

# A retrospective cohort study on dental implant survival in patients with grafted alveolar clefts

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## Abstract

**Objectives:** The aim of this study was to assess the survival rate of dental implants inserted in an alveolar cleft area where one or more bone graft procedures were performed and to identify possible factors that affect the survival rate.

**Materials and Methods:** The available data from 78 implants placed in 64 patients with grafted alveolar clefts were retrospectively analysed. Statistical analyses were performed using Kaplan–Meier survival analysis, log-rank tests and univariable Cox proportional hazard models.

**Results:** The median follow-up period from insertion to the last follow-up appointment was 46 months (IQR: 29–79.3). In five patients, a single implant failed. This resulted in a cumulative survival rate of 95.0% at median follow-up. The factors investigated in this study did not have a significant effect on implant survival.

**Conclusions:** Dental implants placed in patients with alveolar clefts are a reliable treatment option for dental rehabilitation.

## KEYWORDS

cleft lip, cleft palate, dental implants, survival analysis

## 1 | INTRODUCTION

An orofacial cleft is a congenital malformation in which closure of the lip, alveolus, or palate, which normally occurs during the first trimester of pregnancy, does not occur or occurs incompletely (Watkins et al., 2014). This malformation can be observed in various degrees of severity, and its prevalence differs according to sex, race, maternal age and risk factors (e.g. smoking and drinking) (Harkins et al., 1962; Watkins et al., 2014). Orofacial clefts are a rare craniofacial disorder, with an incidence of 15 in 10,000 people born in Europe (European Commission, 2019; Fleurke-Rozema et al., 2016). Patients with alveolar clefts have little or no bone in the cleft area which inhibits dental eruption and alignment. Therefore, alveolar bone graft (ABG) procedures are performed to close bony defects.

ABG is usually performed in children born with a cleft in the alveolus. These patients also commonly have hypodontia, a condition in which one or more teeth are missing. The prevalence of hypodontia in both deciduous and permanent dentitions increases with the severity of orofacial cleft (Ranta, 1986). The most common missing teeth in cleft patients with hypodontia are upper lateral incisors (Tsai et al., 1998). When present, the upper lateral incisors are often underdeveloped and lost early during the patient's life, necessitating dental implants. If a lateral incisor is present and of sufficient quality, the teeth are orthodontically aligned. In cases of agenesis of the lateral incisor, the cuspid can be positioned next to the central incisor. Another option is to maintain the edentulous gap until the patients are fully grown, then insert an implant. When bone volume is insufficient at the time of dental implant placement, an additional guided bone regeneration

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(GBR) procedure is necessary. As a result of (multiple) bone graft procedures, the quality of the grafted bone and surrounding soft tissue is often less optimal than that of the non-cleft area, resulting in lower survival rates of dental implants (Kramer et al., 2005; Tonetti et al., 2008).

Dental implants are a distinguished treatment option for patients in need of dental rehabilitation (Howe et al., 2019). The first successful study of dental implant placement in a cleft patient was published in 1991 (Verdi et al., 1991). In this study, it was stated that there are multiple advantages to this procedure. A single-unit replacement is cosmetically more acceptable than a multiunit bridge. In healthy adjacent teeth, the tooth structure is spared and the problem of large pulp chambers on abutment teeth in patients of this age group is avoided.

Currently, dental implant placement is considered a reliable treatment option for hypodontia in patients with an alveolar cleft because of its safety, good overall prognosis and low morbidity (Sales et al., 2019). Dental implant failure can be divided into early and late failures. Early failures occur within the first 3–5 months post-surgical and late failures occur during the period after successful tissue integration (Buser et al., 1990). In a review paper on 483 implants, Sales et al. (2019) reported a survival rate of 93% for dental implants with a mean follow-up of more than 5 years. Normally, cleft patients receive dental implants at a younger age than non-cleft patients (Sales et al., 2019). Moreover, studies on the survival rate of dental implants in cleft patients have reported a relatively short follow-up period or small sample size, making it difficult to understand the potential predictive factors for these failures (Sales et al., 2019). Only one study reported several factors influencing the survival rate of dental implants in cleft patients, such as implant length, implant diameter and implant surface type (Kramer et al., 2005). However, this study had a relatively small sample size of 45 participants, and there might be more factors affecting dental implant survival apart from those studied by Kramer et al. (2005).

