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Dental implants in patients with ectodermal dysplasia: a systematic review

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ABSTRACT

Purpose. This study sought to assess the clinical outcome and survival rate of oral implants placed in individuals with ectodermal dysplasia (ED), based on previously published studies.

Methods. An electronic search without time restrictions was undertaken in 5 databases (PubMed/Medline, Web of Science, ScienceDirect, J-Stage, Lilacs). Descriptive statistics, Kaplan Meier estimator and implant failure probability were calculated.

Results. 90 publications were included, reporting 228 ED patients that received 1472 implants (1392 conventional, 47 zygomatic, 33 mini-implants). Mean age of the patients was 20.2 ± 6.8 years (2-56). Patients had a mean of 3.2 ± 2.5 maxillary and 2.1 ± 2.6 mandibular permanent teeth (min-max, 0-14). Patients received a mean of 8.2 ± 3.8 implants (1-20). Most implants were placed in the third decade of life, 24.6% of the implants were placed in children (0-17 years of age). 1391 implants had information on follow-up (72 failures, 5.2%). The 20-year CSR was 84.6%. The probability of failure was 4.5% (95%CI 3.5%-5.6%, $p < 0.001$). Additional treatments performed were Le Fort I (99 implants, 20 patients, 3.5% failed), grafting (497 implants, 77 patients, 5.2% failed), distraction osteogenesis (79 implants, 16 patients, 10.1% failed). Mean follow-up was 42.9 ± 41.9 months (min-max, 2-240).

Conclusions. Dental implants placed in ED patients, either infants or adults, present a high survival rate (20-year CSR 84.6%).

KEYWORDS

Ectodermal dysplasia; oral rehabilitation; dental implant; failure

INTRODUCTION

Ectodermal dysplasia (ED) encompasses a number of genetic syndromes characterized by a congenital defect in two or more of the ectodermal structures of the body. The condition is estimated to occur in approximately 1 in 100,000 live births, and approximately 132 different hereditary syndromes related to ED have been identified (Clarke, 1987). The syndromes usually affect the hair, teeth, nails, sweat glands, craniofacial structures, digits, and occasionally mesodermal abnormalities (Clarke, 1987). The impact on the oral and maxillofacial region includes decreased growth of the mandible and maxilla, deficient development of the maxillary and mandibular alveolar ridges, significant reduction in salivary secretions, and malformations and anomalies of number and shape of primary and permanent teeth (Martin et al., 2005).

As many of these patients present oligodontia (absence of 6 or more teeth) or anodontia (complete absence of teeth), a prosthetic rehabilitation is usually desirable. The degree of dentoalveolar tissue deficiency can make an implant-supported prosthesis an appropriate method of definitive occlusal restoration in these patients. However, as the absence of teeth is congenital, this raises the issue of placement of oral implants in growing children, mainly due to the influence of craniofacial growth on the implant's behavior (Singer et al., 2012). The aim of the present review was to assess the clinical outcome and survival rate of oral implants used for the

oral rehabilitation of ED patients.

MATERIALS AND METHODS

This study followed the PRISMA Statement guidelines (Moher et al., 2009).

Search strategies

An electronic search without time restrictions was undertaken in January 2018 in the following databases: PubMed/Medline, Web of Science, Science Direct, J-Stage, and Lilacs. The following terms were used in the search strategies:

("ectodermal dysplasia") AND (implant)

Google Scholar was also checked. A manual search of dental implants-related journals, including *British Journal of Oral and Maxillofacial Surgery*, *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *European Journal of Oral Implantology*, *Implant Dentistry*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Oral and Maxillofacial Surgery*, *International Journal of Paediatric Dentistry*, *International Journal of Periodontics and Restorative Dentistry*, *International Journal of Prosthodontics*, *Journal of Clinical Pediatric Dentistry*, *Journal of Clinical Periodontology*,

Journal of Dental Research, Journal of Craniofacial Surgery, Journal of Cranio-Maxillofacial Surgery, Journal of Maxillofacial and Oral Surgery, Journal of Oral Implantology, Journal of Oral and Maxillofacial Surgery, Journal of Oral Rehabilitation, Journal of Periodontology, Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology, and Quintessence International, was performed.

