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Review

Dental implants in patients suffering from autoimmune diseases: A systematic critical review

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ABSTRACT

Purpose: This systematic review aimed to evaluate complications and survival rates of dental implants placed in patients suffering from autoimmune diseases.
Materials and methods: A systematic review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses systematic review guidelines (PRISMA), using Google scholar and PubMed electronic databases with a stop date of September 2021. The eligibility criteria included all full text human studies in the English language literature reporting on patients with autoimmune diseases treated with dental implants.
Results: Fifty-five studies reporting on nine distinct autoimmune diseases were analyzed: 17 on Sjögren's syndrome (SS), 11 on oral lichen planus (OLP), 8 on Type 1 diabetes, 6 on rheumatoid arthritis (RA), 4 on systemic scleroderma (SSc), 3 on Crohn's disease (CD), 3 on systemic lupus erythematosus (SLE), 2 on mucous membrane pemphigoid (MMB) and 1 on pemphigus vulgaris (PV). Despite the heterogeneity and methodological limitations of most of the studies, results showed that dental implant survival rates were comparable to those reported in the general population. However, patients with secondary SS or erosive OLP were more susceptible to developing peri-mucositis and increased marginal bone loss.
Conclusion: This review suggested that dental implants may be considered as a safe and viable therapeutic option in the management of edentulous patients suffering from autoimmune diseases. Nevertheless, scrupulous maintenance of oral hygiene and long-term follow-up emerge as being the common determinants for uneventful dental implant treatment.

1. Introduction

Dental implants have dramatically improved the quality of life of edentulous patients worldwide by providing stable oral rehabilitation [1–4]. In healthy patients, fixed and removable implant-supported prostheses have proven to be reliable with reported high long-term success and implant survival rates of up to 95% at 10- year follow up [1–4]. In the last two decades, the increase in life expectancy has led to the constant growth of an aging population, thus an increase in the medically compromised population [5–8]. This is especially true with regards to chronic diseases such as heart disease, cancer and diabetes. Although evidence suggests that particular chronic illnesses can unfavorably affect the success and survival of dental implant therapy over time, there is a lack of systematic data supporting which medical conditions should be considered as absolute contraindications for dental implant placement [5–9]. However, the general feeling seems to be that the benefits of such treatment outweigh the possible risks [5–9]. Among medical comorbidities, autoimmune diseases represent a group of disorders with increased risk of oral mucosa diseases, caries and/or periodontal diseases as well as a potential alteration of bone quality related to the associated drug therapy [5–9]. Moreover, the immune system has been shown to play a crucial role in the osseointegration process by balancing the host's inflammatory response as part of the foreign body reaction to dental implants [9]. The immune system has also been shown to be involved in the regulation of the marginal bone loss as well as the soft tissue seal around the implant [9]. These

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considerations highlight the potential deleterious effects on the fate of dental implants to which patients with autoimmune disorders may be exposed. To date, autoimmune diseases encompass nearly 100 distinct entities, which are categorized as organ specific or involving multiple organs, with a worldwide increasing incidence and an overall prevalence of 3–5% in the general population [10–13]. Although differing between geographical regions, the increased frequency of autoimmune diseases affects women predominantly, with a female-to-male ratio ranging from 10:1 to 1:1 [10–13]. For these reasons, the pertinence of dental implant therapy in patients with autoimmune diseases should be questioned by practitioners with regards to potential risks and complications that can affect the final outcome of the dental supported rehabilitation [5–9]. This dilemma is furthermore amplified by the fact that there is no definitive cure for autoimmune diseases, and associated drug therapy regimens represent a challenge given their potential detrimental effects on dental implant osseointegration thus long-term survival [10–13]. Thus far, to our knowledge, only two studies have systemically reviewed the outcome of dental implant therapy in patients with autoimmune diseases [14,15]. Both studies reported on only muco-cutaneous autoimmune diseases. Interestingly, despite the limited number of patients and the low level of evidence and specificity, both studies showed that the implant survival rates seemed comparable to those of healthy patients [14,15].

This study aimed to evaluate complications and survival rates of dental implants placed in patients with selected autoimmune diseases through a systematic review of the published literature.

2. Materials and methods

2.1. Protocol and eligibility criteria

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [16]. The inclusion criteria were organized according to PICO format (Population, Intervention, Control, and Outcome) as follows: Population – subjects in the included review must be humans, with autoimmune diseases, who underwent implant treatment; Intervention – implant placement in patients with autoimmune diseases; Control – all studies with a matched control healthy group when available; Outcome – implant survival and complications at follow-up. All clinical reports, case series, prospective, and retrospective studies on dental implant treatment in humans with autoimmune diseases until September 2021 were included. Animal studies and abstracts were excluded.