Therefore, this study aimed to assess the survival rate of dental implants placed in grafted alveolar cleft patients and to determine the factors influencing their survival rate.

## 2 | METHODS

### 2.1 | Study design

This retrospective cohort study was conducted at the Department of Oral and Maxillofacial Surgery of the Erasmus University Medical Centre Rotterdam. All cleft lip patients with alveolar involvement with or without a cleft palate born between 1983 and 2001, treated for a cleft condition and received at least one dental implant in replacement of one or more of the maxillary incisors or cuspids in the grafted alveolar cleft area were included. Patients who had a disability (mental or physical) that made them unable to maintain basic oral hygiene and those with a condition that affected bone healing were excluded.

### 2.2 | Data collection

For the primary outcome, the implants were considered a failure when the dental implant was lost or when it was determined during follow-up that the implant required removal. The follow-up period was defined as the period between implant insertion and implant failure or the last known follow-up appointment. Data were collected from patient files. The data collected consisted of the patient and implant characteristics. Patient characteristics included sex, age at implant insertion, type of cleft, congenital missing teeth, tooth loss, smoking status at implant insertion and information on bone grafting procedures. Bone grafting procedures were defined as ABG, bone augmentation (BA), or GBR. ABG was defined as an alveolar bone graft procedure that closed the initial alveolar cleft bone defect. Closure of the defect at the cleft area was performed before the eruption of the permanent maxillary cuspid when it was formed for at least two-thirds. The defect was closed with bone harvested from the anterior iliac crest or mandibular symphysis. The BA procedure was defined as the necessary bone graft procedure, performed approximately 3–5 months before implant placement, with (non-) autogenous bone because of an inadequate quantity of surrounding bone volume to support the dental implant. During implant placement, GBR procedures could be performed to ensure the stability of the dental implant.

Implant characteristics included the location of insertion, brand, type, length and diameter of the implant. The lengths and diameters of the implants were grouped in this study into longer ( $\geq 12$  mm)/shorter (8–10 mm) and narrow ( $\leq 3.3$  mm)/wide ( $\geq 3.8$  mm) implants.

### 2.3 | Statistical analysis

Data analysis was performed using R version 3.6.1. (R Core Team, 2019). The packages 'survminer', version 0.4.9. (Kassambara et al., 2021) and 'survival', version 3.2–11 (Therneau, 2021) were used to analyse the data. Missing data were excluded from the sub-analysis. The survival rates of the dental implants were calculated as cumulative survival using the Kaplan–Meier method. Whether the survival rate was influenced by the patient or implant characteristics was analysed using log-rank tests. Tests were considered statistically significant when  $p \leq .05$ .

Statistical tests required individual dental implants to be independent of each other. Therefore, one implant per patient was selected for analysis. The first failed implant was included in the analysis of the patients who had a failed implant. When patients did not have a failing implant, the implant was chosen at random to be included in the analysis.

To increase the power of the study an additional univariable Cox proportional hazards regression was performed with a frailty term to allow the inclusion of multiple dental implants per patient.

### 2.4 | Regulatory approvals

This study was approved by the Medical Ethical Committee of the Erasmus Medical Centre Rotterdam (NL74784.078.20) and was

conducted in accordance with the STROBE guidelines for cohort studies.

