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Systematic Review
Dental Implants

Dental implants in patients with Sjögren's syndrome: a case series and a systematic review

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Abstract. The purpose of this study was to assess the clinical outcomes of dental implants in patients with Sjögren's syndrome (SS). The study consisted of two parts: report of a case series and a systematic review of the literature. The results of the clinical series revealed that 19 patients received 107 implants and were followed for a mean of 125 months. Two patients lost three implants (failure rate 2.8%, 3/107). At the last follow-up, there was a mean marginal bone loss (MBL) of -2.190 ± 1.384 mm; estimated MBL after 30 years was 4.39 mm. The review identified 18 studies, resulting in 19 studies for analysis including the present clinical series. A total of 712 implants were placed in 186 patients; 705 implants were followed up for a mean of 72.5 months (failure rate 4.1%, 29/705; failed at a mean time of 12.9 ± 31.7 months). The probability of failure was 2.8% (95% confidence interval 1.6–4.1%). Primary SS patients had a lower implant failure rate (2.5%, 3/118) than secondary SS patients (6.5%, 12/184). In conclusion, dental implants should be considered by dentists as a viable treatment option for patients with SS, as the failure rate is fairly low. SS patients may, however, present a higher MBL around implants than patients from the general population.

Key words: Sjögren's syndrome; oral rehabilitation; dental implant; failure; marginal bone loss.

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Sjögren's syndrome (SS), primary and secondary, is a systemic disorder characterized by lymphocyte infiltration and progressive destruction of the exocrine glands, leading to mucosal dryness, particularly of the eyes and mouth[1]. SS has a significant impact on oral health, with oral implications including xerostomia due to reduced salivary flow, rampant caries, chronically inflamed and irritated oral mucosa, inflamed, enlarged, and hardened salivary glands, an increased incidence of chronic candidiasis[2,3], angular cheilitis, increased plaque retention, changes in taste perception, difficulty swallowing, chronic tissue discomfort, recurrent denture sores, difficulty masticating, and mandibular denture instability[4]. As a result of the high susceptibility to caries, patients with SS often loose many teeth during their lives and at an earlier age compared to the general population. Due to difficulties or an inability to wear dentures because of the dry and sensitive oral mucosa, many SS patients and dentists opt for oral rehabilitation with dental implants instead.

There is great demand for dental implants among SS patients, but much is conjectured on how successful this treatment may be in these patients[5]. According to the notes of SS patients included in one study[6], a considerable number of dentists

and rheumatologists advised them not to have dental implants, as these professionals were concerned about initial osseointegration or a higher risk of implant failure.

The aim of the present study was to assess the clinical outcomes of dental implants in a series of patients with SS, as well as to review the cases of SS patients receiving dental implants described in the literature.

Materials and methods

This study was performed in two parts: (1) report of a case series, and (2) a systematic review.

Case series

This retrospective study included patients treated with dental implants during the period 1980–2014 at one specialist clinic (Clinic for Prosthodontics, Centre of Dental Specialist Care, Malmö, Sweden). The study was approved by the Regional Ethics Committee of Lund, Sweden.

An implant was considered a failure if it presented signs and symptoms that led to implant removal, i.e. a lost implant.

Implants installed in patients diagnosed with SS were included. The patients could have primary SS (no underlying rheumatic disorder) or secondary SS (associated with an underlying rheumatic disease, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), or systemic sclerosis), and the syndrome needed to have been diagnosed with appropriate tests, usually a combination of some of (but not limited to) the following: blood test for SSA autoantibody, ANA test (antinuclear antibody), lip biopsy (salivary gland biopsy), Schirmer tear test, examination of the surface of the eye with rose bengal and lissamine green staining, sialogram, salivary flow, and salivary scintigraphy.

Modern threaded cylindrical or conical design implants were included, but zygomatic implants were excluded. Only implants for which first radiographs were taken within 12 months after implant installation were considered for the evaluation of marginal bone loss (MBL). Negative values of MBL were considered as bone loss.

The data were entered directly into an SPSS file (IBM SPSS Statistics version 25.0; IBM Corp., Armonk, NY, USA) as the dental records of the patients were read. These included several implant, site, and patient-related factors.

The patients were periodically followed up by a dental hygienist at the clinic, with attendance based on individual needs.

Evaluation of marginal bone levels

Reproducible intraoral radiographs were used for the evaluation of marginal bone levels. When there were no available digital radiographs from the baseline appointment, the analogue peri-apical radiographs were scanned at 1200 dpi (Epson Perfection V800 Photo Color Scanner; Epson, Nagano, Japan). MBL was measured after calibration based on the inter-thread (pitch) distance of each implant type, the Nobel implant being the most common (0.60 mm). Measurements were taken from the implant–abutment junction to the marginal bone level, on both the mesial and distal sides of each implant, and then the mean value of these two measurements was calculated. MBL was determined by comparing bone-to-implant contact levels to those of the radiographic baseline examination. ImageJ software (National Institutes of Health, Bethesda, MD, USA) was used for all measurements.

