62
	No	79	38
Diabetes			
	Yes	24	12
	No	183	88
ASA score			
	1	28	13
	2	120	58
	3	59	29
Tumour location[a]			
	Floor of mouth	70	34
	Tongue	47	23
	Lower alveolar process/lip	53	25
	Maxilla or cheek	37	18
Tumour type			
	Squamous cell carcinoma	199	96
	Osteosarcoma	1	1
	Glandular carcinoma	7	3
Tumour size (cT of TNM)			
	T1	39	19
	T2	104	50
	T3	21	10
	T4	43	21
Nodes (cN of TNM)			
	N0	169	82
	N1	14	7
	N2	24	11

SD, standard deviation; ASA, American Society of Anesthesiologists.
[a] Tumour location can be further subdivided into anterior floor of mouth (47), posterior floor of mouth (23), tongue (47), lower alveolar process (20), retromolar trigone (24), lower lip (9), maxilla (16) and cheek (21).

were also acquired. Sex, age, smoking, diabetes and the American Society of Anesthesiologists Physical Status score (ASA score) as reported at the time of surgery were obtained. A distinction was made between patients who smoked daily and those who smoked less frequently or not at all. Data on tumour type, tumour location, preoperative dental status, pre- and postoperative TNM staging (7th edition), tumour resection, reconstruction, histopathology, radiotherapy, chemotherapy, tumour recurrence, osteoradionecrosis and pathological fractures were assessed. There was mandibular tumour involvement when the tumour was primarily located on the lower alveolar process or the retromolar trigone, and in other tumour locations where a rim or segmental mandibular resection was performed. There was maxillary tumour involvement when the tumour was primarily located on the maxilla and in other locations where a maxillectomy was performed.

Furthermore, implant placement, loading, survival, failure, date of denture placement and denture functionality were recorded. Dentures were considered functional when patients used them to eat their meals. The Dutch population register was accessed to verify the information on patient survival.

Statistical analysis

Binary outcome measures, which included placement of dentures (yes/no), osteoradionecrosis requiring surgery (yes/no) and implant loading (yes/no) were first analysed univariately with logistic regression. All possible factors of influence that had statistical significance ($P < 0.05$) in the univariate analyses, were used in multivariate logistic regression models with backward elimination with 0.05 significance level for removal. The other outcome measures were displayed in days after surgery. These included placement of dentures, survival of dentures, implant loading, implant survival and patient survival. These outcome measures were first analysed univariately with Cox proportional hazard models, using the log-rank test to calculate statistical significance. The factors with a significant influence ($P < 0.05$) in the univariate analyses, were included in multivariate Cox proportional hazard models, using backward elimination with 0.05 significance level for removal. Kaplan–Meier survival curves were constructed for patient survival and implant survival. Patients were censored at the end of the follow-up period, or at the time of death. Timing of denture placement and survival of dentures were analysed with a follow-up period of 5 years, the other outcome measures with a minimum of 5 and a maximum of 17 years. All tests were two-sided, and differences with a P-value <0.05 were considered to be statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

A total of 602 patients had a primary malignancy of the oral cavity, of which 255 were edentulous before tumour surgery and 76 were made edentulous during surgery. Of these 331 edentulous patients, 207 patients received interforaminal implants during ablative surgery. Details regarding the study group and the oncological treatment are displayed in Tables 1 and 2. The average follow-up period was 9.8 years, with a minimum of 5 and a maximum of 17 years. Of the 207 patients, 125 were still alive 5 years after surgery (60.4%). Fig. 1 shows the survival curve of the study group up to 12 years. Patient survival decreased with higher ASA score [ASA 3 versus 1, hazard ratio (HR) 3.559, $P = 0.002$] and higher pN stage (N2 versus N1, HR 2.778, $P < 0.001$). Patients with a tumour of the maxilla or cheek had a lower survival rate compared with those with a tumour of the tongue (HR 2.455, $P = 0.003$).

Functioning dentures

Of 207 patients, 153 patients received functioning dentures (73.9%), 51 patients did not receive functioning dentures (24.6%) and three patients were lost to follow-up. Thirty patients died due to tumour-related causes before dentures could be made. Other reasons that prevented the fabrication of functioning dentures included trismus ($n = 8$), poor soft tissue conditions ($n = 7$), pathological fracture or osteoradionecrosis (ORN) of the mandible ($n = 3$), poor general health ($n = 2$) and lack of motivation ($n = 1$). In the multivariate analysis, ASA score was a good predictor for receiving functioning

Table 2. Details regarding the oncological treatment of 207 edentulous oral cancer patients with implants placed during ablative surgery.

