Review

Surgical Management of Peri-Implantitis: A Systematic Review and Meta-Analysis of Treatment Outcomes

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Background: This systematic review was requested by the Task Force of the American Academy of Periodontology as a follow-up study of the 2013 report, with an aim to investigate the efficacy of different surgical approaches to treat peri-implantitis.

Methods: A search of four electronic databases from January 1990 to May 2013 was performed. Studies included were human clinical trials published in English that applied surgeries for treating peri-implantitis. Parameters evaluated included probing depth (PD) reduction, clinical attachment level gain, bleeding on probing (BOP) reduction, radiographic bone fill (RBF), and mucosal recession. The weighted mean (WM) and the 95% confidence interval of the studied parameters were estimated with the random-effect model.

Results: A total of 1,306 studies were initially identified, after reviewing titles, abstracts, and full texts, and 21 articles, 12 of which were case series, were finally included. Four treatment groups were identified: 1) access flap and debridement; 2) surgical resection; 3) application of bone grafting materials; and 4) guided bone regeneration. The mean initial PD ranged from 4.8 to 8.8 mm, with initial BOP ranging from 19.7% to 100%. Short-term follow-ups (3 to 63 months) revealed that the available surgical procedures yielded a WM PD reduction of 2.04 (group 2) to 3.16 mm (group 4), or 33.4% to 48.2% of the initial PD. The WM RBF was 2.1 mm for groups 3 and 4.

Conclusions: Within the limitation of this systematic review, the application of grafting materials and barrier membranes resulted in greater PD reduction and RBF, but there is a lack of high-quality comparative studies to support this statement. The results might be used to project treatment outcomes after surgical management of peri-implantitis. *J Periodontol 2014;85:1027-1041.*

KEY WORDS

Anti-infective agents; debridement; guided tissue regeneration; osseointegration; peri-implantitis; treatment outcome.

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With an increasing number of implants being placed, peri-implantitis is becoming a prevalent and notable disease, affecting 2.7% to 47.1% of implants.[1-5] Identical to periodontitis, microbial plaque is the main etiologic factor of peri-implantitis.[6] It has been shown that the infected sites harbor a higher proportion of periodontal pathogens.[7,8] Because peri-implantitis shares many features of periodontitis,[9] such as clinical presentations, etiology, and pathogenesis, strategies used to treat periodontitis were adopted for managing peri-implantitis.[10,11] These non-surgical or surgical approaches share common goals of eliminating infection and restoring lost structures and function. Although effective in treating peri-implant mucositis, non-surgical therapy is unable to eradicate peri-implantitis.[12] The surgical therapy is currently the mainstream approach for treating peri-implantitis.[13] A contained, deep defect may be amenable for regeneration, whereas a shallow defect may respond more favorably with resective surgery. With the rising prevalence of peri-implantitis, there is an urgent need to identify an effective treatment procedure.

One of the goals of surgical therapy is to gain access for effective surface decontamination. Surfaces contaminated by microbes are not conducive to bone-forming cells; therefore, surface decontamination is critical for reosseointegration. Mechanical means of

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Table 1.

Summary of the Features of the Included Studies

Study No.–Intervention Arm No.	Author	Study Design	F/U (months)	Patients (n)	Implant Features					Defect Depth (mm)	Surgical Intervention				
					BL (n)	FE (n)	Location	Body Surface	Platform Surface		Anti Used	Surgical Method	Grafting Materials	Barrier Materials	Submerged or not
Access flap + debridement															
1–1	Deppe et al. (2007)[45]	QE	63	6	19	16	NA	NA	NA	NA	N	AA	N	N	Y
1–2				10	22	17	NA	NA	NA			AA + CO_2 laser	N	N	Y
2	Máximo et al. (2009)[50]	CS	3	13	20	20	NA	S	NA	>3 threads	N	PC + AA	N	N	N
3	Heitz-Mayfield et al. (2012)[18]	Cohort	12	24	36	36	NA	S	NA	>2	Y	PC + CHX	N	N	N
4–1	Wohlfahrt et al. (2012)[19]	RCT	12	17	17	16	NA	R	NA	>4	Y	TC + EDTA	N	N	Y
Resective approach															
5–1	Romeo et al. (2005)[16]	RCT	24 to 36	10	19	19	15 max, 4 mand	R	NA	NA	Y	Resective + IP	N	N	N
5–2				7	16	14	10 max, 6 mand	R	NA	NA	Y	Resective only	N	N	
6–1	De Waal et al. (2013)[44]	RCT	12	15	31	31	20 max, 11 mand	R (27) + S (4)	NA	>2	N	CHX + CPC + IP + APF	N	N	N
6–2				15	48	38	24 max, 24 mand	R (47) + S (1)	NA		N	Placebo + IP + APF	N	N	
Bone grafts or substitutes															
7–1	Khoury and Buchmann (2001)[48]	QE	6	7	12	12	NA	R	S	<50% implant length	Y	CHX + CA + H_2O_2 + NaCl	Auto	N	Y
8–1	Schwarz et al. (2009)[55]	CS	48	9	9	9	NA	NA	NA	>3	NA	PC +NaCl	HA	N	N
9–1	Roccuzzo et al. (2011)[52]	CS	12	14	12	12	7 max, 5 mand	R (SLA)	S	NA	Y	PC + EDTA + CHX + NaCl	XG	N	N
9–2				12	14	14	6 max, 8 mand	R (TPS)							
10–1	Roos-Jansåker et al. (2011)[53]	QE	36	15	36	27	NA	R (1) + S (26)	S	>1.8	Y	H_2O_2 + NaCl	PCC	N	N
11	Wiltfang et al. (2012)[56]	CS	12	22	36	36	NA	NA	NA	>4	Y	IP + etching gel + BMP	Auto + XG	N	N
4–2	Wohlfahrt et al. (2012)[19]	RCT	12	16	16	16	NA	R	NA	>4	Y	TC + EDTA	PTG	N	Y
12	Mijiritsky et al. (2013)[51]	Retro CS	6 to 15	16	18	18	NA	NA	NA	NA	Y	TC + tetracycline + APF	PTG	N	N
Grafts + barrier materials															
13	Haas et al. (2000)[47]	CS	9.5	17	24	24	3 max, 21 mand	R	S	>2	Y	Diode laser	Auto	ePTFE	Y
7–2	Khoury and Buchmann (2001)[48]	QE	6	11	20	20	NA	R	S	<50% implant length	Y	CHX + CA + H_2O_2 + NaCl	Auto	ePTFE	Y
7–3				7	9	9								Resorb	
1–3	Deppe et al. (2007)[45]	QE	63	7	15	11	NA	NA	NA	NA	N	AA	Auto+ β-TCP	ePTFE	Y