Systematic review

The guidelines put forward in the PRISMA Statement were followed (Preferred Reporting Items for Systematic Review and Meta-analyses)[7].

The focused question was constructed using the PICO format (participants, interventions, comparisons, and outcomes) and was as follows: What are the clinical outcomes, i.e. implant survival and marginal bone loss, for dental implants installed in patients with Sjögren's syndrome?

A search without time restrictions was undertaken in July 2018 in the following five electronic databases: PubMed/MEDLINE, Web of Science, Science Direct, J-Stage, and LILACS. The following terms were used: (Sjögren's syndrome OR Sjögren syndrome) AND (dental implant OR oral implant). Google Scholar was also checked. A manual search of dental implant-related journals was performed.

With regard to inclusion and exclusion criteria, publications reporting the cases of patients diagnosed with SS who were rehabilitated with implant-retained and/or implant-supported oral prosthetic rehabilitations were included. Publications reporting clinical cases of prosthetic rehabilitation not using dental implants were not included.

The titles and abstracts of all reports identified through the electronic searches were read independently by the authors. 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. Disagreements were resolved by discussion between the authors.

The following data were extracted using a standard form: year of publication, number of patients, patient sex, age, implant type, implants placed and lost in the maxilla and mandible, implant healing period, period between implant placement and loss, type of prosthetic reconstruction, MBL, and follow-up period. If necessary, authors were contacted for possible missing data.

Statistical analyses

The mean $\pm$ standard deviation (SD) values and percentages were calculated for several variables. The following statistical tests were performed: Kolmogorov–Smirnov test (to evaluate the normal distribution), Levene's test (to evaluate homoscedasticity), the Student *t*-test or Mann–Whitney test (for two independent groups of continuous variables), Pearson's χ^2 test or Fisher's exact test (for categorical variables), correlation and linear regression (to determine the relationship between MBL and time of follow-up), and untransformed proportions random-effects DerSimonian–Laird method[8] (for implant failure). The degree of statistical significance was considered $P < 0.05$. All data were analysed statistically using IBM SPSS Statistics version 25.0 software and the software OpenMeta[Analyst][9].

Results

Case series

A total of 19 patients among the 2670 patients treated with implants in the study clinic had been diagnosed with SS. These patients received a total of 107 oral implants: 56 in the maxilla and 51 in the mandible; 11 were placed in one male patient and 96 in 18 female patients. The mean age of the patients was 63.3 $\pm$ 8.1 years (range 50.4–80.3 years). A total of 107 threaded implants with a cylindrical design were installed: 43 Nobel turned, 38 Nobel MK III TiUnite, 13 Astra TiOblast, 10 Astra Osseospeed, two Bego Semados, and one Nobel Active. All implants were inserted with open flap surgery in healed sites with delayed loading. The abutment connection was performed after a mean healing time of

163 ± 46 days (range 74–233 days). The mean length of the implants was 12.8 ± 1.8 mm (range 7–15 mm) and the mean diameter was 3.74 ± 0.17 mm (range 3.3–4.3 mm).

According to the Lekholm and Zarb classification, and concerning bone quantity, 50 implants were placed in type B bone, 41 in type C bone, and eight in type D bone. Concerning bone quality, nine implants were placed in type 1 bone, 35 in type 2 bone, 49 in type 3 bone, and six in type 4 bone. This information was available for 99 implants.

Three implants were used for single-crown restorations, 22 implants for eight fixed partial prostheses with two to six prosthetic elements, six implants for a fixed partial prosthesis with seven to 10 prosthetic elements, 74 implants for 14 full-arch fixed prostheses, and two implants to support an overdenture.

The patients were followed-up for a mean of 125.5 ± 82.5 months (range 5.6–341.2 months). Two patients lost three implants, all due to loss of/lack of osseointegration (failure rate 2.8%, 3/107); no implant fracture was identified. The failures were recorded for three Nobel turned implants, all in the mandible, and they occurred at 36 days, 8.5 months, and 159.6 months after implant installation. One of the lost implants was part of a full-arch prosthesis, and two implants were lost before the abutment connection and were planned for a fixed partial prosthesis of seven to 10 prosthetic elements. These two lost implants were later replaced by another two implants. The three lost implants were installed in bone of type B2 ($n = 1$) and C4 ($n = 2$).

Marginal bone level evaluation

A total of 35 implants were excluded from the analysis of MBL for the following reasons: no radiographs were found in the dental records ($n = 13$), the first radiograph was taken at >1 year after implant installation surgery ($n = 15$), follow-up was very short ($n = 5$), and early implant failure ($n = 2$). A total of 293 MBL measurements were made for the remaining 72 implants, considering multiple radiological follow-ups for each implant, giving a mean of 4.1 MBL measurements per implant. The baseline radiographs were taken at a mean of 4.4 ± 3.2 months (range 0–9.6 months) after implant placement. The implants were radiologically followed up for mean of 125.2 ± 80.5 months (range 0.5–329.9 months).