2.2. Search strategy and source of information

The research was conducted using two electronic databases: Google Scholar and PubMed of the US National Library of Medicine until September 2021. More results were found using Google scholar compared to PubMed. The MeSH terms used were: ("dental implants," "x-autoimmune disease, "or "x-autoimmune disorder") OR ("dental implants AND "x-autoimmune diseases," or "x-autoimmune disorder) OR ("dental implants," "x-autoimmune disease," "complications"). The choice of language was English only.

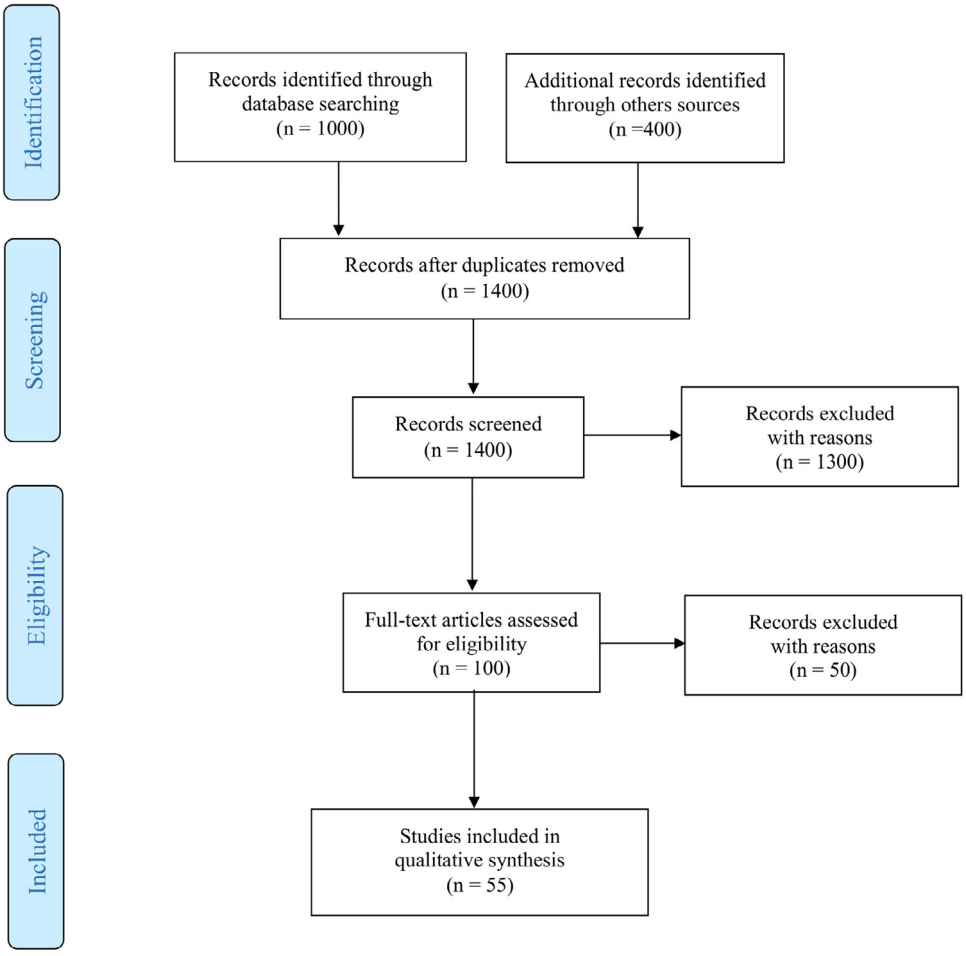

Fig. 1. Patient inclusion flowchart describing the data selection.

Two reviewers (J.F.O.E and P.S.) independently evaluated the abstracts considering formal inclusion criteria and extracted relevant data on the study characteristics (design of the study, year of publication, sample size, follow-up duration, the number and characteristics of implants placed), patient characteristics (age and gender) and outcome data. Primary outcomes were dental implant survival rate and complications.

3. Results

3.1. Study selection

1400 studies were identified through PubMed and Google scholar. During the first phase of selection, titles and all abstracts found through electronic searches relating to the study's objective were screened independently. After that, 1300 were excluded; duplicates, animal studies, *in vitro* studies, and articles published in languages other than English were excluded. Finally, the remaining 100 articles were further analyzed for final inclusion. After full-text reading, 45 additional articles were excluded: 4 meta-analyses and 41 reviews. Thus, 55 studies were considered for qualitative analysis and included the following diseases:

- Sjögren's syndrome (SS) [17–33].
- Oral lichen planus (OLP) [34–44].
- Type-1 Diabetes (T1D) [45–52].
- Rheumatoid Arthritis (RA) [19,21,53–56].
- Systemic scleroderma (SSc) [21,57–59].
- Crohn's disease (CD) [47,60,61].
- Systemic lupus erythematous (SLE) [62–64].
- Mucous membrane pemphigoid (MMP) [65,66].
- Pemphigus vulgaris (PV) [67].

Data were carefully combined and summarized in a PRISMA flow diagram (Fig. 1) showing the different selection processes.