Table 1. (continued)
Summary of the Features of the Included Studies

Study No.–Intervention Arm No.	Author	Study Design	F/U (months)	Patients (n)	Implant Features						Surgical Intervention				
					BL (n)	FE (n)	Location	Body Surface	Platform Surface	Defect Depth (mm)	Anti Used	Surgical Method	Grafting Materials	Barrier Materials	Submerged or not
1–4				9	17	13	NA	NA	NA			AA + CO_2 laser	Auto+ β-TCP	ePTFE	Y
14	Roos-Jansåker et al. (2007)[54]	CS	12	12	16	16	NA	S (16)	S	>1.8	Y	H_2O_2 + NaCl	PCC	Resorb	Y
15–1	Romanos and Nentwig (2008)[20]	CS	27.1	8	10	10	2 max, 8 mand	NA	NA	>2	N	TC + CO_2 laser	Auto	Resorb	4: N
15–2				7	9	9	2 max, 7 mand	NA	NA				XG		others: Y
8–2	Schwarz et al. (2009)[55]	CS	48	11	11	10	NA	NA	NA	>3	NA	H_2O_2 + NaCl	XG	Resorb	N
16–1	Schwarz et al. (2010)[23]	CS	12	27	9	9	2 max, 7 mand	R	S	>3.5	NA	IP + CC + NaCl (Er:YAG 4 weeks before surgery)	XG	Resorb	N
16–2					9	9	5 max, 4 mand	R (8) + S (1)							
16–3					9	9	4 max, 5 mand	R							
10–2	Roos-Jansåker et al. (2011)[53]	QE	36	17	29	29	NA	R (1) + S (28)	S	>1.8	Y	H_2O_2 + NaCl	PCC	Resorb	N
17–1	Aghazadeh et al. (2012)[43]	RCT	12	22	22	22	NA	R	NA	>3	Y	H_2O_2 + NaCl	Auto XG	Resorb	N
17–2				23	23	23									
18–1	Froum et al. (2012)[46]	CS	36 to 91	15	19	19	NA	R	NA	>4	Y	GC + AA + NaCl + PDGF + tetracycline + EMD	XG or Allo	Resorb or SCTG	N
18–2				23	32	32									N
19–1	Schwarz et al. (2012)[21]	RCT	24	14	17	14	NA	R (12) + S (1) + NI (1)	NA	>3	NA	IP + PC + NaCl	XG	Resorb	N
19–2				10	20	10	NA	R (5) + S (4) + NI (1)	NA			IP + Er:YAG	XG	Resorb	N
20	Matarasso et al. (2013)[49]	CS	12	11	11	11	NA	NA	NA	>2	Y	SSC + AA + APF	XG	Resorb	N
21	Schwarz et al. (2014)[22]	CS	6	10	13	13	NA	R (1) + S (9) + NI (3)	NA	>3	NA	IP + PC + CTG (Er:YAG 2 weeks before surgery)	XG	Resorb	N