### 3 | RESULTS

A total of 761 cleft patients born between 1983 and 2001 were treated at the Erasmus University Medical Centre. Patient characteristics are presented in Table 1. Sixty-four patients received a total of 78 dental implants to replace one or more maxillary incisors in the grafted cleft area. Of 78 implants, 64 were included in the Kaplan–Meier analysis as aforementioned in the methods. All implants included in the analysis were of the Straumann (Basel, Switzerland) brand, except for one Dentsply Sirona (Charlotte, USA) implant (Table 2). The median follow-up period was 46 months (IQR: 29.0–79.3) (Table 2). An ABG procedure was performed in all patients (64 out of 64). Before implant insertion, BA procedures were performed in 20 of 64 patients. Implants generally had 5 months to osseointegrate before loading. Five of the 64 implants were lost during the follow-up period: Two implants failed 3 months after insertion and were considered an early failure; the three other implants failed after more than 2 years and were considered late failures. The cumulative survival rate according to the Kaplan–Meier method at the median and last follow-up was 95.0% (95%CI: 89.7%–100.0%) and 88.2% (95%CI: 78.3%–99.3%) (Figure 1).

The dental status of a patient with missing lateral incisors before and after dental rehabilitation is shown in Figure 2. Four out of five lost implants were inserted in the grafted cleft area of patients with cleft lip, alveolus and palate (CLAP). One of the five lost implants was inserted into the grafted cleft area of a patient with unilateral cleft lip and alveolus (CLA). In CLAP patients with implant failure, two patients had a unilateral cleft and two patients had a bilateral cleft.

#### 3.1 | Effect of patient characteristics on dental implant survival

The implant survival rates in males and females were 89.4% (95% CI: 78.3%–100%) and 85.3% (95% CI: 66.8%–100%), respectively, and did not differ significantly ( $p=.90$ ). The mean age at implantation of the dental implants was 19.69 (Table 2). Patients older than 19.69 years ( $n=21$ ) had a survival rate of 92.9% (95%CI: 80.3%–100%) and patients below the age of 19.65 years ( $n=43$ ) had a survival rate of 85.7% (95%CI: 72.7%–100%). The difference in survival rates was not statistically significant ( $p=.60$ ).

Dental implants placed in patients with a unilateral cleft ( $n=43$ ) had a survival rate of 90.4% (95%CI: 80.2%–100%) and did not differ significantly from dental implants placed in bilateral cleft patients ( $n=21$ ) who had a survival rate of 76.2% (95%CI: 48.7%–100%;  $p=.60$ ).

The implants inserted to replace a congenitally missing tooth ( $n=41$ ) had a survival rate of 82.6% (95%CI: 69.0%–98.9%), compared to a survival rate of 100% (95%CI: 100%–100%) for implants inserted to replace a lost tooth ( $n=23$ ). The difference between the

TABLE 1 Patient and implant-related characteristics.

Patient-related	<i>n</i> = 64 (%)
Sex	
Male	<i>n</i> = 39 (60.9)
Female	<i>n</i> = 25 (39.1)
Age at placement, mean (SD)	19.77 (3.0)
Type of cleft	
CLA	<i>n</i> = 13 (20.3)
CLAP	<i>n</i> = 51 (79.7)
Unilateral or bilateral	
Unilateral	<i>n</i> = 43 (67.2)
Bilateral	<i>n</i> = 21 (32.8)
Alveolar bone graft procedure	
Yes	<i>n</i> = 64 (100)
redo	<i>n</i> = 3 (4.7)
Bone augmentation procedure	
Yes	<i>n</i> = 20 (31.3)
No	<i>n</i> = 44 (68.8)
Smoker	
Yes	<i>n</i> = 16 (25.0)
No	<i>n</i> = 45 (70.3)
Missing	<i>n</i> = 3 (4.7)
Implant-related	<i>n</i> = 81 (%)
Location Implant	
Right lateral incisor	<i>n</i> = 32 (39.5)
Right median incisor	<i>n</i> = 1 (1.2)
Left median incisor	<i>n</i> = 5 (6.2)
Left lateral incisor	<i>n</i> = 43 (53.1)
Lost or congenitally missing	
Lost	<i>n</i> = 33 (40.7)
congenitally missing	<i>n</i> = 48 (59.3)
Brand	
Straumann	<i>n</i> = 80 (98.8)
Dentsply Sirona Frialit	<i>n</i> = 1 (1.2)
Type of implant	
Tissue level	<i>n</i> = 17 (21.0)
Bone level	<i>n</i> = 64 (79.0)
Length of implant in mm	
8	<i>n</i> = 9 (11.1)
10	<i>n</i> = 46 (56.8)
12	<i>n</i> = 24 (29.6)
13	<i>n</i> = 1 (1.2)
14	<i>n</i> = 1 (1.2)
Diameter of implant in mm	
2.9	<i>n</i> = 6 (7.4)
3.3	<i>n</i> = 71 (87.7)
3.8	<i>n</i> = 1 (1.2)
4.1	<i>n</i> = 3 (3.7)