3.2. Data synthesis

Given the significant heterogeneity in indications, the unavailability of explicit descriptions and criteria for complication assessment and poor quality of evidence, quantitative data could not be synthesized using meta-analyses. Results were therefore summarized in a qualitative and critical analysis.

3.3. Sjögren syndrome (SS) (Table 1)

The literature search revealed 17 publications reporting on patients with Sjögren syndrome receiving dental implants (one observational prospective cohort study, four retrospective studies, two case series and ten case reports) [17–33].

Krenmair et al. focused on retrospectively assessing the implant-prosthodontic outcome in patients with isolated autoimmune rheumatoid arthritis (RA) compared to those with RA associated with concomitant connective tissue diseases (CTD) [19]. It should be pointed out that among the RA and CTD group, 8 out 9 patients had secondary SS. Although the survival rate was 100% in both groups, patients with RA and CTD showed a significantly increased bone resorption as well as more vulnerable soft-tissue conditions, reflected by a higher bleeding index. Weinlander et al. also reported similar results [21].

Korfage et al. were the only authors comparing clinical outcomes in SS patients (primary and secondary form) with those of control healthy patients [23]. In a retrospective study, they found an overall survival rate of 97% in the SS group versus a 100% success rate in matched healthy controls during a comparable follow-up period of 46 months. The only significant difference between the two groups was related to peri-implant mucositis (PIM) (bleeding on probing at one or more sites around one or more implants), which was diagnosed in 94% of the SS patients versus 62% of the healthy control patients. With regard to the occurrence of peri-implantitis (PID), the incidence was similar in both groups (14% in SS patients and 14% in healthy control group). Moreover, no significant difference in the prevalence of peri-implant mucositis and/or peri-implantitis between patients with primary SS and secondary SS was found.

Albrecht et al., based on oral health questionnaires, compared patient-reported answers related to dental implant treatment (outcome, satisfaction and complications) in SS patients and in healthy control patients [24]. They found a non-significant difference between the two groups (95.2% in SS patients and 100% in control patients), which is a similar rate of success to that reported in the general population.

Siddiqui et al. reported a lower survival rate of dental implants placed in SS patients (87%) [27]. Interestingly, all of the implants were lost in the preloading phase; whereas, the remaining loaded implants had a 100% rate of survival at the 40-month follow-up. Charcanovic et al. found a survival rate of 97.2% as well as an increased marginal bone loss (MBL) at a mean follow-up of 125 months in their case series of 19 patients with SS [29]. Nine out ten case reports had a 100% survival rate in SS patients at different follow-up times (range 2–156 months) [18,20,22,25,26,28,30–33].

3.4. Oral lichen planus (OLP) (Table 2)

Eleven studies focused on the outcome of dental implants in patients with OLP (three prospective controlled studies, one retrospective study, one undetermined study, one case series and five case reports) [34–44].

Only three studies compared OLP patients with healthy controls [36,38,43]. Although not significant, Hernandez et al. found a surprisingly higher rate of survival in the OLP groups compared to the control group (100% and 96.8%, respectively) [36]. Moreover, the prevalence of PIM was also slightly higher in the control group; whereas, the prevalence of PID was higher in the OLP group. Interestingly, the presence of desquamative gingivitis (DG) was associated with a higher rate of PIM on the implants of some patients in the erosive OLP group. Similar results were also reported by Lopez-Jornet et al. who found no significant differences between OLP patients and the control group with regards to implant survival, PIM, PID, and MBL [38]. The overall success rate in the OLP and control groups was 96.42% and 92%, respectively. The PIM and PID prevalence in the OLP group was 17.9% and 25% and in the control group was 18% and 16%. By contrast, they found PID to be more frequent in the mandible and in dental implants placed posteriorly compared to those placed anteriorly either in the maxilla or the mandible. Khamis et al. evaluated the prognosis of implants placed in OLP patients controlled by low-dose systemic corticosteroids in comparison to noncontrolled patients and a control healthy group over a 4-year period [43]. They focused on MBL and found no difference between healthy and controlled patients. However, noncontrolled patients exhibited a significant increase in MBL, and three of them (13.7%) showed recurrence of OLP (erosive and nonerosive types) as demonstrated by histopathological evaluation from biopsy of the cheek and/or gingival tissue opposing the implant placement.

Czerninski et al. evaluated dental implant survival as well as the potential negative influence on the course of the disease in patients suffering from OLP [37]. They found a 100% success rate and no difference of OLP signs and symptoms between patients with and without dental implant rehabilitation.

The positive effect of low doses of corticosteroids on maintenance in OLP patients receiving dental implants was also clearly reported by Aboushelib and Elsafi [39]. They were the only authors to propose a specific protocol (oral corticosteroids and low-energy soft tissue laser irradiation) for dental implant placement in patients with active

OLP. They found a significant improvement of the overall success rate in the controlled treatment group (100%) compared to that of uncontrolled patients (24%). In a retrospective analysis, Anitua et al. reported on the use of short implants (≤ 8.5 mm long) together with a prophylactic regimen of oral corticosteroids in OLP patients to avoid any bony augmentation [40]. Unfortunately, they did not include a control group for comparison. However, they found a 98% success rate with only 1 implant out 66 lost, which was in a patient who had erosive lichen planus with DG.