At the last follow-up, there was a mean MBL of −2.190 ± 1.384 mm (range −7.571 to 0.000 mm) for all implants ($n = 72$). At the last radiological follow-up, 25% of the implants presented >3 mm of MBL (Table 1). There was a steady increase in mean MBL with time of follow-up (Table 2). There was an estimated trend of loss of bone with time (Fig. 1), reaching an estimated 4.39 mm of bone loss at 30 years after implant installation. According to the linear regression equation ($y = -0.79–0.01x$), there was an estimated loss of 0.01 mm of bone for every additional month of follow-up. There was a moderate correlation between MBL and follow-up time ($R = 0.563$, $R^2 = 0.317$, $P < 0.001$; Pearson correlation). At the last radiological follow-up, the mean MBL in primary SS patients (−2.371 ± 1.451 mm ($n = 53$); mean follow-up 133.6 ± 92.3 months) was higher than that in secondary SS patients (−1.686 ± 1.053 mm ($n = 19$); mean follow-up 101.8 ± 13.0 months), although this difference was not statistically significant ($P = 0.093$, Mann–Whitney test).

Systematic review

Literature search

The study selection process is summarized in Fig. 2. At the end of the process, assessment of the full-text reports of the remaining 20 articles led to the exclusion of two publications[10,11]. One of these was excluded because the clinical case was later reported in another publication[4], but with follow-up information. In the second excluded article, the same cases were reported in another published study by the same research group[12]. Thus, a total of 18 publications were selected for the review. As the patients in the present case series were also included in the analyses, a total of 19 studies were included in the review.

Description of the studies and analyses

Table 3 shows detailed data from the included studies. Eighteen publications were included in the review[4–6,12–26], and the 19 patients reported in the present case series were also included in the analyses. These 19 studies involved the placement of a total of 712 implants (45 in men, 644 in women; data on sex not available for 23) in 186 patients (9 men, 166 women; data on sex not available for 11). It was possible to distinguish some patients presenting primary SS (21 patients, 118 implants) and secondary SS (31 patients, 191 implants). The mean age of the

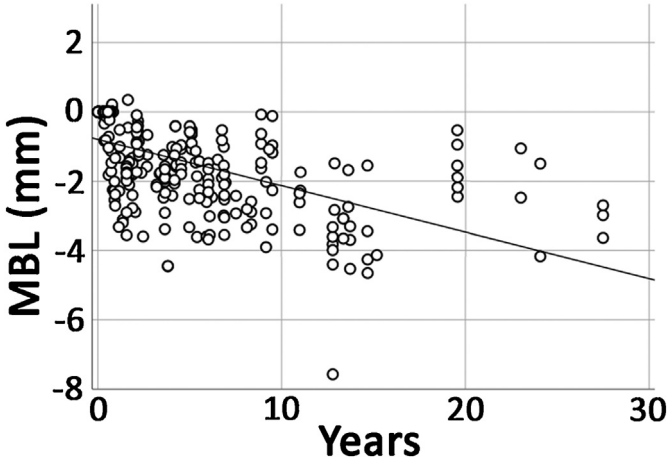

Fig. 1. Scatter plot of 293 marginal bone loss (MBL) measurements for 72 implants. The line represents the estimated MBL along the years of observation, according to linear regression.

Table 1. Marginal bone condition around 72 implants at the last radiological follow-up (mean follow-up of 125.2 months).

Marginal bone condition	Number of implants (%)
Stable (0 mm)	2 (2.8%)
Bone loss	
Up to 1 mm	14 (19.4%)
1–2 mm	17 (23.6%)
2–3 mm	21 (29.2%)
>3 mm	18[a] (25.0%)

[a] Seven out of these 18 implants (9.7% of all implants) presented marginal bone loss of more than 4 mm.

Table 2. Marginal bone condition around 72 implants (293 measurements) during follow-up.

Follow-up period	MBL[a] mean ± SD (min, max)	Number of measurements with MBL of at least 2 mm (%)
<1 year	−0.848 ± 0.961 (−2.706, 0.215) (n = 30[b])	6/30[b] (20.0)
1–3 years	−1.508 ± 0928 (−3.597, 0.346) (n = 51)	11/51 (21.6)
3–5 years	−1.878 ± 0.939 (−4.453, −0.410) (n = 38)	14/38 (36.8)
5–10 years	−2.006 ± 1.002 (−3.902, −0.076) (n = 63)	33/63 (52.4)
>10 years	−2.956 ± 1.318 (−7.571, −0.529) (n = 39)	29/39 (74.4)

MBL, marginal bone loss; SD, standard deviation.
[a] Negative values mean bone loss.
[b] There were 30 MBL measurements at <1 year of follow-up, excluding the initial MBL measurements of the 72 implants at baseline.

patients at the time of implant placement was 62.5 ± 9.3 years (range 38–85 years; 630 implants, 166 patients). Most implants were placed in the seventh decade of life (Fig. 3).