F/U = follow-up; BL = baseline; FE = final examination; Anti = antibiotics; Retro = retrospective; NA = not determined or reported; max = maxilla; mand = mandible; S = smooth; R = rough; TPS = titanium plasma-sprayed; NI = non-identifiable; AA = air abrasive; PC = plastic curet; CHX = chlorhexidine; TC = titanium curet; IP = implantoplasty; CPC = cetylpyridinium chloride; APF = apically positioned flap; CA = citric acid (pH 1); BMP = bone morphogenetic proteins; CC = carbon curet; GC = graphite curet; EMD = enamel matrix derivatives; SSC = stainless steel curet; PDGF = platelet-derived growth factor; Auto = autogenous; HA = hydroxyapatite; XG = xenograft; PCC = phytogenic carbonate calcium; PTG = porous titanium granules; β-TCP = beta tricalcium phosphate; Allo = allograft; ePTFE = expanded polytetrafluoroethylene; Resorb = resorbable membrane; SCTG = subepithelial connective tissue graft.

surface detoxification have been used extensively.[14,15] Implantoplasty is a more radical way of mechanical surface treatment, and it has been shown to halt marginal bone loss effectively.[16,17] Chemotherapy, which includes applications of root conditioners, disinfectants, and antibiotics on the implant surface, has demonstrated equivalent results to mechanical treatment.[18,19] Carbon dioxide (CO_2) and erbium:yttrium–aluminum–garnet (Er:YAG) lasers have shown some promising results,[20-23] yet the most effective protocol for implant surface detoxification has not yet been recognized.[24]

Clinical and radiographic parameters, e.g., the degree of inflammation resolution, probing depth (PD) reduction, and bone fill, are indicators for evaluating the effectiveness of various surgical procedures. The stacking results being presented in recent literature[25,26] enable a systematic investigation of the overall performance of each surgical procedure. As a continuous effort of the 2013 report[27] directed by the Task Force of the American Academy of Periodontology, this systematic review was prepared with a focused question: "What are the radiographic and clinical outcomes of different surgical interventions for the treatment of peri-implantitis?"

Table 2.

Summary of the Outcomes Investigated in This Systematic Review

Study No.–Intervention Arm No.	Authors (Year)	Intervention	No. of Implants	Mean ± SD PD Reduction (mm)	PD Reduction (%)	Mean ± SD Bone Fill (mm)	Mean ± SD CAL Gain (mm)	CAL Reduction (%)	BOP Reduction (%)	Mean ± SD MR (mm)
Access flap + debridement										
1–1	Deppe et al. (2007)[45]	Without laser	16	0.8 ± 0.4	15.7	NA	0 ± 0.3	0	NA	0.8 ± 0.4
1–2		CO_2 laser	17	2.7 ± 0.5	44.3	NA	0.3 ± 0.2	4.3	NA	2.4 ± 0.4
2	Máximo et al. (2009)[50]		20	3.1 ± 0.6	41.3	NA	2.3 ± 1.6	NA	47.5	NA
3	Heitz-Mayfield et al. (2012)[18]		36	2.4 ± 0.3	45.3	NA	NA	NA	37.5	1 ± 0.9
4–1	Wohlfahrt et al. (2012)[19]		16	2.0 ± 2.3	30.8	0.1 ± 1.9	NA	NA	NA	NA
Resective approach										
5–1	Romeo et al. (2005)[16]	With IP	10	2.6 ± 0.4	44.8	NA	0.3 ± 0.5	5.5	NA	1.5 ± 0.4
5–2		Without IP	7	1.0 ± 0.6	15.4	NA	(–)1.1 ± 0.6	–18.3	NA	1.4 ± 0.4
6–1	De Waal et al. (2013)[44]	CHX + CPC	15	2.3 ± 0.5	34.8	NA	NA	NA	19.9	NA
6–2		Placebo	15	1.8 ± 0.2	32.7	NA	NA	NA	22.5	NA
Bone grafts or substitutes										
7–1	Khoury and Buchmann (2001)[48]	Auto	12	5.1 ± 2.7	63.8	2.4 ± 2.7	NA	NA	NA	NA
8–1	Schwarz et al. (2009)[55]	HA	9	1.1 ± 0.3	15.9	NA	0.6 ± 0.5	8.2	34	0.4 ± 0.5

Table 2. (continued)