With regards to the possible malignant transformation of OLP, Noguchi et al. have been the only group to report a single case of an oral squamous cell carcinoma developed in proximity to a dental implant with PID [41]. The four otherwise well-integrated mandibular implants that supported a fixed total prosthesis were removed together with the segmental anterior mandibulectomy, and the defect was reconstructed by a free fibular flap with the patient free of relapse at the 4-year follow-up visit. The remaining studies revealed a 100% survival rate at different intervals of follow-up (range 18–68 months) [34,35,40,42,44].

3.5. Type 1 diabetes (T1D)

The literature search revealed eight publications reporting on diabetic patients receiving dental implants among which only three focused exclusively on type 1 diabetes (one prospective case control, one case series and one single case report) [49,50,52]. The remaining five retrospective studies analyzed data from both type 1 and type 2 diabetic patients [45–48,51].

Only two studies prospectively correlated T1D to the success or failure of dental implants in a controlled setting [51,52]. Sannino et al. investigated the success of mandibular overdenture on three implants in ten type 1 diabetic patients versus ten control non-diabetic patients [51]. They found an 80% survival rate in the study group versus 100% in the control group. Moreover, they also observed a significant decrease in stability as well as a significant increase in amount of average crestal bone loss in the study group as compared to the control group. Sannino et al. evaluated a series of 106 patients with partial edentulous jaws separated into two groups of 53 patients (type 1 diabetic versus healthy patients) [52]. They found no statistically significant differences at the 24-month follow-up in the survival rate between the diabetic and the control group (95.19% and 97.03%, respectively), nor in infections occurrence or in marginal bone loss. Shimoda et al. reported on a type 1 diabetic patient receiving one mandibular dental implant [49]. They unfortunately did not report whether the implant was successfully osseointegrated nor any peri-implant complications. Conversely, they focused on the occurrence of acute severe hypoglycemia that occurred during dental implant surgery, stressing the importance of monitoring glycemic levels in these patients to ensure adequate management.

By contrast, five retrospective studies reported on both type 1 and type 2 diabetic patients with no significant difference in the success and the survival rate between the two groups [45–48,51].

Fiorellini et al. found in a series of 40 patients with well-controlled diabetes at the time of implant insertion an overall 6.5-year success rate of 85.7% with most of the failures occurring within the first year of functional loading [45]. The survival rate was considered by the authors to be reasonable although lower than that reported in the general population. However, no differences were found between type 1 and 2 diabetic patients. Farzad et al. reported a success rate of 96.3% during the healing period in 25 diabetic patients with normal glucose levels as assessed by personal interviews [46]. Unfortunately, no information was given regarding long-term survival. In a retrospective study, Alsaadi et al. assessed the influence of different systemic factors on implant success [47]. Despite the limited number of diabetic patients included in this series (n = 10), they found a 100% survival rate of the 34 implants 2 years after the abutment connection. de Araújo Nobre et al. were the first to report a significantly lower survival rate in type 1 diabetics when compared to type 2 diabetics (80% versus 90.5%, respectively) [48]. Moreover, type 1 diabetics showed higher MBL between the 1st and 5th years of function of more than 0.2 mm per year failing to fulfill the criteria for implant success. However, no information was given regarding glycemic control during the follow-up period. Alberti et al. analyzed the results of 204 patients, 19 of which were diabetics [52]. They reported 10-year survival rates of 96.51% and 94.74%, respectively for diabetic and non-diabetic patients. Moreover, only one type 2 diabetic patient developed PID; whereas, one type 1 diabetic patient experienced multiple implant failures due to a failure of osseointegration. Interestingly, this patient was the only one who had poor glycemic control (HbA1c ≥ 8.0%). Although not unequivocally demonstrated, the relationship between glycemic control and dental implant survival has been strongly suggested by several reports.

3.6. Rheumatoid arthritis (RA) (Table 3)

Six studies on the use of dental implants in RA patients were found in the literature search (one prospective study, two retrospective studies, and three case reports) [19,21,53–56].

Results from the Krenmair et al. and Weinlander et al. studies were discussed previously in the section on SS patients [19,21]. El-Sherbini was the only author to compare survival rate prospectively between RA and non-RA patients with no difference found between the two groups [56]. The remaining three case reports had results similar to those found in the general population with a 100% survival rate [53–55].