Information on follow-up was provided for 705 implants (mean 72.5 ± 59.2 months, range 5–341.2 months), of which 29 failed (4.1%). The failure rate was higher for implants installed in the maxilla (4.8%, 11/228) than for implants placed in the mandible (3.5%, 13/373), but the difference was not statistically significant (P = 0.416; Pearson χ^2 test). Patients presenting primary SS had a lower implant failure rate (2.5%, 3/118) than patients presenting secondary SS (6.5%, 12/184), but this difference was also not statistically significant (P = 0.120; Pearson χ^2 test).

Implants failed at a mean time of 12.9 ± 31.7 months (range 1–160 months; n = 24) after implant placement. Considering the implants with information on the precise time of failure, 79.2% (19/24) occurred within 6 months after installation surgery or at abutment connection. One implant failed at 9 months, two at 16 months, and one implant each at 24 months and 160 months after installation. There was no information on the time of failure for the five failed implants reported in the study by Albrecht et al. (2016)[6].

The probability of failure (Fig. 4) was 2.8% (95% confidence interval 1.6–4.1%, standard error = 0.006, $P < 0.001$; heterogeneity: $\tau^2 = 0.000$, $\chi^2 = 16.106$, $P = 0.446$, $I^2 = 0.66\%$) for the observed mean follow-up of these studies altogether. Only the clinical cases for which the

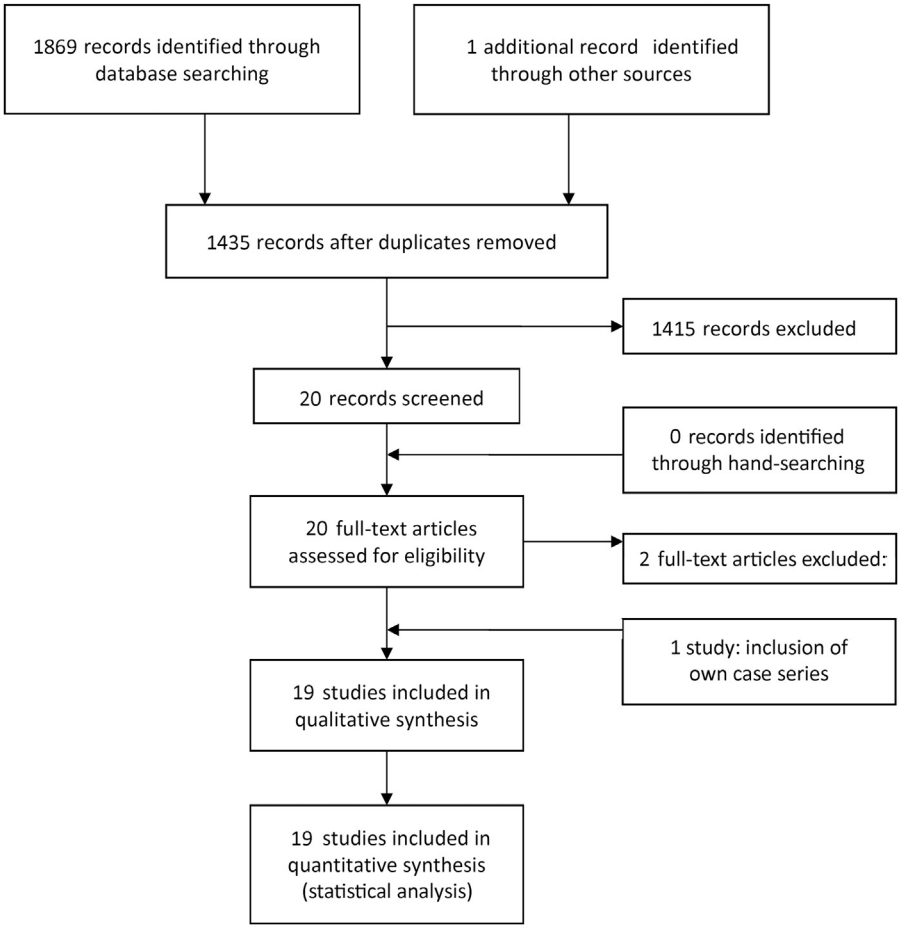

Fig. 2. Study screening process for the review.

Table 3. Detailed data of the included studies.

