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Systematic Review
Dental Implants

Survival of dental implants placed in HIV-positive patients: a systematic review

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Abstract. No consensus has been reached on the use of dental implants in human immunodeficiency virus (HIV)-positive patients. This systematic review evaluated dental implants in HIV-positive patients in terms of implant survival and success rates, marginal bone loss, and complications. The review was conducted according to the PRISMA checklist. Two independent reviewers performed a comprehensive search of the PubMed/MEDLINE, Scopus, and Cochrane Library databases for studies published until October 2017. Six studies were selected for review. In total, 821 implants were placed: 493 in 169 HIV-positive patients, and 328 in 135 HIV-negative patients. The mean duration of follow-up was 47.9 months. Weighted mean survival rate, success rate, and marginal bone loss values were calculated for the HIV-positive patients. Mean survival and success rates at the patient level (according to the number of patients) were 94.76% and 93.81%, respectively; when calculated at the implant level (according to the number of implants), these rates were 94.53% and 90.37%, respectively. Mean marginal bone loss was 0.83 mm at the patient level and 0.99 mm at the implant level. Thus, dental implants are suitable for the rehabilitation of HIV-positive patients with controlled risk factors and normal CD4+ cell counts.

Key words: dental implant; human immunodeficiency virus; complications; success; marginal bone loss; systematic review.

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Dental implants are considered a favourable treatment option for the rehabilitation of patients who present partial or total edentulism, as survival and success rates are high[1]. However, treatment longevity can be reduced in patients with a compromised medical status or systemic conditions[2]. In addition, the effects of general health problems on implant failure rates are still poorly documented[2], especially in human immunodeficiency virus (HIV)-positive patients[3].

Infection with HIV may lead to the development of acquired immunodeficiency syndrome (AIDS), which is associated with increased morbidity and mortality rates[4]. The virus attacks the immune system, especially CD4+ T-cells, and causes a reduction in host resistance to different pathogens[5,6]. Furthermore, some studies have linked the presence of HIV/AIDS to an increased risk of complications from oral surgical procedures[6,7].

Such an increased risk of complications may compromise implant survival and contribute to failures[8,9]. However, as a result of the introduction of highly active

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antiretroviral therapy (HAART), HIV/AIDS is becoming a chronic disease, and the life expectancy of patients with HIV/AIDS has increased due to an increase in their immunological resistance[6,10]. As a result, more HIV-positive patients are likely to seek dental treatment, including dental implants, for oral rehabilitation.

No consensus has been reached concerning the risks associated with dental implant placement in HIV-positive patients. This systematic review was performed to evaluate the clinical performance of implants placed in HIV-positive patients. The null hypotheses were as follows: (1) the survival rate of implants in HIV-positive patients is similar to that in HIV-negative patients; (2) marginal bone loss and complications in HIV-positive patients are similar to those in HIV-negative patients.

Materials and methods

Registry protocol

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist[11] and in accordance with models proposed in the literature[12–14]. Furthermore, the methods used in this systematic review have been registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42017059318).

Eligibility criteria

The focused question addressed was ''Are dental implants placed in HIV-positive patients at increased risk of implant failure, marginal bone loss, and complications?'' The primary outcome evaluated was the implant survival rate, and secondary outcomes were the implant success rate, marginal bone loss, and complication rate.

Study types eligible for inclusion were randomized controlled trials (RCTs), prospective studies, and retrospective studies (retrospective studies were included because of the limited number of RCTs and prospective studies available). All studies reported the survival rates of implants in HIV-positive patients and were published in English. In vitro studies, animal studies, case series, case reports, and reviews were excluded.