3.7. Miscellaneous: (systemic scleroderma (SSc); Crohn's disease (CD); systemic lupus erythematosus (SLE); mucous membrane pemphigoid (MMB); pemphigus vulgaris (PV)) (Table 4)

The literature search revealed four studies on patients with SSc [21,57–59], three on patients with CD [47,60,61], three on patients with SLE [62–64], two on patients with MMB [65,66], and one on patients with PV receiving dental implants [67]. Ten out thirteen were single case reports [57–60,62,64–67], which showed a 100% survival rate with the exception of a case report on an SLE patient with concomitant common variable immunodeficiency (CVID), who had a 93% survival rate [63]. With regards to CD patients, Alsaadi et al. in two different studies on the influence of systemic diseases on dental survival found a success rate clearly lower (66.7%) than that encountered in the general population [47–61] (
Table 5).

4. Discussion

This review aimed to evaluate complications and survival rate of dental implants in patients with autoimmune diseases. The results suggest that dental implants can be considered a safe and reliable solution in this category of patients, who in the majority of cases have shown a success rate similar to that found in the general population. These findings seem to contradict a general tendency that emerged from some previous reports, which called for some caution with respect to implant placement in patients suffering from systemic disorders [5,9]. Actually, some authors warn about the predominant role that systemic factors could play in an increased risk of early failure for implant placement [5,9]. As a consequence, dental implant placement was often considered as being contraindicated in such patients. However, there is still uncertainty about the exact nature of systemic factors that jeopardize implant osseointegration as well as its preservation over time.

Our review has several methodological limitations, which unfortunately prevented a robust comparison between studies and thus

Table 1
Patient characteristics and clinical data (Sjögren's syndrome (SS)).

Authors	Type of study	Diseases	Sample						Follow up(Months)	Survival rate (%)	Complications
			Patients			Implants					
			No	Gender	Mean Age (y)	No	Type	Surface			
Payne et al. [17]	CS										
	Pt I	SF	1	F	38	6	NR	Rough	96	50%	NR
	Pt II	PF	1	F	38	6	NR	Rough	12	100%	NR
	Pt III	SF	1	F	40	8	NR	Rough	12	100%	NR
Binon P et al. [18]	CR	NR	1	M	67	6	NR	Rough	156	100%	NR
Krenmair et al. [19]	R	RA+SF	8	F	52.4	39	Camlog	NR	96	100%	RA + SS : ↑ MBL and higher BI
Spinato et al. [20]	CR	PF	1	F	62	6	Zimmer TPS	Rough	12	100%	NR
Weinlander et al. [21]	R	RA+SF	21	83	NR	21	Camlog	Rough	72	100%	RA + SS : ↑ MBL and higher BI
de Mendonça Invernici et al. [22]	CR	SF	1	F	58	2	Systhex Sistema	Rough	72	100%	NR
Korfage et al. [23]	CCR	PF (41) SF (9)	50	F(46) M(4)	67	140	NR	NR	46	97%	PID (14%) PIM (94%)
Albrecht et al. [24]	OPCS	PF + SF	32	F (32)	64.5	104	NR	NR	NR	95.2%	NR
Chochlidakis et al. [25]	CR	SF	1	F	71	6	Straumann	SLA	14	100%	NC
Peron et al. [26]	CR	SF	1	F	62	5	Zimmer TM	Rough	NR	NR	NR
Siddiqui et al. [27]	R	PF SF	11	NR	63.7	23	NR	NR	40	87%	Implant mobility PIM MBL
Mori et al. [28]	CR	PF	1	F	50	8	Straumann Zimmer SDIS	Rough	36	100%	NC
Chrcanovic et al. [29]	CS	NR	19	M(1) F(18)	63.3	107	NB turned (43) NB MK III (38) Astra TiOblast (13) Astra Osseospeed (10) Bego Semados (2) NB Active (1)	Rough	125	97.2%	↑ MBL
Coman et al. [30]	CR	PF	1	F	71	12	NR	NR	6	100%	NC
Zaghal and Doufish [31]	CR	NR	1	F	28	4	CDDI	Rough	2	100%	NC
Turkyilmaz et al. [32]	CR	NR	1	M	80	15	NR	Rough	12	100%	↑ MBL
Daneshparvar et al. [33]	CR	NR	1	F	46	6	NR	NR	84	100%	NC

Abbreviations: R: retrospective; CR: case report; CS: case series; CCR: Case control retrospective study; OPCS: observational prospective cohort study; F, female; M, male; NR, not reported; Pt., patient; PF: primary form of SS; SF: secondary form of SS; RA: rheumatoid arthritis; TPS: Tapered Screw-Vent HA; SDIS: Spline Dental Implant System; NB: Nobel Biocare; TM: Trabecular Metal; NC: no complications; MBL: marginal bone loss; SLA: sandblasted and acid-etched; PIM: peri-implant mucositis; PID: peri-implantitis.

Table 2
Patient characteristics and clinical data (Oral lichen planus (OLP)).