Summary of the Outcomes Investigated in This Systematic Review

Study No.–Intervention Arm No.	Authors (Year)	Intervention	No. of Implants	Mean ± SD PD Reduction (mm)	PD Reduction (%)	Mean ± SD Bone Fill (mm)	Mean ± SD CAL Gain (mm)	CAL Reduction (%)	BOP Reduction (%)	Mean ± SD MR (mm)
9–1	Roccuzzo et al. (2011)[52]	XG, R (SLA)	12	3.4 ± 1.7	50	1.9 ± 1.3	NA	NA	60.4	NA
9–2		XG, R (TPS)	14	2.1 ± 1.2	29.2	1.6 ± 0.7	NA	NA	33.9	NA
10-1	Roos- Jansåker et al. (2011)[53]	PCC	27	NA	NA	1.3 ± 1.3	NA	NA	NA	NA
11	Wiltfang et al. (2012)[56]	Auto + XG	36	4.0 ± 1.8	NA	3.5 ± 2.4	NA	NA	36	1.3 ± 0.2
4–2	Wohlfahrt et al. (2012)[19]	PTG	16	1.7 ± 1.7	26.2	2.0 ± 1.7	NA	NA	NA	NA
12	Mijiritsky et al. (2013)[51]	PTG	18	NA	NA	2.0 ± 2.3	NA	NA	NA	NA
Grafts + barrier materials										
13	Haas et al. (2000)[47]	Diode laser + Auto + ePTFE	24	NA	NA	2.0 ± 1.9	NA	NA	NA	NA
7–2	Khoury and Buchmann (2001)[48]	Auto + ePTFE	20	5.4 ± 3.0	65.9	2.8 ± 3.1	NA	NA	NA	NA
7–3		Auto + Resorb	9	2.6 ± 1.6	33.8	1.9 ± 3.2	NA	NA	NA	NA
1–3	Deppe et al. (2007)[45]	Auto + β-TCP + ePTFE	11	2.3 ± 0.5	47.9	NA	2.1 ± 0.4	35.6	NA	0.2 ± 0.6
1–4		CO_2 laser + Auto + β-TCP + ePTFE	13	2.5 ± 0.5	50	NA	2.7 ± 0.5	42.9	NA	(–)0.2 ± 0.5
14	Roos- Jansåker et al. (2007)[54]	PCC + Resorb	16	4.2 ± 1.5	82.4	2.3 ± 1.2	1.4 ± 1.7	NA	NA	NA
15	Romanos and Nentwig (2008)[20]	CO_2 laser + Auto/XG + Resorb	19	3.5 ± 0.5	58.3	NA	NA	NA	NA	NA

Table 2. (continued)

Summary of the Outcomes Investigated in This Systematic Review

Study No.–Intervention Arm No.	Authors (Year)	Intervention	No. of Implants	Mean ± SD PD Reduction (mm)	PD Reduction (%)	Mean ± SD Bone Fill (mm)	Mean ± SD CAL Gain (mm)	CAL Reduction (%)	BOP Reduction (%)	Mean ± SD MR (mm)
8–2	Schwarz et al. (2009)[55]	XG + Resorb	10	2.5 ± 0.9	35.2	NA	2.0 ± 1.0	26.7	51	0.5 ± 0.4
16–1	Schwarz et al. (2010)[23]	XG + Resorb, Class Ib	9	1.6 ± 0.9	23.9	NA	1.2 ± 1.1	16.9	38.9	0.4 ± 0.7
16–2		XG + Resorb, Class Ic	9	1.6 ± 0.7	22.5	NA	1.1 ± 0.9	14.7	25.9	0.5 ± 0.5
16–3		XG + Resorb, Class Ie	9	2.7 ± 0.7	38.6	NA	2.4 ± 1.0	32	61.1	0.3 ± 0.6
10–2	Roos-Jansåker et al. (2011)[53]	PCC + Resorb	29	NA	NA	1.6 ± 1.2	NA	NA	NA	NA
17–1	Aghazadeh et al. (2012)[43]	Auto + Resrob	22	2.0 ± 1.2	33.3	0.2 ± 1.8	NA	NA	44.8	NA
17–2		XG + Resorb	23	3.1 ± 1.2	50	1.1 ± 1.9	NA	NA	50.4	NA
18–1	Froum et al. (2012)[46]	XG + Resorb, interproximal bone loss	19	5.4 ± 1.5	61.4	3.8 ± 1.5	NA	NA	NA	NA
18–2		XG + Resorb, buccal/facial bone loss	32	5.1 ± 1.9	64.6	3.0 ± 0.8	NA	NA	NA	NA
19–1	Schwarz et al. (2012)[21]	XG + Resorb	14	1.5 ± 2.0	28.8	NA	1.2 ± 2.2	18.5	54.9	0.3 ± 0.6
19–2		Er:YAG + XG + Resorb	10	1.1 ± 2.2	22.4	NA	1.0 ± 2.2	15.6	75	0.1 ± 0.4
20	Matarasso et al. (2013)[49]	XG + Resorb	11	4.1 ± 0.7	50.6	2.8 ± 1.4	3.0 ± 1.1	33	13.6	1.3 ± 0.7
21	Schwarz et al. (2014)[22]	XG + Resorb	13	2.5 ± 1.8	40.3	NA	2.1 ± 1.9	31.3	74.4	0.1 ± 0.5

IP = implantoplasty; CHX = chlorhexidine; CPC = cetylpyridinium chloride; Auto = autogenous; HA = hydroxyapatite; XG = xenograft; R = rough; TPS = titanium plasma-sprayed; PCC = phytogenic carbonate calcium; PTG = porous titanium granules; ePTFE = expanded polytetrafluoroethylene; Resorb = resorbable membrane; β-TCP = β-tricalcium phosphate; NA = not determined or reported.

MATERIALS AND METHODS

Inclusion and Exclusion Criteria

Included studies were human clinical trials comprising case series (CS), cohort studies, quasi-experiments (QEs), and randomized controlled trials (RCTs) that 1) were published in the English language; 2) applied surgeries for treating peri-implantitis; 3) reported on at least one clinical or radiographic parameter; 4) had a minimum sample size of eight implants; and 5) followed the treated implants for at least 3 months for surgical interventions other than regenerative procedures, which had a follow-up period of 6 months or more.