Variable		*n*	%
Postoperative radiotherapy			
	No	93	45
	Yes[a]	114	55
Tumour size (pT of TNM)			
	T1	56	27
	T2	95	46
	T3	16	8
	T4	40	19
Nodes (pN of TNM)			
	N0	140	68
	N1	19	9
	N2	48	23
Mean tumour diameter, cm (SD)			
Mandibular resection			
	No resection	127	61
	Rim	64	31
	Segment	16	8
Reconstruction of soft tissue			
	Primary closure	65	31
	Local flap	5	2
	Split-thickness skin graft	73	36
	Vascularized flap[b]	64	31
Reconstruction of bone defect			
	No reconstruction needed	174	84
	Fibula flap	4	2
	Reconstruction plate	12	6
	Obturator prosthesis	17	8
Edentulous			
	Before ablative surgery	151	73
	During ablative surgery	56	27
Mandibular implants			
	2	133	64
	3	66	32
	4	8	4
Radiation dose on tumour area			
	<50 Gy	4	4
	≥50 and <55 Gy	2	2
	≥55 and <60 Gy	22	19
	≥60 Gy and ≤70 Gy	86	75

SD, standard deviation; Gy, gray.

[a] Six patients received postoperative chemoradiotherapy.

[b] Vascularized flap reconstruction can be further subdivided into radial free forearm flap (40), anterolateral thigh flap (16), fibula flap with skin paddle (4), platysma flap (2), pectoralis major flap (2).

dentures, because all patients with ASA score 1 had functioning dentures (Table 3). For patients with ASA score 2 or 3, the odds of receiving functioning dentures were lower with higher age at baseline [odds ratio (OR) 0.947 per year increase, $P = 0.006$]. The odds were higher in patients with lower pN stage (N0 versus N2, OR 6.275, $P < 0.001$), less extensive soft tissue reconstruction (primary closure versus vascularized flap, OR 5.546, $P = 0.003$) and when less mandibular implants were placed (two versus three implants, OR 3.062, $P = 0.007$).

The median time of functioning denture placement was 336 days after surgery. In the multivariate analysis, receiving radiotherapy significantly delayed the placement of dentures (233 versus 420 days, $P = 0.005$). Placement of dentures was faster with less advanced pT stage [T1 (289 days) versus T4 (400 days), $P = 0.027$], pN stage [N0 (290 days) versus N2 (463 days), $P = 0.002$] and reconstruction of soft tissue [primary closure (259 days) versus vascularized flap (435 days), $P = 0.001$]. Of 153 functioning dentures placed, 103 were still functional 5 years after surgery (67.3%). Reasons why patients lost their functioning dentures included patient death ($n = 37$), surgery due to tumour recurrence ($n = 11$), ORN ($n = 1$) and soft tissue problems ($n = 1$). Higher age significantly reduced denture survival (HR 1.051 per year increase of age, $P < 0.001$). Survival of the functioning dentures is displayed in Fig. 1. The percentage of surviving patients with functioning dentures was 62.2% 1 year after surgery, 81.9% after 2 years, 81.6% after 5 years and 86.3% after 10 years.

Implant loading and survival

A total of 548 implants were placed, 496 in the mandible and 52 in the maxilla. In one patient, a virtual implant planning and surgical template was used to place the implants in the maxilla. In total, 383 implants were loaded (69.9%), 156 implants were not loaded (28.5%) and three patients with a total of nine implants were lost to follow-up. A total of 64 implants (11.7%) were not loaded because satisfactory dentures could not be made, and 83 implants (15.1%) were not loaded