Authors	Type of study	Diseases	Sample Patients No	Gender	Mean Age (y)	Implants No	Implants Type	Implants Surface	Follow up(Months)	Survival rate	Complications
Esposito et al. [34]	CR	E	1	F	72	2	Straumann	NR	18	100%	NC
		E	1	F	78	2	Straumann	NR	21	100%	
Reichart et al. [35]	CR	R	1	F	63	4	HaTi	Tapered	Pt I: NR	100%	Pt I: Delayed wound healing
		RA	1	F	68	1	Camlog	Rough	Pt II: 36	100%	Pt II: Bone resorption and gingivitis
		AWE	1	F	79	5	ZLMicro	Rough	Pt III: NR	100%	Pt II: NC
Hernandez et al. [36]	PCS	E	18	M(4) F(14)	53.7	56	NB Ti-Unite		56.5	100%	PIM (66.6%) PID (27%)
Czerninski et al. [37]	R	R, E, A	14	M(3) F(11)	59.5	54	NR	NR	12–24	100%	BOP and gingivitis (3pts)
López-Jornet et al. [38]	CSS	R(11) AE(5)	16	M(6) F(10)	64.5	56	NR	NR	12–24	96.4%	PIM (17.9%) PID (25%)
Aboushelib et al. [39]	NR	Active	23	M(11) F(12)	54.3	55	Zimmer	Rough	1–4 36	24% UP 100% CP	No OI NC
Anitua et al. [40]	CS	E(8) R(15)	23	M(3) F(20)	58	66	BTI	NR	68	98%	Recurrent gingivitis (1pt)
Noguchi et al. [41]	CR	NR	1	F	78	4	NR	NR	48	0%	Post-treatment evolution of OLP to OSCC with loss of implants
Fu et al. [42]	CR		1	F	65	4	NB	Rough	36	100%	NC
Khamis et al. [43]	PCS	NEOLP EOLP	22 (LDSC) 20 (No LDSC)	NR	NR	NR	NR	NR	48	100%	No LDSC: ↑ MBL and recurrence of the oral lesions
Martin-Cabezas [44]	CR	Erosive	1	F	83	3	NR	NR	12	100%	PID

Abbreviations: R: retrospective; PCS: prospective-controlled study; CSS: Cross-Sectional control study; CR: case report; F, female; M, male; NR, not reported; NS: not specified; Pt., patient. R: reticular form; RS: reticular atrophic form; A: atrophic form; AWE: atrophic without erosions; AE: atrophic erosive form; E: Erosive form; NEOLP: atrophic/erosive, bullous, and ulcerative; EOLP: atrophic/erosive, bullous and ulcerative; LDSC: low doses of systemic corticosteroids NB: Nobel Biocare; NC: no complications; BOP: Bleeding on probing; OSCC: Oral squamous cell carcinoma; MBL: marginal bone loss; PIM: peri-implant mucositis; PID: peri-implantitis: OI: osseointegration; UP: uncontrolled patients (no oral corticosteroids and no low-energy soft tissue laser irradiation at the implant insertion); CP: controlled patients (oral corticosteroids and no low-energy soft tissue laser irradiation at the implant insertion).

Table 3
Patient characteristics and clinical data (Diabetes).

Authors	Type of study	Diseases	Sample						Follow up(Months)	Survival rate	Complications
			Patients			Implants					
			No	Gender	Mean Age (y)	No	Type	Surface			
Fiorellini et al. [45]	R	T1 (6) T2 (34)	40	M(29) F(11)	48.7	215	NB Straumann	TPS SLA	78	85.6%	Yes (NS)
Farzad e al. [46]	R	T1 (9) T2 (16)	25	M(5);F(4) M(7);F(9)	63	136	NR	NR	12	94.1%	Yes (NS)
Alsaadi et al. [47]	R	T1 (1) T2 (9)	10	NR	NR	T1(1) T2(33)	NB	Machined TiUnite	NR	100%	NR
de Araújo Nobre et al. 2016 [48]	R	T1 (6) T2 (64)	70	F(33) M(37)	59	352	NB	Machined TiUnite	60	T1 (80%) T2 (90.5%)	Yes (NS)
Shimoda et al. [49]	CR	T1	1	M	60	1	NR	NR	NR	NR	NR
Eldidi et al. [50]	CCP	T1	10	M(20)	NR	30	Dentium NR line	SLA	12	80%	Yes (NS)
Sannino et al. [51]	CCP	T1	106	M(59) F(47)	38.4	205	NR	NR	24	95.2%	5 Implant failures
Alberti et al. [52]	RCS	T1 (2) T2 (17)	19	M(90) F(114)	57.3	NR	NR	NR	2–180	NR	T1 : PID T2 : MIF

Abbreviations: R: retrospective; CR: case report; CCP: Case control prospective study; RCS: retrospective control study; F, female; M, male; NR, not reported; NS: not specified; T1: Diabetes Type 1; T2: Diabetes type 2; NB: Nobel Biocare; TPS: Tapered Screw-Vent HA; SLA: sandblasted and acid-etched; MIF: multiple implant failure; PIM: peri-implant mucositis; PID: peri-implantitis.

the possibility of a true conclusive meta-analysis and led us to perform a narrative review. Most of the time, the studies were retrospective and nonrandomized, and there was a large proportion of small case series and case reports. Moreover, information on the design of the studies, with clearly predetermined end points, was rarely defined. Therefore, studies were highly subject to potential bias and associated with a low level of evidence. Moreover, the exact role played by confounding factors (e.g., smoking, alcohol, different concomitant systemic diseases, pharmacologic therapy) was never taken into account separately, thus compromising the evaluation of their effect on dental implant survival and the potential to draw sound conclusions. These limitations make any combination of results difficult and inappropriate, thus preventing an observational study of the evidence to be conducted.