Information sources and search

Two independent authors (C.A.A.L. and R.S.C.) conducted an electronic search of the PubMed/MEDLINE, Scopus, and Cochrane Library databases for articles published up until October 2017. The key words used were: (HIV [MeSH Terms] and Dental implants [MeSH Terms]) OR (Human Immunodeficiency Virus [All Fields] and Dental implants [MeSH Terms]) OR (AIDS [All Fields] and dental implants [MeSH Terms]) OR (Acquired Immunodeficiency Syndrome [MeSH Terms] and dental implant [MeSH Terms]). The same researchers performed a manual search of the following journals: *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *Implant Dentistry*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Oral and Maxillofacial Surgery*, *Journal of Clinical Periodontology*, *Journal of Dentistry*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Oral Implantology*, *Journal of Oral Rehabilitation*, *Journal of Periodontology*, and *Periodontology 2000*. In addition, OpenGrey (http://www.opengrey.eu) was used to search the grey literature.

Data collection process

One author (C.A.A.L.) collected relevant information from the articles and a second author (L.P.F) checked all of the information collected. A careful analysis was performed to check for disagreements among the authors. Any such disagreements were resolved through discussion with a third author (J.F.S.J) until a consensus was reached.

Risk of bias

Two investigators (C.A.A.L. and F.R.V.) assessed the methodological quality of the studies using the Newcastle–Ottawa scale (NOS) for cohort studies, which is based on three major components: selection, comparability, and outcome. According to the NOS, a maximum of nine stars can be given to a study, which represents the highest quality. A score of five or fewer stars indicates a high risk of bias, while a score of six or more stars indicates a low risk of bias[15].

Additional analyses

The kappa statistic (κ) was used to determine inter-reader agreement during the article selection process in the database search. Weighted mean values for marginal bone loss, survival rate, and success rate were calculated using Microsoft Excel (Microsoft Corp., Redmond, WA, USA).

Results

Study selection

The database search retrieved 360 articles: 143 from PubMed/MEDLINE, 145 from Scopus, 57 from the Cochrane Library, and 15 from other sources (hand-search and grey literature). After reading the titles and abstracts against the eligibility criteria, eight articles remained. Two articles were excluded after full-text reading: one reported a duplicate sample of patients and data from another included article[16], and one was an editorial article[17]. Ultimately, six articles reporting four observational studies[3,8,9,18] and two retrospective studies[19,20] were included in this systematic review (Fig. 1). Three of the studies only evaluated HIV-positive patients[8,9,20], and three compared HIV-positive and HIV-negative patients[3,18,19].

The inter-investigator agreement for articles selected from PubMed/MEDLINE ($\kappa = 1.0$), Scopus ($\kappa = 0.81$), and the Cochrane Library ($\kappa = 1.0$) indicated a high level of agreement[21].

Study characteristics

A total of 821 implants were placed in 304 patients: 493 implants in 169 HIV-positive patients, and 328 implants in 135 HIV-negative patients. The mean age of the patients was 51.6 years. The mean follow-up period was 47.9 months (range 6–120 months). Implants were most often placed in the mandible. There were several variations in the implant systems used, including length (range 8–16 mm) and diameter (range 3.3–5 mm). The quantitative and qualitative study data are summarized in Tables 1 and 2.

The patients had a mean CD4+ T-cell count of <550 cells/mm^3 in the majority of studies. However, in the study by Gherlone et al.[9], the mean count was 726.3 cells/mm^3. Antiretroviral therapy was reported in four studies[3,8,18,20], all of which used HAART. One of the selected studies compared two groups: group 1 patients had been treated with protease inhibitor (PI)-based HAART and group 2 patients had been treated with non-nucleoside reverse transcriptase inhibitor (NNRTI)-based HAART (without a PI)[3]. The study found that antiretroviral therapy did not influence the implant survival rate.