Abbreviations: CLA, cleft lip and alveolus; CLAP, cleft lip, alveolus and palate; SD, standard deviation. Percentages may not total 100 due to rounding.

TABLE 2 Characteristics included in the Kaplan–Meier analysis.

	<i>n</i> = 64 (%)
Sex	
Male, failed	<i>n</i> = 39 (60.9), <i>n</i> = 3
Female, failed	<i>n</i> = 25 (39.1), <i>n</i> = 2
Age at placement, mean (SD)	19.69 (3.1)
Above average, failed	21 (32.8), <i>n</i> = 1
Below average, failed	43 (67.2), <i>n</i> = 4
Unilateral or bilateral	
Unilateral, failed	<i>n</i> = 43 (67.2), <i>n</i> = 3
Bilateral, failed	<i>n</i> = 21 (32.8), <i>n</i> = 2
Location Implant	
Right lateral incisor	<i>n</i> = 23 (35.9)
Right median incisor	<i>n</i> = 1 (1.6)
Left median incisor	<i>n</i> = 2 (3.1)
Left lateral incisor	<i>n</i> = 38 (59.4)
Smoker	
Yes, failed	<i>n</i> = 16 (25.0), <i>n</i> = 2
No, failed	<i>n</i> = 45 (70.3), <i>n</i> = 2
Lost or congenitally missing	
Lost, failed	<i>n</i> = 23 (35.9), <i>n</i> = 0
congenitally missing, failed	<i>n</i> = 41 (64.1), <i>n</i> = 5
Procedures	
ABG, failed	<i>n</i> = 44 (68.8), <i>n</i> = 3
ABG + BA, failed	<i>n</i> = 20 (31.3), <i>n</i> = 2
Brand	
Straumann	<i>n</i> = 63 (98.4)
Dentsply Sirona Frialit	<i>n</i> = 1 (1.6)
Type of implant	
Tissue level, failed	<i>n</i> = 15 (23.4), <i>n</i> = 2
Bone level, failed	<i>n</i> = 49 (76.6), <i>n</i> = 3
Length of implant in mm	
8	<i>n</i> = 6 (9.4)
10	<i>n</i> = 37 (57.8)
12	<i>n</i> = 19 (29.7)
13	<i>n</i> = 1 (1.6)
14	<i>n</i> = 1 (1.6)
Shorter, failed	<i>n</i> = 43 (67.2), <i>n</i> = 4
Longer, failed	<i>n</i> = 21 (32.8), <i>n</i> = 1
Diameter of implant in mm	
2.9	<i>n</i> = 4 (6.3)
3.3	<i>n</i> = 57 (89.1)
3.8	<i>n</i> = 1 (1.6)
4.1	<i>n</i> = 2 (3.1)
Narrow, failed	<i>n</i> = 61 (95.3), <i>n</i> = 5
Wide, failed	<i>n</i> = 3 (5.7), <i>n</i> = 0
Median Follow-up, months (IQR)	46 (29.0–79.3)

Abbreviations: ABG, alveolar bone grafting; BA, bone augmentation; IQR, Interquartile Range; SD, standard deviation. Percentages may not total 100 due to rounding.

two survival rates was not statistically significant ( $p = .10$ ). Non-smokers ( $n = 45$ ) and smokers ( $n = 16$ ) had implant survival rates of 95.6% (95% CI: 89.7%–100%) and 83.0% (95% CI: 63.5%–100%), respectively. The difference in the survival rates was not statistically significant ( $p = .40$ ).