Despite the absence of a true meta-analysis, the literature reviewed did allow for the following general observations regarding the autoimmune diseases presented:

4.1. Sjögren syndrome (SS)

Of all the autoimmune diseases reviewed, most were on patients with SS. Overall, with the exception of one study, data showed an overall survival rate similar to that reported for the general population [17–33]. However, two specific peculiarities related to SS patients receiving implants emerged [19,21,23,27,29]. First is the marked susceptibility to continuous inflammation of the peri-implant marginal soft-tissues in comparison to healthy matched controls [19,21,23,27,29]. This gingival vulnerability is probably elicited by the most important sequela caused by the disease in the oral cavity, which is the decrease of salivary secretion. As a result, the self-clearance of the oral cavity is impaired allowing the collection of food debris within the peri-implantar gingival sulcus with a consequent local chronic inflammation. This dysfunction was clinically reflected by a greater prevalence of PIM (high bleeding index and pocket probing depths) and MBL in SS patients. By contrast, no significant difference in the prevalence of PID between SS and healthy patients was revealed. Second, no significant difference was found with regard to the survival rate between patients with primary and secondary SS [19,21,23,27,29]. However, patients with SS and concomitant RA showed increased MBL and PIM. Chronic use of corticosteroids as well as the compromised dexterity related deformation of the hands that is often present in RA patients have been mentioned as possible detrimental factors explaining the pronounced difference in the MBL and PIM rate between the two categories of SS patients. In light of these results, it seems that there are no reasons to contraindicate dental implant rehabilitation in SS patients. Nevertheless, the intrinsic vulnerability of the soft tissue that characterizes SS patients and *a fortiori* those with the secondary form of the disease, makes meticulous oral hygiene and regular monitoring essential for the long-term success of implant-supported rehabilitation.

4.2. Oral lichen planus (OLP)

Similar to SS patients, implant survival among OLP patients was essentially the same as that reported in the general population [34–44]. Again, these results contradict the conjectures of some authors who have claimed that the potential risk of dental implant failure in OLP patients was greater than in healthy patients [68]. These conjectures are mainly based on the hypothesis that the damaged epithelium can fail to adhere correctly to the implant's surface [68]. This being said, three main messages came out of the analysis [36,38,43]. The first is related to the predisposing role of DG in erosive OLP patients to develop PIM and a higher rate of PID compared to that found in the healthy control group [36,38,43]. Second is the beneficial effect of low doses of "prophylactic" oral corticosteroids on the dental implant survival rate as well as on the control of the disease in terms of limiting its recurrence was outlined by some authors [39,43]. Finally, dental implant placement does not seem to influence the course of the disease negatively [37]. These findings converge again on the crucial issue of the maintenance of a good state of oral hygiene as the *conditio sine qua non* for long-term success.

4.3. Type 1 diabetes (T1D)

The paucity of studies focusing exclusively on type 1 diabetics prevented a well-structured analysis of the dental implant outcomes in this category of patients [49,50,52]. Moreover, most of the studies combined both types 1 and 2 diabetes, systemic diseases, periodontal diseases, or evaluated the effect of HbA1c on implants making it impossible to analyze data on type 1 diabetics separately [45–48,51]. However, some considerations, which must be interpreted with caution, may be appropriate. First is that there is not an explicit predisposition to a higher rate of failure in diabetic patients in general [45–52]. Secondly, it would seem that failures occur in the early phases either during the healing period or within the first year of implant loading [45–52]. Thirdly, no significant differences were revealed

Table 4
Patient characteristics and clinical data (Rheumatoid arthtritis (RA)).