Authors, year	Number of patients	Sex	Age (years)	Implant type	Healing (months)	Prosthesis[a]
Payne et al., 1997[22]	3	F	38	Turned Brånemark (Nobel Biocare AB, Göteborg, Sweden)	6	FAP ($n = 2$)
		F	38		6	FAP
		F	40		6	OV ($n = 2$)
Isidor et al., 1999[20]	8	F	53–70	Turned Brånemark (Nobel Biocare AB, Göteborg, Sweden)	6 (Mx)	OV
		F			4 (Md)	OV (Mx), FAP (Md)
		F				FAP ($n = 2$)
		F				FAP
		F				FAP
		F				FAP
		F				FAP
		F				OV (Mx), FAP (Md)
Binon, 2005[4]	1	M	67	Turned Brånemark (Nobel Biocare AB, Göteborg, Sweden)	4	FAP
Oczakir et al., 2005[21]	2	F	63	NA	NA	FPP (Mx), SC (Md)
		F	64	NA	NA	OV (Mx), FPP (Md)
Weber et al., 2008[26]	1	F	NA	Brånemark	6	OV
Krennmair et al., 2010[12]	8	F	68	NA (Camlog Biotechnologies AG, Basel, Switzerland)	NA	OV
		F	48		NA	FPP
		F	42		NA	FPP
		F	72		NA	FAP
		F	41		NA	FPP
		F	52		NA	FPP
		F	55		NA	FAP
		F	41		NA	FPP ($n = 2$)
Spinato et al., 2010[25]	1	F	62	Tapered Screw-Vent HA (Zimmer Dental, Carlsbad, USA)	2.5	FAP
Corigliano et al., 2014[17]	2	F	60	TMI, Italy	NA	FAP ($n = 2$)
		F	74		2	OV
de Mendonça Invernici et al., 2014[19]	1	F	58	Acid-etched implants (Systhex, Curitiba, Brazil)	4	FPP
Albrecht et al., 2016[6]	32	32 F	Mean 64.5	NA	NA	NA
Aravena, 2016[13]	1	F	65	NA	3	FAP
Chatzistavrianou and Shahdad, 2016[15]	2	F	51	SLActive Straumann	3	FAP (Mx), OV (Md)
		F	53		3	FPP
Chochlidakis et al., 2016[16]	1	F	71	Bone Level SLA Straumann	Immediate	FPP (Mx), FAP (Md)
Korfage et al., 2016[5]	50	4 M, 46 F	Mean 67	NA	NA	SC ($n = 27$)
						OV ($n = 36$)
						FPP ($n = 2$)
						FAP ($n = 1$)
Carr et al., 2017[14]	41	3 M, 38 F	60 (36–81)[b]	NA	NA	NA
Cuifen et al., 2017[18]	1	F	62	ITI Straumann, Dengtu implants, Denton implants	1	FPP ($n = 5$)
Peron et al., 2017[23]	1	F	62	Trabecular Metal (Zimmer Dental Inc., Carlsbad, USA)	Immediate	FPP
Siddiqui et al., 2017[24]	11	NA	NA	NA	NA	NA
Present study, 2018	19	1 M, 18 F	63.3 (50–80)[b]	Several (see text)	Mean 163 days	SC ($n = 3$)
						OV ($n = 1$)
						FPP ($n = 9$)
						FAP ($n = 14$)

Authors	Number of patients	Implants, lost/total		Time at loss (months)	MBL (mm)	Follow-up (months)	Sjögren's syndrome type	Symptoms, medications (for SS and associated rheumatic disease only)
		Mx	Md					
Payne et al.[22]	3	2/6	1/6	2nd stage ($n = 2$) 24 ($n = 1$)	NA	96	Secondary	Xerostomia, xerophthalmia, RA, dramatic bilateral swelling of the parotid glands, cervical caries and recurrent peri-apical infection, recurrent colds, influenza, bronchitis, and pneumonia, smoker (>20 cig./day), chemotherapy 6 years after implants, surgical resection of all parotid and submandibular glands, cortisone over an 8-year period, salivary substitute, sialogogues
		0/6	0	–	NA	12	Primary	Extensive caries, swelling of the salivary glands, dryness of the mouth and eyes, submandibular glands were removed, anetholtrithione (to help stimulate salivary flow)
		0/4	0/4	–	''good marginal bone levels''	12	Secondary	Xerostomia, painful joints, arthritic erosion of both TMJs, dental caries, osteomyelitis after extraction of some teeth
Isidor et al.[20]	8	3/6	0	2nd stage ($n = 7$) 1 year of function ($n = 2$)	0.7 (implant to 1 year) 0.9 (4 years)	48	Secondary	Dry eyes and dry mouth, 7 patients with RA and 1 with scleroderma, constant feeling of fatigue
		2/5	0/5				Secondary	
		0/6	0/4				Secondary	
		0	0/6				Secondary	
		0	0/4				Secondary	
		0	2/7				Secondary	
		0	0/6				Secondary	
		1/3	1/5				Secondary	
Binon[4]	1	0	0/6	–	NA	156	Primary	Xerostomia, generalized reddened, dry, sticky oral mucosal tissues, angular cheilitis, dry scaly lips, a red, cobblestone, fissured texture to the tongue, extensive cervical caries
Oczakir et al.[21]	2	0/3	0/1	–	NA	24	Primary	Caries in remaining teeth
		0/4	0/4	–	NA	60	Secondary	Patient also presented scleroderma
Weber et al.[26]	1	0	NA/2	–	NA	NA	Secondary	Xerostomia, RA, SLE, DM, angular cheilitis, salivary stimulant, prednisone, hydroxychloroquine
Krennmair et al.[12]	8	0/6	0	–	2.8 ± 0.6[c]	96	Secondary	RA, corticosteroid
		0/3	0	–		48	Secondary	RA, corticosteroid
		0/4	0	–		50	Secondary	RA, corticosteroid, immunosuppressants
		0	0/8	–		44	Secondary	RA
		0/3	0	–		49	Secondary	RA
		0/4	0	–		52	Secondary	RA
		0	0/4	–		34	Secondary	RA
		0/7	0	–		42	Secondary	RA
Spinato et al.[25]	1	0	0/6	–	''there was no peri-implant bone loss''	12	Primary	Xerostomia, xerophthalmia, artificial tears and pilocarpine to control the xerophthalmia and xerostomia, respectively
Corigliano et al.[17]	2	0/7	0/7	–	NA	6	Primary	Xerostomia, non-smoker, Raynaud's phenomenon
		0	0/2	–	NA	48	Primary	Xerostomia, non-smoker