Inclusion and Exclusion Criteria

Eligibility criteria included publications (either retrospective or prospective studies) reporting cases of patients with ectodermal dysplasia rehabilitated with implant-retained and/or implant-supported oral prosthetic rehabilitation. Publications reporting clinical cases of prosthetic rehabilitation not using dental implants were not included.

Study selection

The titles and abstracts of all reports identified through the electronic searches were read by the author. For studies appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, the full report was obtained.

Data extraction

The review author independently extracted data using specially designed data extraction forms. For each of the identified studies included, the following data were then extracted on a

standard form, when available: year of publication, number of patients, patient's sex, age, type of Implant used (conventional, zygomatic, mini-implant), implants placed and lost in maxilla and mandible, implant healing period, period between implant placement and loss, number of permanent teeth in maxilla and mandible, performance of additional procedures (grafting, distraction osteogenesis, Le Fort I), grafting donor site or material, time between grafting and/or distraction osteogenesis and dental implant placement, type of prosthetic reconstruction, and follow-up period. Contact with authors for possible missing data was performed.

Analyses

The mean, standard deviation (SD), and percentages were presented as descriptive statistics. Kolmogorov–Smirnov test was performed to evaluate the normal distribution of the variables, and Levene's test evaluated homoscedasticity. The performed tests for two independent groups were Student's t-test or Mann-Whitney test, depending on the normality. Pearson's chi-squared or Fisher's exact tests were used for categorical variables, depending on the expected count of events in a 2x2 contingency table. Kaplan–Meier survival curve was plotted for the outcome implant failure. The interval survival rate (ISR) of implants was calculated using the information for the period of failure extracted from the included studies, and the cumulative survival rate (CSR) was calculated over the maximal period of follow-up reported, in a life-table survival analysis. The untransformed proportion (random-effects DerSimonian-Laird method (DerSimonian and Laird, 1986)) for implant failure was calculated, considering the different variables. The degree of statistical significance was considered $p < 0.05$. All data were statistically analyzed using the Statistical Package for the Social Sciences

(SPSS) version 23 software (SPSS Inc., Chicago, IL, USA) and the software OpenMeta[Analyst] (Wallace et al., 2012).

RESULTS

Literature search

The study selection process is summarized in Figure 1. The search strategy in the databases resulted in 991 papers. Search in Google Scholar resulted in 5 eligible papers not found in the five main databases. A number of 162 articles were cited in more than one database (duplicates). The reviewers independently screened the abstracts for those articles related to the aim of the review. Of the resulted 834 studies, 720 were excluded for not being related to the topic or not presenting clinical cases. Additional hand-searching of journals and of the reference lists of selected studies did not yield additional papers. The full-text reports of the remaining 114 articles led to the exclusion of 24 because they did not meet the inclusion criteria. Thus, a total of 90 publications were included in the review (for the full list of publications, see Supplemental Appendix).

Description of the Studies and Analyses

Table S1 shows detailed data of the included studies (see Supplemental Appendix). Table 1 shows the summarized data of the included studies. 90 publications were included in the present review, reporting the placement of 1472 implants (929 in men, 543 in women) in 228

patients (152 men, 76 women). There were 1392 conventional implants, 47 zygomatic implants (in 22 patients), and 33 mini-implants (in 9 patients). The mean age of the patients at the placement of the implants was 20.2 ± 6.8 years (min-max, 2-56); this information was available for 1398 implants in 214 patients. One study (Garagiola et al., 2007) provided only range of age of the patients (16-45 years) and another one (Clauss et al., 2014) did not inform the patient's age. 24.6% of the implants were placed in children (0-17 years of age). Figure 2 shows the distribution of implants according to the age of the patient at the time of implant placement surgery; most implants were placed in the third decade of life.

Information on follow-up was provided for 1391 implants, of which 72 failed (5.2%), all conventional implants. Implants failed at a mean time of 11.8 ± 19.9 months (min-max, 2-84; n=52) after implant placement. Table 2 shows the comparison of the distribution of implants in gender, jaw, age and healing time groups, implant failure rates for the cases with available information for both failure and the variables here included, and mean time of follow-up. There was no statistically significant difference in the failure rates between implants placed in the maxilla and mandible, and between implants placed in men and women. With regard to age groups, the lowest failure rates occurred in the oldest group of patients. Other group ages until 25 years of age presented similar failure rates.