Four studies reported the use of prophylactic drug therapy with antibiotics (amoxicillin with or without clavulanic acid)[3,9,18,20]. Two studies reported the use of anti-inflammatory drugs postoperative (sodium diclofenac, paracetamol, or piroxicam)[3,20]. One study did not use pro-

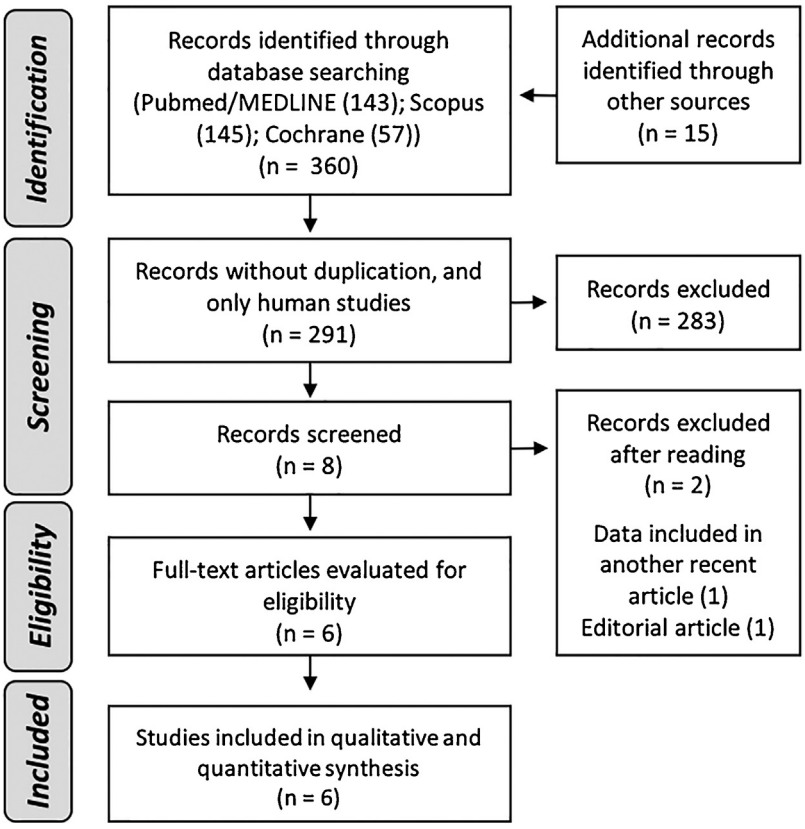

Fig. 1. Flowchart of the search strategy.

phylactic or postoperative medication[8]. Rinsing with chlorhexidine was reported in three studies[8,9,20].

Risk of bias/quality analysis of the studies included

Four studies were awarded seven stars and two studies were awarded eight stars on the NOS, indicating a low risk of bias for the included studies. Categories most frequently missing stars were non-exposed cohort (absence of a non-exposed cohort), additional comparison factors, and the duration of follow-up (insufficient) (Table 3).

Survival and success rates of implants

All of the studies assessed reported the survival rates of implants in HIV-positive patients. Specifically, 27 of 493 implants failed (5.5%). In the studies that reported HIV-negative patients[3,18,19], 16 of 328 implants failed (4.9%). Two studies reported 100% survival of implants placed in HIV-positive patients[3,18], while all of the other studies reported survival rates of >90%[8,9,19,20]. The implant failure rates for each study are illustrated in Fig. 2.

Regarding the success rate of implants, three studies[3,18,20] used the success criteria defined by Albrektsson et al.[22]. One article did not report success rate data[9], while four studies reported success rates that were the same as the implant survival rates[3,8,18,19]. Only one study reported success and survival rates that were different[20]. In that study, there was one implant failure (98.3%); however, due to the large number of complications, the implant success rate was 68.4%.

The weighted mean values of the implant survival and success rates were calculated at the patient level (according to the number of patients) and at the implant level (according to the number of implants). At the patient level, the mean survival rate was 94.76% and the mean success rate was 93.81%. At the implant level, the mean survival rate was 94.53% and the mean success rate was 90.37% (Table 1).

Marginal bone loss

Three studies evaluated marginal bone loss[3,9,18]. One study evaluated only HIV-positive patients, and these patients showed a mean marginal bone loss of 1.19 mm[9]. The two other studies observed no difference in marginal bone loss between HIV-positive and HIV-negative patients, with a mean loss of <0.55 mm in both groups[3,18]. Weighted mean values of marginal bone loss were calculated: the mean loss at the patient level was 0.83 mm and at the implant level was 0.99 mm (Table 1).