Screw-shaped implants with either smooth or rough surfaces were included. There was no restriction on the methods for surface detoxification used. Animal studies, reviews, and case reports were excluded, but the bibliographies of these studies were screened for potential articles to be included. The parameters included the following: 1) PD reduction (in millimeters); 2) clinical attachment level (CAL) gain (in millimeters); 3) bleeding on probing (BOP) reduction (percentage); 4) radiographic bone fill (RBF) (in millimeters); and 5) mucosal recession (MR) (in millimeters).

Search Strategy

A search of four electronic databases, including Ovid MEDLINE, PubMed, EMBASE, and Dentistry and Oral Sciences Source, for relevant studies published in the English language from January 1990 to May 2013 was performed. The search terms used, in which mh represented the MeSH terms and tiab represented title and/or abstract, included the following: (“peri-implantitis”[mh] OR “peri-implantitis”[ti] OR ((“dental implantation, endosseous”[mh] OR “dental implants”[mh]) AND (“peri implant”[tiab] OR “peri-implantitis”[tiab]))) AND (“treatment”[tiab] OR “therapy”[tiab] OR “therapeutics”[tiab] OR “surgery”[tiab] OR “surgical”[tiab] OR “regeneration”[tiab] OR “regenerative”[tiab] OR “guided tissue regeneration”[mh] OR “bone graft”[tiab] OR “bone grafts”[tiab] OR “bone substitute”[tiab] OR “bone substitutes”[tiab] OR “access flap”[tiab] OR “open flap”[tiab] OR “debridement”[tiab] OR “resective”[tiab] OR “implantoplasty”[tiab] OR “laser”[tiab] OR “lasers”[tiab]).

A hand search was also performed in dental and implant-related journals from January 2000 to April 2013, including the following: 1) *Journal of Periodontology*; 2) *Clinical Implant Dentistry and Related Research*; 3) *International Journal of Oral and Maxillofacial Implants*; 4) *Clinical Oral Implants Research*; 5) *Implant Dentistry*; 6) *International Journal of Oral and Maxillofacial Surgery*; 7) *Journal of Oral and Maxillofacial Surgery*; 8) *Journal of Dental Research*; 9) *Journal of Prosthetic Dentistry*; 10) *International Journal of Prosthodontics*; 11) *Journal of Oral Implantology*; 12) *Journal of Clinical Periodontology*; and 13) *International Journal of Periodontics & Restorative Dentistry*. *European Journal of Oral Implantology* was searched from January 2008 to April 2013. Furthermore, a search in the references of included papers was conducted for publications that were not electronically identified. One examiner (G-HL) performed all the searches. Potential articles were examined in full text by two reviewers (G-HL and H-LC), and their eligibility for this review was confirmed after discussion. The level of agreement between the reviewers regarding study inclusion was calculated using κ statistics. The screening process was shown in supplementary Figure 1 in online *Journal of Periodontology*.

Risk of Bias Assessment

The criteria used to assess the quality of the selected RCTs were modified from the RCT checklist of the Cochrane Center[28] and the CONSORT (Consolidated Standards of Reporting Trials) statement.[29] The degree of bias was categorized as follows: 1) low risk if all the criteria were met; 2) moderate risk when only one criterion was missing; and 3) high risk if two or more criteria were missing. Two reviewers (G-HL and H-LC) assessed all the included articles independently, and final assessment was achieved with discussion.

Data Extraction

Data were extracted by two observers (G-HL and H-LC) independently. Disagreements were resolved with discussion after carefully reviewing the studies in question. Demographic information was recorded for each study, including the following: 1) study design; 2) sample size; 3) number of fixtures placed; 4) location of the implants; 5) surgical technique used; 6) loading protocols; and 7) follow-up period.

Data Analyses

The primary outcome was the amount of PD reduction. The percentage of PD reduction was calculated as the amount of PD reduction divided by the amount of initial PD. The same calculation was performed for the percentage of CAL gain. The weighted mean (WM) and the 95% confidence interval (CI) of the variables were estimated using a computer program.‡ The random-effect model was applied when performing meta-analyses to account for methodologic differences among studies. Forest plots were produced to graphically represent WM and

‡ Comprehensive Meta-Analysis v.2, Biostat, Englewood, NJ.