Le Fort I was concomitantly or previously performed with the placement of 99 implants in 20 patients (failure rate of 3.5%; 3/85). 497 implants were placed in grafted sites in 77 patients, with a failure rate of 5.2% (25/481). 79 implants were in 16 patients placed in sites previously submitted to distraction osteogenesis, with a failure rate of 10.1% (8/79).

Figure 3 shows the survival analysis, using the Kaplan-Meier estimator, with a high

survival rate after 20 years of follow-up. Pooled data from the 1391 implants with information on follow-up (Table 3) showed that 47.2% of the failures (34/72) occurred within 6 months after installation surgery or at the abutment connection, resulting in a 6-month ISR of 97.5%. The 20-year CSR was 84.6%. The probability of failure (Figure 4) was 4.5% (95% CI 3.5%, 5.6%, standard error = 0.005, $p < 0.001$; heterogeneity: $\tau^2 = 0.000$, $\text{Chi}^2 = 70.426$, $p = 0.717$, $I^2 = 0\%$), according to the DerSimonian-Laird method. Only the clinical cases for which the follow-up was informed were included in this analysis.

DISCUSSION

The oral rehabilitation of patients with implants is generally delayed until the cessation of growth because an implant does not exhibit dentoalveolar adaptation in response to vertical alveolar growth or local bony remodeling as would occur in the case of a tooth (Björk and Skieller, 1972; Thilander et al., 1992). However, the use of removable dentures in the deficient residual basal bone structures usually observed in individuals with ED could be a cause of functional and psychological problems. Moreover, the salivary gland hypoplasia in ED patients typically leads to mucosal drying, which can cause poor removable denture retention and make it difficult for children to use removable dentures (Wang et al., 2016). Therefore, the use of dental implants before the cessation of growth in ED patients is encouraged by some dentists (Guckes et al., 1998).

Results of the present review show that dental implants placed in children with ED have relatively low failure rates (5.3%-7.2%, depending on the age group) after reasonable mean follow-up times (52.8-70 months, depending on the age group). Implants placed in adult ED

patients presented a slightly lower failure rate (46/1030; 4.5%) than children. These numbers suggest that the use of implants in ED patients has a high predictability with good clinical results, with failure rates similar to the ones when non-ED patients are considered (Chrcanovic et al., 2018). Almost half of the failures occurred within 6 months after installation surgery, showing failures in ED-patients follow a similar pattern of failures as in non-ED patients (Chrcanovic et al., 2016b; 2018).

The congenital absence of teeth often leads to a deficit of functional stimulation, resulting in alveolar bone atrophy and an absence of supporting bone, both significant limitations in dental implant therapy (Wang et al., 2016). The amount of additional therapies performed in these patients, such as grafting procedures, distraction osteogenesis, and inferior alveolar nerve lateratization reflects the concern of surgeons to increase the quantity of bone available for implants. The performance of Le Fort I in 20 patients shows that orthognathic surgery approaches may become necessary in some ED patients in order to correct the incorrect jaw relationship characteristic of the craniofacial dysmorphology usually seen in this group of patients. Zygomatic implants were used to avoid grafting of the maxilla in 22 patients, and none of them failed. A recent publication on the subject reviewing more than 4500 zygomatic implants observed that these are a good option to avoid grafting of the maxilla and present a high survival rate (Chrcanovic et al., 2016a).

The results of the present study have to be interpreted with caution because of its limitations. First of all, all confounding factors may have affected the long-term outcomes (Chrcanovic et al., 2017) and not just the fact that implants were placed in patients with ED. To precisely assess the effect of a risk factor on implant outcomes, it would be ideal to eliminate all other risk factors from the study population. Not only does the coexistence of multiple risk

factors within a study population create an inability to assess the specific effect of one individual risk factor, but there is a possibility that certain risk factors together may be more detrimental than the individual risk factors alone (Klokkevold and Han, 2007). Second, most of the included studies had a retrospective design, and the nature of a retrospective study inherently results in flaws, such as gaps in information and incomplete records. Third, much of the research in the field is limited by small cohort size and short follow-up periods. A longer follow-up period can lead to an increase in the failure rate, especially if it extended beyond functional loading, because other prosthetic factors can influence implant failure from that point onward (Chrcanovic et al., 2016b; 2018).