In this study, we investigated the effect of an additional BA next to ABG on the survival of dental implants. Implants inserted in patients who underwent both ABG and BA ( $n = 20$ ) had a non-significant lower survival rate compared to patients who underwent solely ABG ( $n = 44$ ) (85.5% (95%CI: 67.9%–100%) and 89.7% (95%CI: 78.6%–100%), respectively;  $p = .70$ ).

### 3.2 | Effect of implant characteristics on dental implant survival

Of the 64 inserted implants, 49 were bone-level implants and 15 were tissue-level implants (Table 2). The survival rate of bone-level implants was 89.5% (95%CI: 77.3%–100%) which was not significantly ( $p = .60$ ) higher than that of tissue-level implants (85.1% (95%CI: 68.0%–100%)). Twenty-one implants were categorised as longer implants ( $\geq 12$ mm) and 43 as shorter implants (8–10mm) (Table 2). Longer implants had a non-significantly higher survival rate (93.3% (95%CI: 81.5%–100%)) than shorter implants (85.9% (95%CI: 72.5%–100%);  $p = .30$ ). Sixty-one implants were categorised as narrow implants ( $\leq 3.3$ mm) and three as wide ( $\geq 3.8$ mm) (Table 2). Narrow implants had a lower survival rate (87.6% (95%CI: 77.3%–99.3%)) than wider implants (100% (95%CI: 100%–100%)).

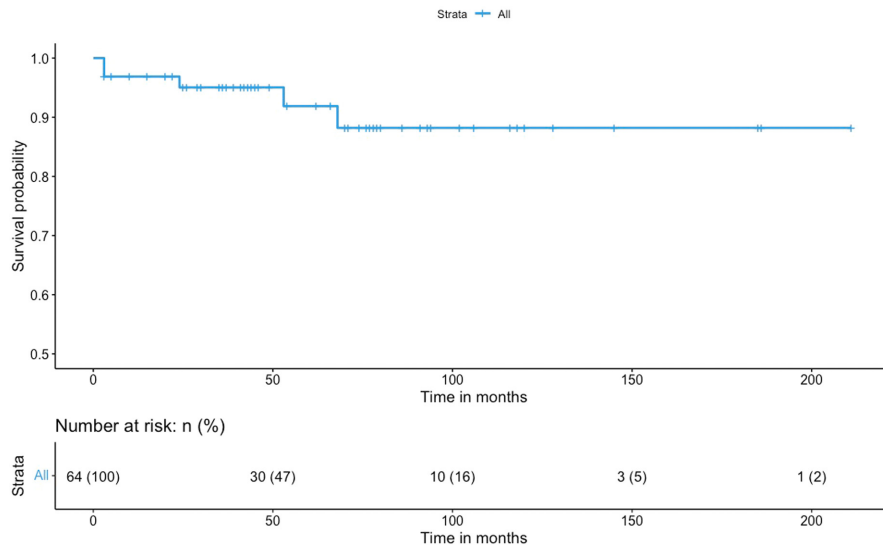
### 3.3 | Cox proportional hazards regression

For the univariable Cox proportional hazard regression, all implants inserted in the grafted alveolar cleft were included. Characteristics are shown in Table 3. An additional 14 implants were included. Hazard ratios and corresponding 95% confidence intervals are shown in Table 4. The hazard ratio for dental implants replacing lost teeth was 1.67e-18 and had an infinite 95% confidence interval (Table 4). From three patients, with a single implant, the smoking status during implantation was not known and therefore excluded from the analysis. Complete case analysis was chosen to handle missing data since only three implants would be excluded and it was assumed missingness was completely at random. None of the variables had a significant effect on survival.