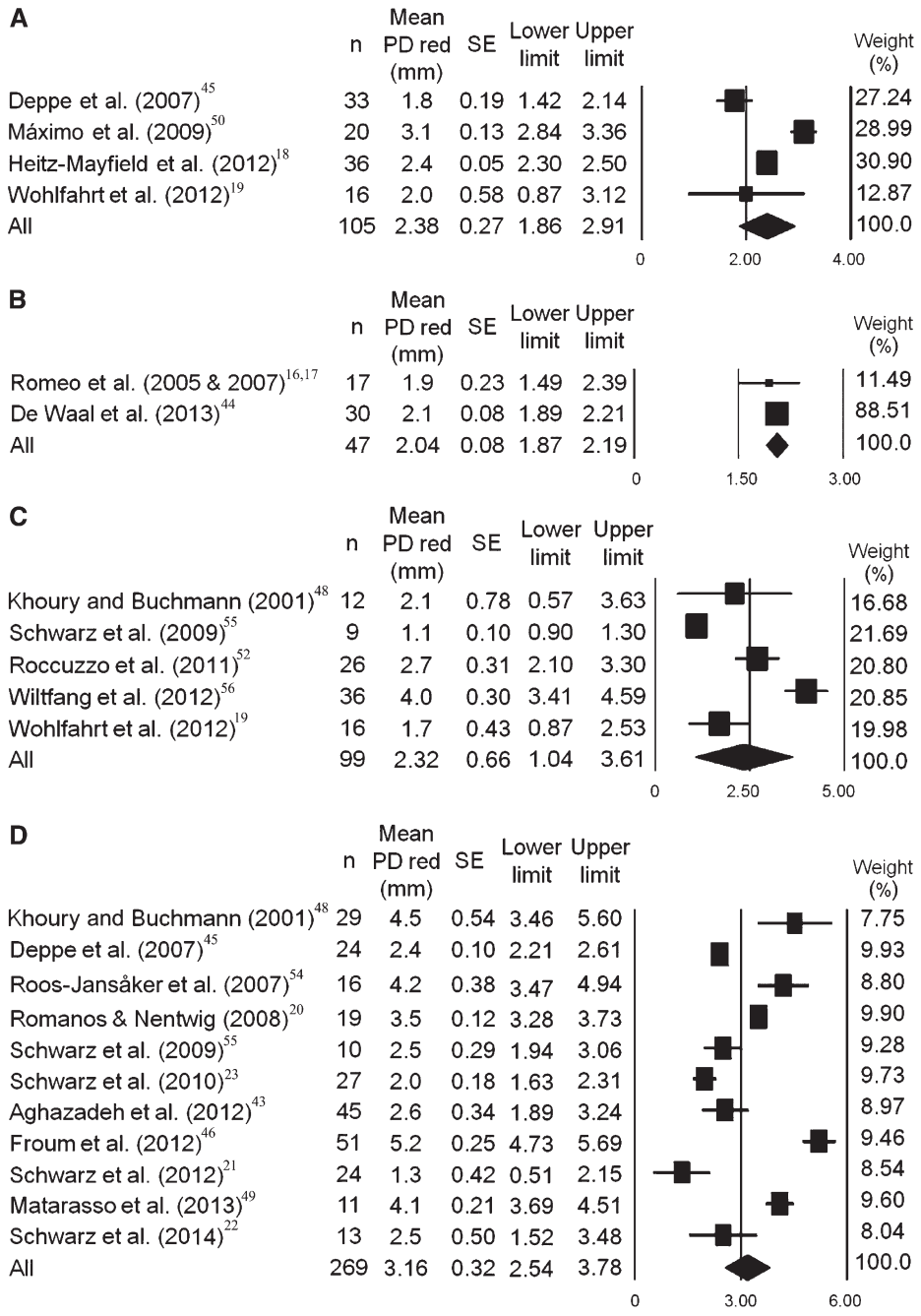

Figure 1.
A) *Meta-analysis for the amount of PD reduction among selected studies using intervention of access flap and debridement. The WM was 2.38 mm, with a 95% CI of 1.86 to 2.91 mm.* ***B)*** *Meta-analysis for the amount of PD reduction among selected studies using intervention of resective approach. The WM was 2.04 mm, with a 95% CI of 1.87 to 2.19 mm.* ***C)*** *Meta-analysis for the amount of PD reduction among selected studies using intervention of regenerative treatment with grafting materials. The WM was 2.32 mm, with a 95% CI of 1.04 to 3.61 mm.* ***D)*** *Meta-analysis for the amount of PD reduction among selected studies using intervention of regenerative treatment with both grafting materials and barrier membranes. The WM was 3.16 mm, with a 95% CI of 2.54 to 3.78 mm. red = reduction.*

95% CI of the outcomes using "implant" as the analysis unit. For studies with multiple treatment groups, the results from groups of the same category were combined together. Heterogeneity was assessed with the I^2 test, which ranges from 0% to 100%, with a lower value representing less heterogeneity. The reporting of these meta-analyses adhered to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement.[30]

RESULTS

The screening process was shown in supplementary Figure 1 in the online *Journal of Periodontology*. Electronic and hand searches yielded 1,306 articles, of which 34 articles were selected for full-text evaluation after screening their titles and abstracts. Thirteen articles[15,31-42] were further excluded; the reasons for exclusion are listed in supplementary Table 1 in online *Journal of Periodontology*. Twenty-one[16,18-23,43-56] articles were finally included. The main features and conclusions of the included studies are summarized in Table 1. The outcomes of various parameters for each included study are presented in Table 2.