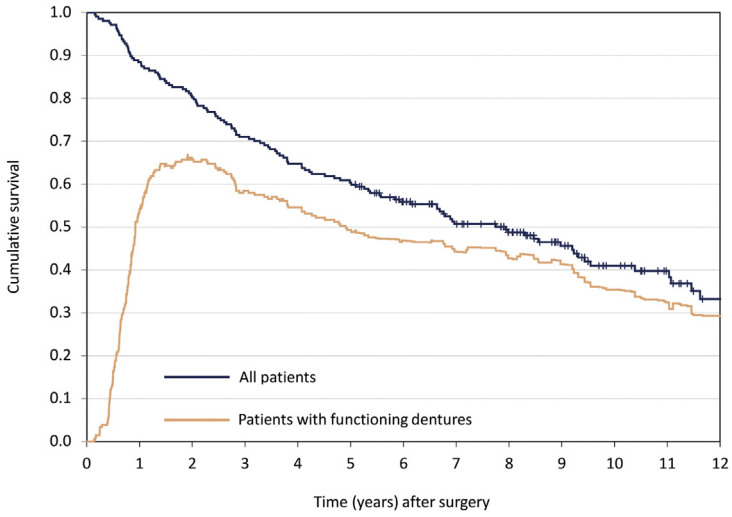

Fig. 1. Kaplan–Meier survival curve of 207 patients, with an observational period of 12 years after tumour surgery (upper line). Censored observations, due to the end of the follow-up or patient death, are cross-hatched. The lower line represents the proportion of surviving patients with functioning dentures.

because patients had died before possible denture rehabilitation. In nine patients functioning dentures were made, while one of the implants was not loaded; eight implants were not loaded due to improper positioning (seven in the mandible, one in the maxilla), and one implant was removed due to ORN of the mandible before dentures could be made. Improper positioning of one mandibular implant occurred more frequently in patients with three (7.6%) or four mandibular implants (12.5%), compared with patients with two mandibular implants (0.8%).

In the total follow-up period, 51 of 548 implants were lost (9.3%). Figs 2 and 3 show survival curves of the 548 implants up to 5 years after placement. Reasons for implant loss were tumour recurrence requiring surgery ($n = 18$), ORN of the mandible ($n = 16$), peri-implantitis ($n = 13$), failed osseointegration ($n = 2$) and mandibular fracture ($n = 2$). The only factor with a significant influence on implant loss in the multivariate analysis was tumour involvement of the jaw in which the implant was placed. A total of 251 of 548 implants were placed in a jaw involved in the tumour. Thirty-two of these implants were lost (12.7%), compared with 19 of 297 implants that were placed in a jaw without tumour involvement (6.4%). The risk of implant loss was higher when there was tumour involvement compared with no tumour involvement (HR 2.760, $P = 0.006$). Implant placement in the mandible or the maxilla did not influence implant loading, loss or failure significantly.

ORN of the mandible requiring surgery under general anaesthesia occurred in 14 of 114 patients who received radiotherapy (12.3%). Smoking had a significant effect on the occurrence of ORN in the univariate analysis ($P = 0.040$), because 12 of 14 patients with ORN were smokers. However, this effect was not significant in the multivariate analysis ($P = 0.058$). Furthermore, a more advanced mandibular bone reconstruction significantly increased the occurrence of ORN in the multivariate analysis ($P = 0.042$).

Discussion

In this study, immediate placement of implants in oral cancer patients who were edentulous or became edentulous during tumour surgery led to a high percentage of functioning implant-retained dentures (73.9%). Two years after tumour surgery, 81.9% of the survivors wore functioning implant-retained dentures, a number that further increased after 10 years (86.3%). The median time of functioning denture placement was 336 days after surgery, and was longer in patients who did not receive postoperative radiotherapy. In the total follow-up period, implant survival was 90.7%, which is comparable to studies on postponed implant placement[15,18,24].

The number of patients rehabilitated with functioning dentures is higher following the immediate implant placement protocol (73.9%) compared with postponed implant placement, where half of the patients did not receive functioning dentures[5]. It is likely that patients often refrain from postponed implant placement, due to a lack of motivation for an additional surgical procedure or hyperbaric oxygen therapy when necessary. Furthermore, when the site-specific radiation dose was too high, implant placement is sometimes not possible due to the risk of osteoradionecrosis. The percentage of sur-

Table 3. Multivariate logistic regression model for receiving functioning dentures.[a]

Variable		OR	95% CI	*P*
Age (per year increase)		0.947	0.910–0.983	0.006
Reconstruction of soft tissue				
	Primary closure	5.546	1.949–17.575	0.003
	Local flap	0.601	0.060–5.259	0.237
	Split-thickness skin graft	1.673	0.703–4.032	0.819
	Vascularized flap	1	N/A	N/A
Nodes (pN of TNM)				
	N0	6.275	2.627–15.853	<0.001
	N1	1.992	0.536–7.962	0.714
	N2	1	N/A	N/A
Mandibular implants				
	2	3.062	1.356–6.912	0,007
	3	1	N/A	N/A
	4	1.805	0.290–15.625	0.138

CI, confidence interval; N/A, not applicable; OR, odds ratio estimates for receiving functioning dentures.