## 4 | DISCUSSION

After a median period of 46 months, the cumulative survival rate of implants was 95.0%. After 68 months, the cumulative survival rate of the dental implants was 88.2% and remained the same till the end of follow-up at 211 months. Consistent with the results of other studies, this finding confirms the good survival of dental implants





**FIGURE 1** Overall Survival of dental implants placed in cleft Lip and alveolus and cleft lip, alveolus and palate patients. The implant survival rate after 46 months was 95.0% and after 68 months was 88.2%.



**FIGURE 2** (a-d) Orthopantomograph (OPG) of a patient with missing lateral incisors. (a) OPG before dental implantation. (b) OPG after bone augmentation (BA) at the site of the right lateral incisor and implant insertion on the left lateral incisor. (c) Secondary implant insertion of the right lateral incisor. (d) Implants are loaded with prostheses (e) Intraoral view before implant insertion. (f-i) Intraoral view 6 years after implantation. (j) Appearance of the patient at the age of 24.

inserted in cleft patients (Alberga et al., 2020; Kramer et al., 2005; Landes, 2006; Lilja et al., 1998; Matsui et al., 2007; Takahashi et al., 2008).

Patient-related characteristics (sex, age, type of cleft, congenital missing teeth, tooth loss, smoking and the number of procedures in the cleft area) did not significantly influence implant survival. However, interesting trends were observed, such as better survival rates among implants inserted as a replacement for lost teeth and implants inserted in non-smokers. In the present study, dental implants that were inserted as a replacement for lost teeth appeared to have a better, but not significant, survival rate than dental implants inserted as a replacement for congenitally missing teeth. The hazard ratio for the survival of dental implants inserted as replacement of a lost tooth was extreme. This was most likely caused by the lack of events in the group with lost teeth. Patients with cleft palates have hypoplasia of the maxilla on the defective side (Wang et al., 2020; Woods et al., 2018). Additionally, after tooth extraction, alterations of the alveolar ridge occur, such as horizontal and vertical reduction (Masaki et al., 2015). Hypoplasia of the maxilla, alterations in the alveolar ridge and impaired soft tissue conditions may affect the survival rate of dental implants. However, further research is needed to explain whether maxillary hypoplasia or alteration of the alveolar ridge has a negative effect on the survival rate of dental implants. Consistent with the results obtained by Kramer et al. (2005), patients with a bilateral cleft in the present study had a lower survival rate than those with a unilateral cleft. From the univariable Cox regression, a contradicting result in comparison to the Kaplan–Meier analysis was observed. However, this is likely due to the inclusion of multiple implants per patient in the Cox regression, which was only the case in patients with a bilateral cleft. Furthermore, the results of this study suggest that smoking negatively influences implant survival rates. Similarly, Landes (2006) reported a possible negative effect of smoking on dental implant survival.

In this study, dental implants placed in areas with additional BA procedures apart from the ABG procedures led to an insignificantly lower survival rate than dental implants placed in areas with solely ABG procedures. Similarly, Lilja et al. (1998) stated that patients in whom dental implants can be inserted without an additional BA have an excellent success rate. Possible explanations could be that with more procedures, more scarring may be present, which was similarly described by Härtel et al. (1999), and with GBR, it is difficult to increase the height of the alveolar ridge (Horváth et al., 2013). Multiple studies have argued the importance of bone grafting for the survival of dental implants (Kearns et al., 1997; Kramer et al., 2005; Landes, 2006; Lilja et al., 1998). For example, Landes (2006) argued that a short interval of 4–6 months after the BA procedure could be beneficial for implant survival due to the fact that transplant ossification and minor bone resorption are then combined. Additionally, Kramer et al. (2005) argued the prognostic importance of bone grafting on implant survival, because all the implants in their study failed within the first year after insertion, with a possible explanation that the remodelling in the graft is the most intense in the first year (Gordh & Alberius, 1999). However, the