The κ value for inter-reviewer agreement for potentially relevant articles was 1 (titles and abstracts) and 0.85 (full-text articles), indicating an "almost perfect" agreement between the two reviewers according to the criteria of Landis and Koch.[57]

Study Design, Participants, and Implant Features

Twelve CS,[20,22,23,46,47,49-52,54-56] one cohort study,[18] three QEs,[45,48,53] and five RCTs[16,19,21,43,44] were

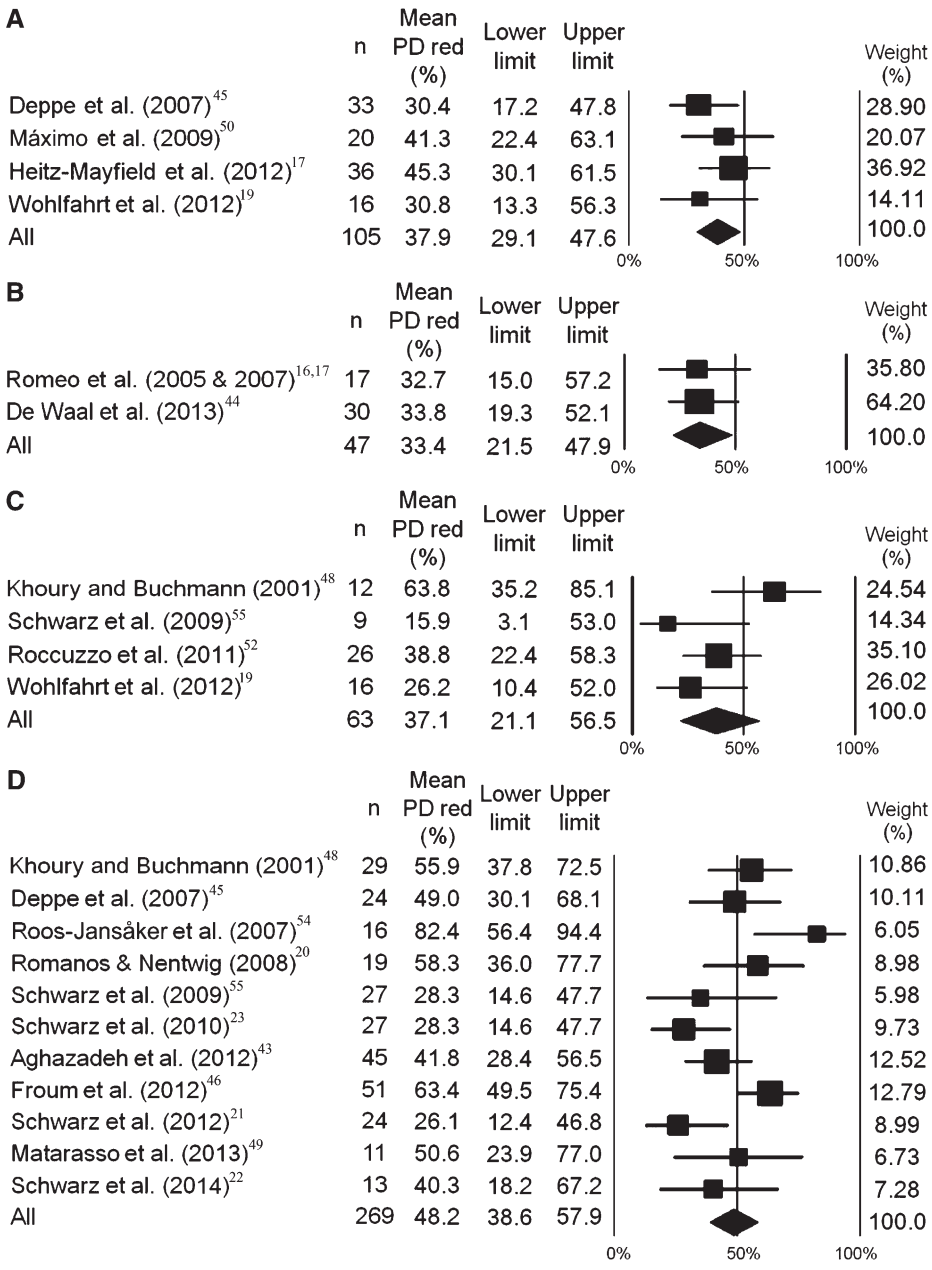

Figure 2.
A) *Meta-analysis for the percentage of PD reduction among selected studies using intervention of access flap and debridement. The WM was 37.9%, with a 95% CI of 29.1% to 47.6%.* ***B)*** *Meta-analysis for the percentage of PD reduction among selected studies using intervention of resective approach. The WM was 33.4%, with a 95% CI of 21.5% to 47.9%.* ***C)*** *Meta-analysis for the percentage of PD reduction among selected studies using intervention of regenerative treatment with grafting materials. The WM was 37.1%, with a 95% CI of 21.1% to 56.5%.* ***D)*** *Meta-analysis for the percentage of PD reduction among selected studies using intervention of regenerative treatment with both grafting materials and barrier membranes. The WM was 48.2%, with a 95% CI of 38.6% to 57.9%. red = reduction.*

included. Patient age ranged from 24 to 83 years.[56] Fourteen studies[16,18,19,21-23,43,44,49,51-55] included smokers, one study included non-smokers[50] exclusively, and six studies[20,45-48,56] did not report the smoking status of the participants. Information about the location of the treated implants is listed in Table 1. Four studies[20,49,51,56] did not report information about the features of the treated implants; some implants were reported as having non-identifiable features in two studies.[21,22] Three studies[18,50,54] included smooth and rough surface implants, whereas in seven studies,[16,19,43,46-48,52] only rough-surface implants were included. In two studies,[45,55] the information about the implant features was not available because the features of the failed implants excluded at the final examination were not released.