[a] Patients with ASA score 1 all received functioning dentures. Therefore, only patients with ASA score 2 or 3 were included in this model.

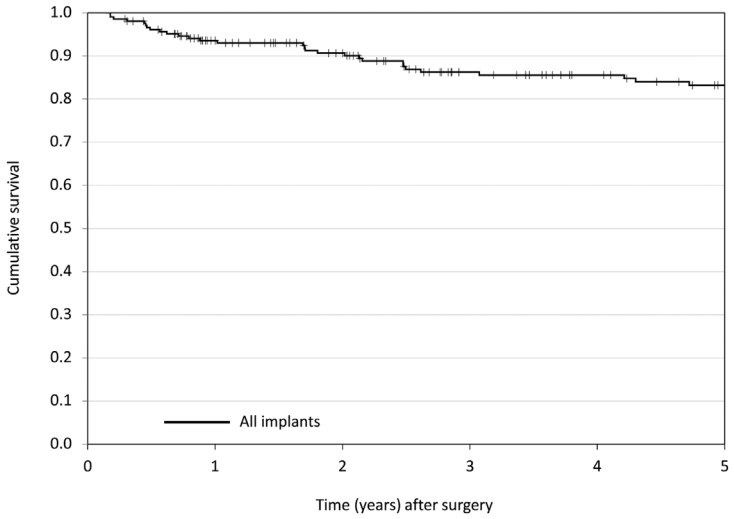

Fig. 2. Kaplan–Meier survival curve of 548 implants, with an observational period of 5 years after implant placement. Censored observations due to patient death, are cross-hatched.

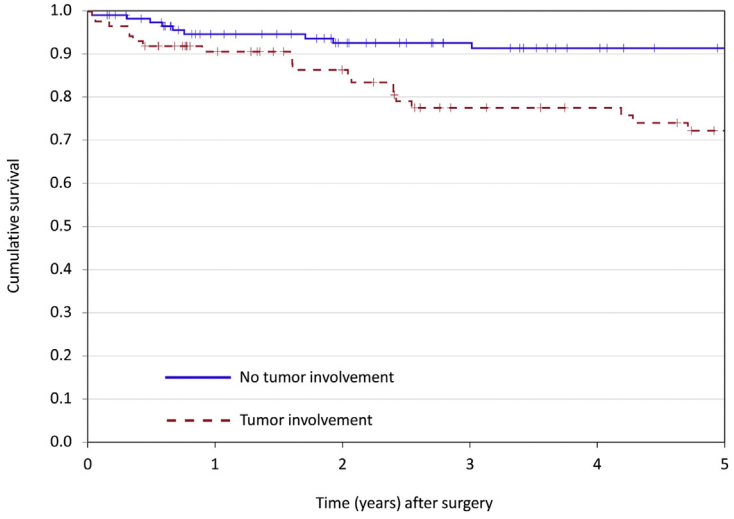

Fig. 3. Kaplan–Meier survival curve of 297 implants placed in a jaw without tumour involvement (solid line) and 251 implants placed in a jaw with tumour involvement (dashed line), with an observational period of 5 years after implant placement. Censored observations due to patient death, are cross-hatched.

vivors with functioning dentures in this study further increased at 2-year (81.9%) and 10-year follow-up (86.3%), because patients with a worse oncological prognosis and worse survival received dentures less frequently. Furthermore, good general health (ASA score 1) and lower age at baseline were predictors for receiving functioning dentures.