Complications

Three studies reported complication rates[3,9,20]. One of these studies found no complications in the patients evaluated[3]. The other two studies reported peri-implantitis ($n = 35$), mucositis ($n = 6$), and prosthetic failure ($n = 2$) as the most prevalent complications in patients with HIV[9,20].

Discussion

The oral rehabilitation of patients using dental implants is now a routine treatment in clinics. However, limited scientific evidence is available to guide clinicians regarding the risks associated with dental implant placement in HIV-positive patients[9].

The first null hypothesis of this review was accepted, since the survival rate of implants in HIV-positive patients was similar to that in HIV-negative patients[23]. Of the six selected studies, three performed a direct comparison between HIV-positive and HIV-negative patients; none found any difference in implant survival rate between the two groups[3,18,19].

Some factors may be related to these favourable results observed in HIV-positive patients, such as antiretroviral therapy (HAART), which increases the number of CD4+ T-cells and consequently reduces immunosuppression in the patient[24]. Four studies reported the use of HAART in HIV-positive patients, which may have contributed to the increase in mean CD4 + cells[3,8,18,20]. However, the other two studies reported that the CD4+ cell count did not influence the implant survival rate[3,9].

A greater risk of complications has been related to the presence of substantial immunosuppression (CD4+ cell count <200 cells/mm^3) and to severe neutropenia (absolute neutrophil count <500 cells/mm^3)[6,25]. However, the selected studies in this systematic review reported mean CD4 + T-cell counts of >400 cells/mm^3, except for one study that reported a mean CD4+ T-cell count of <200 cells/mm^3 (mean 141.25 cells/mm^3); this study showed the highest rate of implant failure among the included studies (9.1%)[8]. In addition,

Table 1. Summary of the quantitative analysis of included studies.

Study	Patients, *n*	Implants, *n*	Mean age, years	Arch	CD4+ count (cells/mm^3), mean (SD)	Complications, *n*	MBL (mm), mean (SD)	Survival rates of implants, *n* (%)	Weighted mean values of the outcomes for HIV-positive patients		
									MBL	Survival	Success
May et al. 2016[8]	16	33	36.2	28 Mx 6 Md	141.25 (35.5)	NR	NR	30 (90.9%)	Based on number of patients		
Gherlone et al. 2016[9]	66	190	55.3	Mx Md	726.3 (201.4)	PI (10) PF (2)	1.19 (0.87)	175 (92.1%)	0.83 mm	94.76%	93.81%
Gay-Escoda et al. 2016[20]	9	57	42	4 Mx 8 Md	436 (NR)	Mucositis (6) PI (25)	NR	56 (98.2%)	Based on number of implants		
Rania et al. 2015[19]	145			NR	>300[b] (NR)	NR	NR	HIV(+): 126 (94.0%) HIV(−): 274 (94.5%)	0.99 mm	94.53%	90.37%
	34 HIV(+) 111 HIV(−)	134 290	54 52								
Oliveira et al. 2011[3,a]	39 11 HIV(+)[1] 13 HIV(+)[2] 15 HIV(−)	 20 19 20	46.2	59 Md	HIV(+)[1]: 400 (NR) HIV(+)[2]: 543.5 (NR)	None	HIV(+)[1]: 0.49 HIV(+)[2]: 0.47 HIV(−): 0.55	HIV(+)[1]: 20 (100%) HIV(+)[2]: 19 (100%) HIV(−): 20 (100%)			
Stevenson et al. 2007[18]	29 20 HIV(+) 9 HIV(−)	 40 18	57.1	58 Md	467 (NR)	NR	HIV(+): 0.06 (0.09) HIV(−): 0.18 (0.17)	HIV(+): 40 (100%) HIV(−): 18 (100%)			

MBL, marginal bone loss; Md, mandible; Mx, maxilla; NR, not reported; PF, prosthetic failure; PI, peri-implantitis; SD, standard deviation.