The ideal timing of implant placement in children is a matter of debate. For the young patient with severe oligodontia or anodontia, such as individuals with ED, the oral rehabilitation has the impact of improving the patient's masticatory efficiency, quality of life, self-confidence, and social acceptability. The results of the present review suggest that the use of dental implants in these present a relatively low failure rate after a reasonable mean follow-up period. However, professionals need to take into consideration that implants cannot participate in the maxillary and mandibular growth processes of drift and displacement in patients with residual craniofacial growth, usually resulting in infra-occlusion of the implants during growth (Thilander et al., 1994).

CONCLUSIONS

Dental implants placed in ED patients, either infants or adults, present a high survival rate (20-year CSR 84.6%).

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Declaration of conflicting interests

There are no conflicts of interest to declare.

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FIGURE LEGENDS

Figure 1. Study screening process.

Figure 2. Distribution of implants according to the age of the patient at the time of implant placement surgery.

Figure 3. Survival analysis (Kaplan-Meier estimator; +: censored observations).

Figure 4. Probability of implant failure - only clinical cases with information about follow-up were included.

Table 1. Summarized data of the included studies.

Variable	
Patients (n)	228
Implants (n)	1472
Age (years), mean±SD (min-max)	20.2±6.8 (2-56; n=214)
Gender, n (%)	
Men	152 (66.7)
Women	76 (33.3)
Permanent teeth (n), mean±SD (min-max)	
Maxilla	3.2±2.5 (0-14)
Mandible	2.1±2.6 (0-14)
Implants per patient (n), mean±SD (min-max)	8.2±3.8 (1-20)
Implant type, n (%)	
Conventional	1392 (94.6)
Zygomatic	47 (3.2)
Mini-implant	33 (2.2)
Follow-up (months), mean±SD (min-max)	42.9±41.9 (2-240; n=1379)
Implant failure (n), failure/total (%)	72/1391 (5.2)
Time of failure (months), mean±SD (min-max)	11.8±19.9 (2-84; n=52)
Additional treatment	
Le Fort I	99 implants, 20 patients
Implant failure/total (%)	3/85 ^a (3.5)
Grafting	497 implants, 77 patients
Implant failure/total (%)	25/481 ^b (5.2)
Time between grafting and implant placement (months), mean±SD (min-max)	-3.3±4.6 (-36 to 6)
Distraction osteogenesis	79 implants, 16 patients
Implant failure/total (%)	8/19 (10.1%)
Time between distraction and implant placement (months), mean±SD (min-max)	-4.6±1.1 (-7 to -4)
Inferior alveolar nerve lateratization	8 implants, 1 patient ^c
Grafting donor site, number of implants placed (%)	
Iliac crest	136 (28.5)
"Autogenous bone" + DFDBA	73 (15.3)
Iliac crest + DFDBA	59 (12.3)
Ilium	42 (8.8)
Fibula + DFDBA	40 (8.4)
DFDBA	39 (8.2)
Fibula	26 (5.4)
Rib	16 (3.3)
Mandible	9 (1.9)
Calvaria	8 (1.7)
Bone rests of operation + DFDBA	8 (1.7)
Femur	8 (1.7)
Bone rests of operation	5 (1.0)
"Autogenous bone"	5 (1.0)
Tibia	4 (0.8)
Total	478 (100)
Not informed	19
Type of prosthetic rehabilitation, number of implants used (%)	
Single crown	19 (2.1)

Fixed partial prosthesis (2-6 units)	169 (19.2)
Fixed partial prosthesis (7-10 units)	63 (7.1)
Fixed full-arch prosthesis	475 (53.9)
Overdenture	156 (17.7)
Total	882 (100)
Not informed	590

SD – standard deviation, DFDBA - demineralized freeze-dried bone allograft (Bio-Oss, Osteo-Pure, Regenaform)

^a There was no information of follow-up for 14 implants

^b There was no information of follow-up for 16 implants

^c No information on follow-up

Table 2. Comparison of the distribution of implants in gender, jaw, age and healing time groups, implant failure rates for the cases with available information for both failure and the variables here included, and mean time of follow-up.