Most patients received functioning dentures within 1 year of surgery, and radiotherapy was one of the main delaying factors (233 versus 420 days after surgery). This is in accordance with another study on immediate implant placement[11]. Studies on postponed implant placement show a markedly slower prosthodontic rehabilitation, ranging from 24 to 60 months after surgery[5,14,25]. The main reason for this is that in most head and neck oncology centres, implants are placed after a disease-free period of at least 6–12 months. Most systematic reviews indicate that the risk of implant failure is higher when implants are placed within 6 months after finishing radiotherapy[23,26], and some even show higher failure rates within 12 months[27]. However, it seems undesirable to further postpone implant placement, because tissue fibrosis due to ischaemia and reduced cell reproduction starts 6 months after radiotherapy and increases over time[28]. Because prosthodontic rehabilitation is faster with immediately placed implants, the recovery of the masticatory function is also quicker[6], which in turn may lead to a better function in the long-term.

Of the 548 implants placed, 383 were loaded (69.9%). Studies on postponed placement report slightly higher implant loading, between 73% and 91%[5,22,25,29,30]. This advantage of postponed placement, can be explained by the fact that patients with a poor oncological prognosis, trismus and bad soft tissue conditions do not receive implants in this protocol. Only eight implants in our study were not loaded due to improper positioning, and this was more frequent in patients with three or four mandibular implants. However, in all of these patients, functioning dentures could still be made. Implant survival was 90.7% in the total follow-up period, which is comparable to both another study on immediate placement[11] and to studies on postponed placement, which report survival rates between 83% and 96%[14,15,18,24]. Some of these studies report that survival is lower in irradiated bone[20] or in the maxilla compared to the mandible[13,16], although our study found no significant differences between these groups. This can be explained by the relatively small number of implants lost (51), and it is possible that a future study with more participants will identify a statistically significant effect for both factors. In our current study however, implants placed in a jaw involved in the tumour had significantly lower implant survival (87.3%) than implants in a jaw without tumour involvement (93.6%).

Strengths of this study are the large number of patients (207), the long follow-up (5–17 years), and the use of multivariate Cox proportional hazard models, in which we analysed many possible factors of influence. A limitation is the retrospective design of this chart study. If the data had been collected prospectively, more accurate estimates of treatment outcome and risk factors could have been calculated. Furthermore, subgroups such as chemotherapy, diabetes, tumour type and fibula flap reconstruction had only a small number of patients, making it more difficult to identify them as factors with statistically significant influence.

Reconstructive protocols after ablative surgery have been optimized in recent decades. Free flap reconstruction has become the standard of care for large surgical defects, including a hemiglossectomy, a segmental mandibular defect or a defect involving three or more functional anatomical units[31,32]. It is likely that in future studies, more patients will be rehabilitated with a vascularized flap than the 31% in our study, which in turn will positively affect oral functions such as

speech, swallowing and masticatory function. Furthermore, implants can be placed more accurately using a virtual implant planning and surgical template, allowing the implant positioning to better suit the prosthodontic needs. Such virtual planning can also be used to immediately place implants in vascularized bone at the time of the tumour resection and reconstruction, and appears to be a reliable treatment technique[33]. By carefully planning the positioning of the implants, interference with the fixation screws is avoided and implants are placed in the most optimal bone.

The Dutch healthcare system up to 2019, provides total coverage of costs for the oncological treatment and rehabilitation of oral cancer patients, including placement of implants and dentures when needed. The authors acknowledge that reimbursements for healthcare can be very different in other countries, where patients often have to contribute to the expenses for oral rehabilitation. Due to the current differences between health insurance systems, many oral cancer patients might not be able to profit from the functional benefits of (immediate) implant placement, and end up without functioning dentures. Future research should focus on further individualizing the prosthodontic rehabilitation of these patients, thereby reducing the total costs for rehabilitation, and increasing the number of patients that can receive the best treatment.

In conclusion, this study demonstrated that implant placement during oral cancer surgery results in a large number of edentulous patients rehabilitated with implant-retained dentures, which are placed at an early stage. Patient age, ASA score and tumour involvement of the jaw might increase the cost-effectiveness when taken into account before implant placement.

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Competing interests

None.

Ethical approval

This study was approved by the Ethics Committee of the Radboud University Medical Center (reference number 2020-6210).

Patient consent

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Address:
Caroline M. Speksnijder
Department of Oral and Maxillofacial Surgery and Special Dental Care
University Medical Center Utrecht
G05.122
P.O. Box 85.500
3508 GA Utrecht
The Netherlands
Tel.: +31 88 7568040
E-mail: c.m.speksnijder@umcutrecht.nl