[a] This study compared two groups: group 1 patients treated with protease inhibitor-based HAART and group 2 patients treated with non-nucleoside reverse transcriptase inhibitor-based HAART (without a protease inhibitor).

[b] The authors mentioned only that ''all patients received surgery after achieving a CD4+ count >300 cell/mm^3''.

Table 2. Summary of the qualitative analysis of included studies.

Study	Study design	Follow-up, months	Implant system Diameter (D) Length (L)	Antiretroviral therapy	Medication	
					Prophylaxis	Postoperative
May et al. 2016[8]	Observational	60	Bicon D: 4, 4.5, 5 mm L: 8, 11 mm	HAART	No medication	Chlorhexidine gluconate 0.12% rinse
Gherlone et al. 2016[9]	Observational	12	WinSix D: 3.3, 3.8, 4, 5 mm L: 9, 11, 13 mm	NR	Amoxicillin–clavulanic acid (2 g 1 h before surgery)	Amoxicillin–clavulanic acid (1 g twice per day for 7 days); chlorhexidine (0.2% rinse for 15 days)
Gay-Escoda et al. 2016[20]	Retrospective	77.4	Nobel, Defcon, Astra, Straumann D: NR L: NR	HAART	Amoxicillin (2 g 1 h before surgery)	Amoxicillin (750 mg every 8 h for 7 days); sodium diclofenac (50 mg every 8 h for 5 days); paracetamol (1 g every 8 h for 4 days); chlorhexidine 0.12% (every 12 h for 15 days)
Rania et al. 2015[19]	Retrospective	120	NR	NR	NR	NR
Oliveira et al. 2011[3,a]	Observational	12	Serson Implus D: 3.5 L: 10–16 mm	HIV(+)[1]: PI-based HAART HIV(+)[2]: NNRTI-based HAART (without PI)	Amoxicillin (500 mg 1 h before surgery); piroxicam (20 mg 1 h before surgery)	Amoxicillin (500 mg three times per day for 5 days); piroxicam (20 mg every 24 h for 3 days)
Stevenson et al. 2007[18]	Observational	6	BioHorizons D: NR L: NR	HAART	Amoxicillin (1 h before surgery)	Amoxicillin (500 mg 3 per day for 7 days)

HAART, highly active antiretroviral therapy; NR, not reported; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Table 3. Quality assessment of the included studies based on the Newcastle–Ottawa scale.

Study	Selection				Comparability		Outcome			Total
	Exposed cohort	Non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start	Main factor	Additional factor	Assessment of outcome	Follow-up long enough[a]	Adequacy of follow-up	
May et al. 2016[8]	☆	0	☆	☆	☆	0	☆	☆	☆	7
Gherlone et al. 2016[9]	☆	0	☆	☆	☆	☆	☆	0	☆	7
Gay-Escoda et al. 2016[20]	☆	0	☆	☆	☆	0	☆	☆	☆	7
Rania et al. 2015[19]	☆	☆	0	☆	☆	0	☆	☆	☆	7
Oliveira et al. 2011[3]	☆	☆	☆	☆	☆	☆	☆	0	☆	8
Stevenson et al. 2007[18]	☆	☆	☆	☆	☆	☆	☆	0	☆	8

[a] Five years was considered an adequate time period over which to observe the outcome 'implant failure'.