**TABLE 3** Characteristics included in the Cox Proportional Hazards regression analysis.

	n = 78 (%)
<b>Sex</b>	
Male, failed	n = 47 (60.3), n = 3
Female, failed	n = 31 (39.7), n = 2
<b>Age at placement, mean (SD)</b>	19.71 (3.0)
Above average, failed	25 (32.1), n = 1
Below average, failed	53 (67.9), n = 4
<b>Unilateral or bilateral</b>	
Unilateral, failed	n = 44 (56.4), n = 3
Bilateral, failed	n = 34 (43.6), n = 2
<b>Location Implant</b>	
Right lateral incisor	n = 30 (38.5)
Right median incisor	n = 1 (1.3)
Left median incisor	n = 5 (6.4)
Left lateral incisor	n = 42 (53.8)
<b>Smoker</b>	
Yes, failed	n = 20 (26.7), n = 2
No, failed	n = 55 (73.3), n = 2
<b>Lost or congenitally missing</b>	
Lost, failed	n = 33 (42.3), n = 0
congenitally missing, failed	n = 45 (57.7), n = 5
<b>Procedures</b>	
ABG, failed	n = 49 (62.8), n = 3
ABG + BA, failed	n = 29 (37.2), n = 2
<b>Brand</b>	
Straumann	n = 77 (98.7)
Dentsply Sirona Frialit	n = 1 (1.3)
<b>Type of implant</b>	
Tissue level, failed	n = 17 (21.8), n = 2
Bone level, failed	n = 61 (78.2), n = 3
<b>Length of implant in mm</b>	
8	n = 9 (11.5)
10	n = 45 (57.7)
12	n = 22 (28.2)
13	n = 1 (1.3)
14	n = 1 (1.3)
Shorter, failed	n = 54 (69.2), n = 4
Longer, failed	n = 24 (30.8), n = 1
<b>Diameter of implant in mm</b>	
2.9	n = 5 (6.3)
3.3	n = 69 (89.1)
3.8	n = 1 (1.6)
4.1	n = 2 (3.1)
Narrow, failed	n = 74 (96.2), n = 5
Wide, failed	n = 3 (3.8), n = 0
<b>Median Follow-up, months (IQR)</b>	49 (29.0–78.8)

Abbreviations: ABG, alveolar bone grafting; BA, bone augmentation; IQR, Interquartile Range; SD, standard deviation. Percentages may not total 100 due to rounding

**TABLE 4** Univariable cox proportional hazards model for dental implant survival.

Effect	HR	95% LB	95% UB	p-value	Frailty p-value
Female	1.05	0.17	6.37	0.96	0.27
Below Mean Age	1.63	0.18	14.64	0.66	0.56
Bilateral Cleft	0.97	0.16	6.00	0.98	0.31
Lost Tooth	1.67e-18	0	inf	1.00	0.74
Smoker	2.3	0.32	16.53	0.41	0.76
ABG	0.80	0.13	4.88	0.80	0.31
BoneLevel Implant	0.57	0.09	3.56	0.54	0.33
Longer Implant	0.37	0.04	3.47	0.38	0.29

Abbreviations: ABG, alveolar bone grafting; HR, hazard ratio; inf, infinite; LB, lower bound; UB, upper bound.

present study had contradictory results with only two of the five implants failing within the first year.