Table 3 (*Continued*)

Authors	Number of patients	Implants, lost/total		Time at loss (months)	MBL (mm)	Follow-up (months)	Sjögren's syndrome type	Symptoms, medications (for SS and associated rheumatic disease only)
		Mx	Md					
de Mendonça Invernici et al.[19]	1	0	0/2	–	''no bone loss''	72	Secondary	Xerostomia, xerophthalmia, RA, type 2 DM, smoking right after receiving the SS diagnosis, dryness of the vaginal mucosa, hands, and feet, use of eye drops and water day and night to keep her eyes and mouth moist, prednisone
Albrecht et al.[6]	32	5/104		NA	NA	Mean 59	Primary and secondary	Xerostomia, some smokers and ex-smokers, 1 diabetic patient, 1 patient taking bisphosphonates, 1 under chemotherapy, 17 patients taking corticosteroids, 4 patients with hyperthyroidism
Aravena[13]	1	0	NA/5	NA	NA	NA	Secondary	Xerostomia, caries, advanced tooth erosion, RA, angular cheilitis, candidiasis, tongue depapillation, salivary stimulant, artificial tears, corticosteroids
Chatzistavrianou and Shahdad[15]	2	0/6	0/2	–	''stable bone levels''	18	Secondary	Xerostomia, caries
		0	0/2	–	''stable bone levels''	24	Primary	Xerostomia, caries, altered taste
Chochlidakis et al.[16]	1	0/2	0/4	–	NA	14	Secondary	Xerostomia, xerophthalmia, hypothyroidism, SLE, Raynaud's disease, bipolar 2 disorder, chronic cystitis, actinic keratosis, SCC of the skin, heart murmur, use of topical moistening preparations, oral bisphosphonates (for 2 years, 15 years before implants)
Korfage et al.[5]	50	0/20	4/120	<3 ($n = 4$)	0.89 (0.25–1.56)[b] ($n = 26$) Mean 42 months	Mean 45.6	Primary ($n = 41$) and secondary ($n = 9$)	1 smoker, corticosteroids (8 patients), hydroxychloroquine (14 patients), immunosuppressants (5 patients), NSAIDs (13 patients)
Carr et al.[14]	41	0/45	2/91	3 ($n = 1$) 4.5 ($n = 1$)	NA	76.8 (3.6–313)[b]	NA	NA
Cuifen et al.[18]	1	0/6	0/4	–	NA	16	Primary	Dry mouth and dry eyes, artificial tear drops and prescribed long-term prednisone
Peron et al.[23]	1	0/5	0	–	NA	36	Secondary	Xerostomia, xerophthalmia, type 2 DM, RA, corticosteroids, use of artificial saliva and lubricants
Siddiqui et al.[24]	11	2/12	1/11	2 ($n = 1$) 5 ($n = 2$)	NA	Mean 40	NA	NA
Present study	19	0/56	3/51	1.2 ($n = 1$) 8.5 ($n = 1$) 159.6 ($n = 1$)	2.19 (range 0.00–7.57)[b] Mean 125.2 months	125.5 (5.6–341.2)[b]	Primary ($n = 13$) and secondary ($n = 6$)	6 patients with RA, 1 patient with sarcoidosis, 3 smokers, 1 former smoker, 1 patient type 1 DM, 4 patients type 2 DM, 6 patients taking antidepressants, 1 patient taking bisphosphonates, 2 bruxers, 6 patients taking medications to reduce gastric acid production, 2 patients irradiated in the head and neck region

DM, diabetes mellitus; F, female; M, male; MBL, marginal bone loss; Md, mandible; Mx, maxilla; NA, not available; NSAIDs, non-steroidal anti-inflammatory drugs; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; TMJ, temporomandibular joint; SCC, squamous cell carcinoma; SS, Sjögren's syndrome

[a] FAP, fixed full-arch prosthesis; FPP, fixed partial prosthesis; OV, overdenture; SC, single crown.