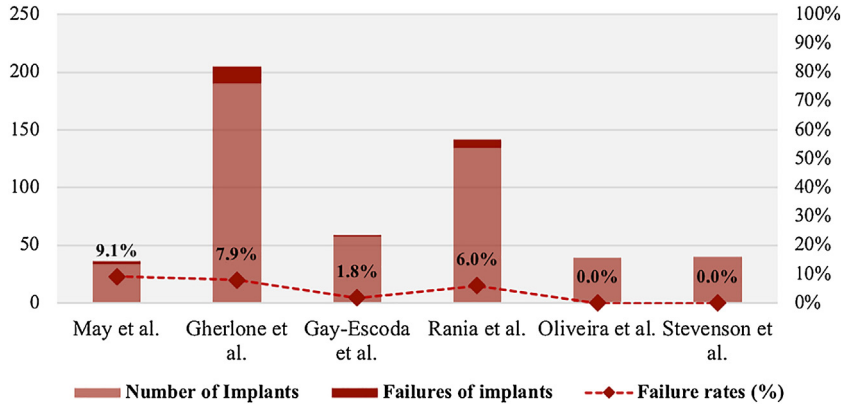

Fig. 2. Number of implants that survived, number that failed, and the implant failure rate in HIV-positive patients for each of the six studies.

the same study reported no usage of prophylactic or postoperative medications[8]. These factors may have been responsible for the failures, since patients with a CD4+ T-cell count <200 cells/mm^3 would usually be given broad-spectrum antibiotics[25]. In a systematic review, Esposito et al.[26] reported that prophylactic antibiotics reduce the failure of dental implants placed in ordinary conditions, but that there are no apparent differences in the occurrence of postoperative infections. Thus, the use of antibiotics before surgery is recommended, especially because the inflammatory process at the site of surgery causes a temporary reduction in the CD4+ T-cell count after implant placement[5].

Marginal bone loss is considered an important parameter in implantology[27]. In this review, the mean marginal bone loss was below the 1.2 mm considered acceptable in the literature[23]. In studies that conducted a comparison between patients with and without HIV, there was no difference in marginal bone loss[3,18]. Therefore, the second null hypothesis was also accepted.

Clinical analysis of bone resorption levels is especially important in HIV-positive patients because HAART causes different bone disorders and thus reduces bone mineral density[3]. Oliveira et al.[3] compared NNRTI-based HAART and PI-based HAART, since reduced bone mineral density has been shown to correlate significantly with PI-based HAART. Although these authors observed low bone mineral density in HIV-positive patients, there was no difference in marginal bone loss between patients with and without HIV infection, regardless of the antiretroviral therapy used. However, it is important to note that the longest follow-up period in the three studies evaluating marginal bone loss was 1 year. Thus, additional clinical studies with longer follow-up periods are necessary to verify the clinical stability of bone tissue in HIV-positive patients.

The most frequently reported complication in the selected studies was peri-implantitis[9,20]. Implant failures were most often related to postoperative complications that led to infection and/or peri-implantitis and consequent implant loss[8,9,20]. However, the high risk of peri-implantitis in these patients may have been associated with factors other than immunosuppression. Gay-Escoda et al.[20] reported the highest number of peri-implantitis cases ($n = 25$); most involved patients who had advanced periodontal disease and had failed to comply with periodontal/peri-implant maintenance visits. These results are in agreement with those of another systematic review, which reported that supportive implant treatment (maintenance visits) prevents the occurrence of tissue disease around implants[28].

Gherlone et al.[9] also presented a high number of patients with peri-implantitis (10 cases). Such a high risk of complications was observed in patients who smoked (>10 cigarettes per day), which also contributed significantly to implant failure in HIV-positive patients. These results corroborate those of another study, which found that smoking affects implant survival rates and the incidence of postoperative infections[29].

The results of this review should be interpreted with caution, as there were a number of uncontrolled confounding factors in the included studies, no RCT studies were included, and three studies had short follow-up periods. Thus, in the future, more studies with longer follow-up periods should be conducted to compare HIV-positive and negative patients.

In conclusion, within the limitations of this study, this systematic review indicates that dental implants are suitable for HIV-positive patients with controlled risk factors and normal CD4+ cells counts, because implant survival rates and levels of marginal bone loss were similar to those of HIV-negative patients.

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Competing interests

The authors declare that there was no conflict of interest in the elaboration of this study.

Ethical approval

Not applicable.

Patient consent

Not applicable.

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