Variable	n (%)	Implant failure failure/total (%)	Follow-up (months) mean±SD (min-max; n)
<i>Gender</i>			
Men	929 (63.1)	49/888 (5.5) ^a	39.8±35.5 (2-216; n=888)
Women	543 (36.9)	23/503 (4.6) ^a	49.4±52.3 (6-240; n=503)
<i>Jaw</i>			
Maxilla	560 (38)	30/527 (5.7) ^b	44.9±42.6 (2-240; n=527)
Mandible	912 (62)	42/864 (4.9) ^b	42.3±42.5 (2-240; n=864)
<i>Age group</i>			
2-5 years of age	21 (1.5)	1/19 (5.3)	52.8±21.7 (24-94; n=19)
6-10 years of age	93 (6.7)	6/87 (6.9)	66.1±61.4 (2-236; n=87)
11-17 years of age	228 (16.3)	13/181 (7.2)	70.0±60.9 (6-216; n=181)
18-25 years of age	889 (63.6)	44/870 (5.1)	35.9±34.3 (5-240; n=870)
≥26 years of age	167 (11.9)	2/160 (1.3)	43.0±41.1 (3-216; n=160)
Not informed	74		
<i>Healing time</i>			
Immediate loading	76 (6.9)	1/66 (1.5)	28.6±18.3 (3-72; n=66)
0.5-3 months	195 (17.7)	1/185 (0.5)	36.1±26.2 (6-132; n=185)
4-6 months	753 (68.3)	47/739 (6.4)	32.9±24.4 (2-144; n=739)
≥7 months	78 (7.1)	5/78 (6.4)	83.3±70.1 (2-236; n=78)
Not informed	370		

^a Comparison of the difference of failure of between implants placed in men and women: $p = 0.442$; Pearson chi-square test

^b Comparison of the difference of failure of between implants placed in maxilla and mandible: $p = 0.492$; Pearson chi-square test

Table 3. Life-table survival analysis showing the cumulative survival rate of implants in ectodermal dysplasia patients, including all 1391 implants with information of follow-up.

Interval start time (years)	Number entering interval	Number withdrawing during interval	Number exposed to risk	Implant failures	Survival rate within each interval – ISR (%)	Cumulative proportion surviving at end of interval – CSR (%)
0	1391	22	1380	34	97.5	97.5
0.5	1335	58	1306	12	99.1	96.6
1	1265	134	1198	3	99.7	96.4
1.5	1128	358	949	2	99.8	96.1
2	768	72	732	0	100	96.1
3	696	250	571	12	97.9	94.1
4	434	240	314	2	99.4	93.5
5	192	19	183	2	98.9	92.5
6	171	20	161	0	100.0	92.5
7	151	52	125	2	98.4	91.0
8	97	2	96	0	100.0	91.0
9	95	0	95	0	100.0	91.0
10	95	10	90	0	100.0	91.0
11	85	21	75	0	100.0	91.0
12	64	17	56	0	100.0	91.0
13	47	0	47	0	100.0	91.0
14	47	0	47	0	100.0	91.0
15	47	4	45	0	100.0	91.0
16	43	1	43	3	92.9	84.6
17	39	7	36	0	100.0	84.6
18	32	16	24	0	100.0	84.6
19	16	2	15	0	100.0	84.6
20	14	14	7	0	100.0	84.6

ISR - interval survival rate, CSR - cumulative survival rate

HIGHLIGHTS

- Review of implants in ectodermal dysplasia patients: 1472 implants, 228 patients
- 72/1391 implants (5.2%) failed; 20-year cumulative survival rate: 84.6%
- 24.6% of implants placed in children (0-17 years of age), 7% failure rate
- Probability of failure: 4.5% (95%CI 3.5%-5.6%, $p < 0.001$)
- Implants in infant/adult ectodermal dysplasia patients present a high survival rate