[b] Mean (range) values.

[c] Mean ± standard deviation.

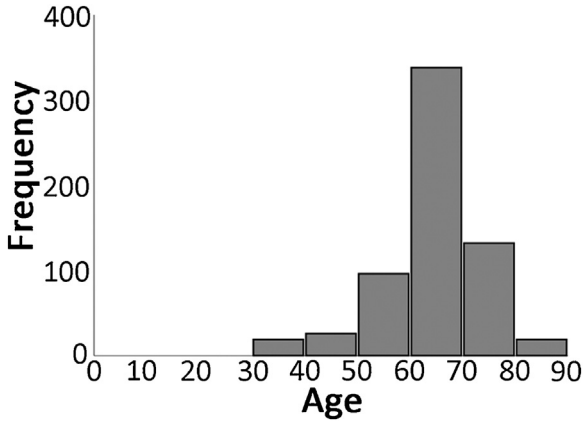

Fig. 3. Distribution of implants according to the age of the patient at the time of implant placement surgery.

follow-up was reported were included in this analysis.

Discussion

The aim of this study was to assess the clinical outcomes of dental implants in a series of patients with SS, as well as to review the cases of SS patients receiving dental implants described in the literature. In relation to previous reviews on the subject[27,28], the present study performed a more careful systematic search of the literature, thus resulting in a greater number of included studies. Systematic reviews are insufficiently informative if they do not include all available current evidence. This failure to rigorously synthesize the totality of relevant evidence may have a detrimental effect on treatment decisions and future research planning[29]. Moreover, the present study performed a more in-depth and detailed statistical analysis of the compilation of included studies in comparison to these previous reviews.

After reviewing 712 implants placed in 186 patients with SS, it was observed that the failure rate was fairly low in this population: 4.1% over a mean of 72.5 ± 59.2 months of follow-up. Moreover, in the majority of cases in which an implant failed to integrate, the cause was unknown. Most of the implant failures occurred within 6 months after implant installation, in agreement with other studies in which most of the lost implants failed within a couple of months after placement surgery[30,31]. In general, SS patients have reported a significant improvement in their quality of life after oral rehabilitation with dental implants, with regard to satisfaction, chewing, self-assurance, and appearance[6,16,20]. It is, however, important to stress that oral functioning is impaired in patients with SS and continues to be impaired in patients with implant-retained prostheses[5].

Only a few studies reported data on MBL[5,12, 15,19,20,22,25], and still most of the publications provided only vague information such as ''good marginal bone levels''[22], ''there was no peri-implant bone loss''[25], ''no bone loss''[19], ''stable bone levels''[15]. Only three previous studies provided data[5,20], as well as the present one. The results of these two publications suggested that MBL is not a major problem in SS patients[5,20]. The present study, however, observed a very fast initial MBL in comparison to the general population followed up for at least 20 years in another study[31]. This loss was found to be considerable in the short- and medium-term observations, with many implants showing MBL of 2 mm during the first years after installation and many presenting MBL of around 4 mm within the first 10 years of follow-up.

Korfage et al.[5] have previously reported that there is probably an increased risk of peri-implant infection in SS patients in the long term. Salivary secretion and the associated self-clearance of the oral cavity is reduced in SS patients, which results in debris being collected more quickly and remaining on the implant surfaces in SS subjects compared to patients with no xerostomia[5]. In the study by Korfage et al.[5], SS subjects presented more gingi-