Similarly, multiple implant-related characteristics (length and type of implant) did not significantly influence the survival of the dental implants. Owing to the small number of implants with diameters wider than 3.3 mm, it was not possible to analyse the effect of the diameter of the dental implant on the survival rate. A non-significant trend was observed in this study, showing a higher survival rate for longer implants. Kramer et al. (2005) reported a significantly longer survival time with longer dental implants. Landes (2006) also argued that the dental implant loss in two patients in his study was likely due to the small implant dimensions and subsequent overloading, which could have been prevented if larger implants were inserted. Furthermore, after analysing the case of implant failure, Takahashi et al. (1997) reported that one of the major factors affecting dental implant survival is the dental implant length. Matsui et al. (2007) argued that the high survival rate of 98.6% could be attributed to the fact that dental implants longer than 13 mm were used in almost all cases. Importantly, the difference between the present study and that of Kramer et al. (2005) is the cut-off value for the two groups of lengths that were compared (8–10 vs.  $\geq 12$  compared to  $\leq 12$  vs.  $\geq 13$ ). As a result, it was difficult to compare this study with that of Kramer et al. (2005) on the effects of implant length. In addition, by dichotomising the effect of length on dental implant survival, it is difficult to conclude the true effect of length increase on dental implant survival. Moreover, the low number of failing implants made it impossible to determine the true effect of length on dental implant survival by modelling length as a continuous variable. Finally, based on the results of this study alone, it was not possible to conclude whether the length of a dental implant was important for the survival rate. However, the results of this study, in combination with those of other groups, suggest that longer implants should preferably be chosen to increase survival rates (Kramer et al., 2005; Landes, 2006; Matsui et al., 2007; Takahashi et al., 1997).

It was difficult to draw strong conclusions due to the limitations of this study. For example, considering the incidence of 15 in 10,000 and the fact that not all cleft patients receive dental implant treatment, it is challenging to include a sufficient number of

cleft patients with dental implants (European Commission, 2019; Fleurke-Rozema et al., 2016). Therefore, the non-significant results were probably due to a lack of power, and it was only possible to recognise trends from the data. From the univariable Cox regressions, broad 95% confidence intervals were observed. This is probably due to heterogeneity and a lack of power, so no conclusions can be made about effect sizes. Additionally, multivariable regression was not performed due to the high risk of overfitting which enhanced the risk of confounding bias in this present study. Furthermore, the study population was relatively young. Resulting in a short follow-up period and subsequently an inability to draw conclusions about the long-term follow-up. Moreover, the external validity of the findings is limited due to the selection of patients from a monocentric setting, the use of the same brand of dental implants except for one and no implants inserted in the cuspid area despite the inclusion criteria. Additionally, this study primarily looked at the survival of dental implants and did not consider aesthetic results, peri-implant diseases, or the incidence of mechanical complications which are important additional outcomes when studying the survival of dental implants. Considering these limitations, a multicentre prospective cohort study would be a suitable solution to increase the sample size, and, therefore, the power of the study.

This study confirmed that the use of dental implants in patients with cleft palate with missing teeth is a well-established treatment option for dental rehabilitation. Furthermore, this study has shown the necessity for more prospective clinical studies with larger sample sizes to study the potential effect of different factors on implant survival rate. Interesting trends were observed but their statistical significance must be proven by more studies.

#### ETHICS APPROVAL STATEMENT

This study was approved by the Medical Ethical Committee of the Erasmus Medical Centre Rotterdam (NL74784.078.20) and conducted in accordance with the declaration of Helsinki.

#### PATIENT CONSENT STATEMENT

If necessary, informed consent was received from the patients verbally and written.

## AUTHOR CONTRIBUTIONS

**Yordi van Putten:** Data curation (lead); formal analysis (equal); methodology (equal); visualization (equal); writing – original draft (lead); writing – review and editing (equal). **Antoinette V.J. Rozeboom:** Conceptualization (equal); methodology (equal); supervision (equal); visualization (equal); writing – review and editing (equal). **Elske M. Strabbing:** Data curation (supporting); methodology (equal); writing – review and editing (equal). **Maarten J. Koudstaal:** Methodology (equal); visualization (equal); writing – review and editing (equal). **Ali Tahmaseb:** Conceptualization (equal); formal analysis (equal); methodology (equal); supervision (equal); visualization (equal); writing – original draft (supporting); writing – review and editing (equal).

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## CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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