Authors	Type of study	Diseases	Sample Patients No	Gender	Mean Age (y)	Implants No	Type	Surface	Follow up(Months)	Survival rate	Complications
Eder and Watzek [53]	CR	chronic polyarthritis	1	F	80	2	Friadent Frialoc	Rough	48	100%	NC
Yokokoji et al. [54]	CR	Isolated RA	1	F	83	5	Astra Tech	Rough	96	100%	NC
Krennmair et al. [19]	R	Isolated RA	25	F(25)	46.7	85	Camlog	Rough	42	100%	RA + SS :
		RA + CTD	9	F(9)	53.4	41					↑ MBL and higher BI
Weinlander et al. [21]	R	Isolated RA	16	F(16)	55.6	83	Camlog	Rough	36	100%	RA + SS :
		RA+CTD	5	F(6)							↑ MBL and higher BI
El-Sherbini [55]	CCP	Isolated RA	14	NR	47.5	28	Neo Biotech	Rough	3	100%	NC
Shokri et al. [56]	CR	Isolated RA	1	F	65	8	Biodenta	Rough	4	100%	NC
			1	F	51	6	SIC invent		48	100%	↑ MBL

Abbreviations: R: retrospective; CR: case report; CCP: case control prospective study F, female; M, male; NR, not reported; NS: not specified; NC: no complications; SS: Sjögren's syndrome; MBL: marginal bone loss; BI: bleeding index.

Table 5
Patient characteristics and clinical data (Systemic Scleroderma (SSc); Crohn's disease (CD); Systemic lupus erythematosus (SLE); Mucous Membrane Pemphigoid (MMB); Pemphigus Vulgaris (PV)).

Authors	Type of study	Diseases	Sample Patients No	Gender	Mean Age (y)	Implants No	Type	Surface	Follow up(Months)	Survival rate (%)	Complications
Weinlander et al. [21]	R	SSc	1	NR	NR	6	Camlog	Rough	46	100%	NC
Zigdon et al. [21]	CR	SSc	1	F	45	12	MIS implant	Rough	36	100%	NC
Nam et al. [58]	CR	SSc	1	F	71	14	NB	Rough	NR	100%	NC
Baptist et al. [59]	CR	SSc	1	F	61	6	Implant direct	Rough	24	100%	NC
Nayyar Singh et al. [60]	CR	CD	1	NR	NR	10	NA	smooth surfaced	12	100%	NR
Alsaadi et al. [61]	R	CD	NR	NR	NR	NR	NB	NR	NR	↑ risk of early implant failures	NR
Alsaadi et al. [47]	R	CD	2	NR	NR	9	NB	NR	NR	66.7%	NR
Ergun et al. [62]	CR	SLE	1	F	49	6	Zimmer	microtextured MTX	24	100%	NC
Drew et al. [63]	CR	SLE	1	F	28	15	Zimmer	microtextured MTX	18	93%	NC
Todorovic et al. [64]	CR	SLE	1	F	66	6	Straumann	SLA	36	100%	NC
Megarbane et al. 2017 [65]	CR	MMP	1	F	60	14	NB	Ti-Unite	180	100%	NC
Fuschetto et al. [66]	CR	MMP	1	F	68	4	BioHorizons	Rough	8	100%	NC
Altin et al. [67]	CR	PV	1	F	70	2	Zimmer	Micro-surfaced	32	100%	NC

Abbreviations: R: retrospective; CR: case report; F, female; M, male; NR, not reported; Pt., patient; NB: Nobel Biocare; NC: no complications; SLA: sandblasted and acid-etched; PIM: peri-implant mucositis; PID: peri-implantitis.

between the two types of diabetic populations [45–52]. Finally, the positive role played by a good glycemic control on long-term success became apparent [45–52]. Despite this limited information, it seems reasonable that dental implantation in T1D patients should not be contraindicated, provided the comorbidities are controlled. The susceptibility to infection and the glycemia together with a strict and regular maintenance follow-up for oral hygiene control must occur.

4.4. Rheumatoid arthritis (RA)

Although heterogeneous, all of the six studies revealed by the literature search showed a 100% survival rate of dental implants in RA patients [19,21,53–56]. As mentioned in the previous section on SS patients, the primary information is related to the susceptibility of RA patients with concomitant SS to develop PIM and higher MBL [19,21].

4.5. Miscellaneous: (systemic scleroderma (SSc); Crohn's disease (CD); systemic lupus erythematosus (SLE); mucous membrane pemphigoid (MMB);pemphigus vulgaris (PV))

In this category, the majority were case reports or general studies reporting on various systemic conditions precluding any definitive conclusions [47, 60–67]. Nevertheless, all of these heterogeneous studies [47] except one revealed a high survival rate comparable to that found in the general population.

5. Conclusion

The findings of our analysis suggest that dental implants may be considered as a safe and viable therapeutic option in the management of edentulous patients suffering from the autoimmune diseases that were reviewed. As a matter of fact, globally, the survival rate was found to be similar to that found in healthy patients Thus, no specific contraindications seem supported by current knowledge. With the exception of rigorous glycemic control for diabetic patients to prevent chronic complications, which can potentially negatively influence dental implant survival, and the use of corticosteroids in OLP patients, no other extraordinary measures were advocated. Finally, the scrupulous maintenance of oral hygiene and long-term follow-up emerge as being the common determinants for uneventful dental implant treatment. However, further well-structured controlled studies with larger sample sizes and matched cohorts allowing for more robust results on the long-term outcomes are needed.

Declaration of Competing Interest

None.

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