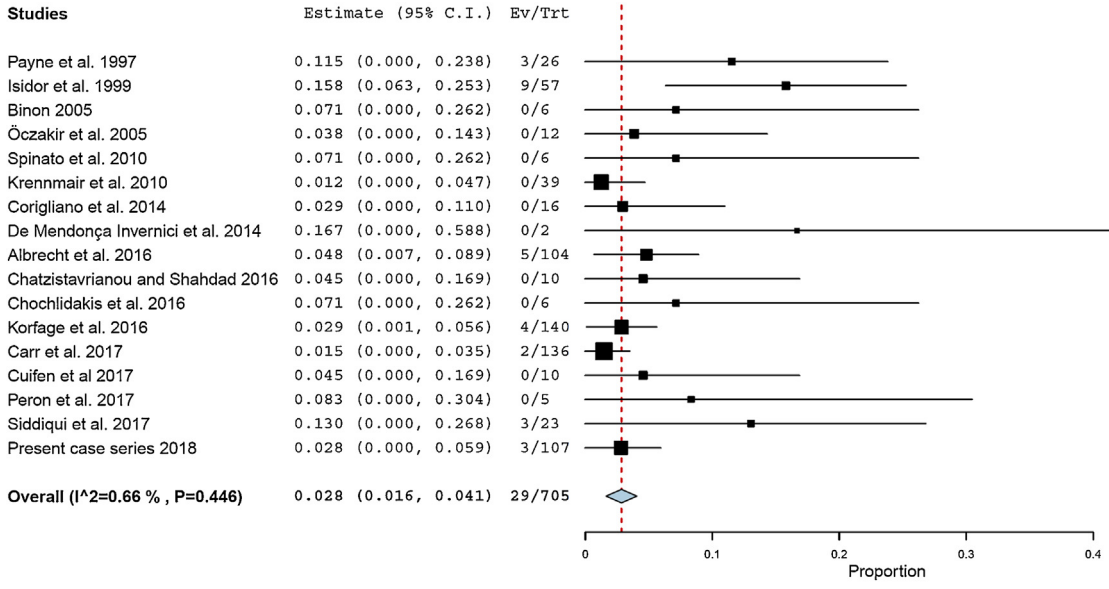

Fig. 4. Probability of implant failure. Only clinical cases with information about follow-up were included.

val swelling and bleeding, as well as increased pocket probing depths than the controls with no salivary problems. As a consequence, the marginal peri-implant tissue is more prone to continuous inflammatory insults than the peri-implant tissue in healthy patients. The reported more frequent presence of peri-implant mucositis in SS patients may be associated with an increased prevalence of peri-implantitis later on[5].

Smoking could have been a factor influencing implant failure[32] and MBL[33] in these patients. The same is true for a series of other conditions such as bruxism[34], diabetes[35], and the intake of antidepressants[36] or of medications to reduce gastric acid production[37]. Detailed information about these conditions and habits among the patients was, however, not provided for every patient in the publications.

Another point to consider is that patients with secondary SS showed a higher implant failure rate than patients with primary SS. Although the difference was not statistically significant, there might be some clinical relevance and significance. The usual intake of corticosteroids for the management of underlying rheumatic diseases in patients with secondary SS could be partly associated with impaired osseointegration. Corticosteroids induce apoptosis of osteoblasts[38], reduce the number of pre-osteoblasts[39], and promote the differentiation of bone marrow stromal cells into adipocyte lineage cells[40]. Moreover, corticosteroids increase the life-span of osteoclasts[41] and suppress bone formation via the osteoclast[42]. Besides corticosteroids, methotrexate[43] and biological targeted therapies, including tumour necrosis factor alpha (TNF-α) inhibitors and rituximab[44], have been used in patients with primary SS-associated inflammatory arthritis. Methotrexate has been shown to be a potent inhibitor of osteoblast proliferation and mitochondrial metabolism in vitro[45], and to have the potential to interfere with the osseointegration process[46]. Concerning biological agents, these have been found to have effects on human chondrocytes and osteocytes in vitro[47], and to cause a significant suppression of bone turnover[48]. These drugs can have some impact on wound healing and osseointegration, and not only on the underlying SS itself. The higher MBL in primary SS patients in comparison to secondary SS patients could either be a true finding, i.e. related to the negative effects of the drugs mentioned above in primary SS patients, or could be related to the shorter radiological follow-up for the secondary SS patients and the much smaller sample size at the last follow-up. More balanced groups are necessary in order to confirm this difference.

Overall, the findings of this study suggest that SS itself does not impair the biology of osseointegration. It may, however, result in a higher MBL than in non-SS patients, which may require an increased number of recall visits and shorter intervals between professional hygiene appointments.

The limitations of this study include (1) the presence of confounding factors that may have affected and influenced the outcomes[49], (2) the retrospective design of the studies included in the systematic review, as well as the case series of 19 patients presented, (3) the lack of standardized timing for evaluating the radiographs and the low percentage of MBL measurements due to the retrospective nature of the case series, and (4) the fact that most studies reported a small number of patients followed up for a limited period of time.

In conclusion, dental implants should be considered by dentists as a viable treatment option for patients with SS, as the failure rate is fairly low: 4.1% over a mean 72.5 $\pm$ 59.2 months of follow-up. Patients with SS may, however, present a higher MBL around implants than patients from the general population.

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Competing interests

There are no conflicts of interest to declare.

Ethical approval

Regional Ethics Committee, Lund, Sweden (Dnr 2014/598; Dnr 2015/72).

Patient consent

Not required.

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