Defect Features

The mean initial defect depth was measured radiographically or clinically in most studies; four studies[16,45,51,52] did not report it. The mean initial PD was also reported in most studies, except for four studies.[47,51,53,56] It ranged from 4.8[45] to 8.8[46] mm. Nine articles[16,20-22,45,49,50,54,55] measured the mean initial CAL, with a range of 5.5[16] to 9.1[49] mm. Eleven studies[18,21-23,43,44,49,50,52,55,56] reported the mean initial BOP in percentage, with a range of 19.7%[49] to 100%.[50]

Surgical Features

Four treatment groups were identified: 1) access flap and debridement only;[18,19,45,50] 2) resective approach;[16,44] 3) application of bone grafting material;[19,48,51-53,55,56] and 4) guided bone regeneration (GBR).[20-23,43,45-49,53-55] Bone grafting materials used included autografts,[20,43,45,47,48] a combination of autografts and xenografts,[56] allografts,[46] alloplastic materials,[55] xenografts,[20-23,43,46,49,52,55] and others.[19,51,53,54] Non-resorbable[20-23,43,46,48,49,53-55] and resorbable[45,47,48] membranes were used. Five studies[19,45,47,48,54] submerged the implants. In one study,[20] four implants were submerged, whereas

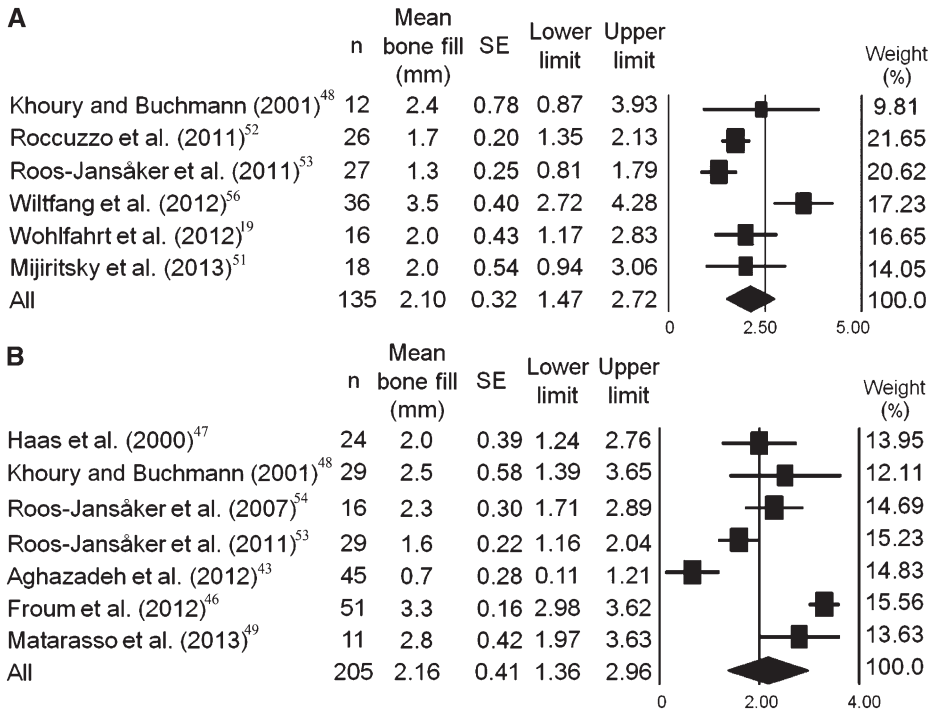

Figure 3.
A) *Meta-analysis for the amount of defect fill among selected studies using intervention of regenerative treatment with grafting materials. The WM was 2.10 mm, with a 95% CI of 1.47 to 2.72 mm.* ***B)*** *Meta-analysis for the amount of defect fill among selected studies using intervention of regenerative treatment with both grafting materials and barrier membranes. The WM was 2.16 mm, with a 95% CI of 1.36 to 2.96 mm.*

12 implants were not. Implants were not submerged in the remaining studies.

Surface Treatment

The contaminated implant surfaces were primarily treated with mechanical means, including air abrasives,[45,46,49,50] curets made of different materials (plastics,[18,21,22,50,52,55] carbon,[23] stainless steel,[49] graphite,[46] and titanium[19,20,51]), and implantoplasty.[16,21-23,44,56] Chemotherapy was commonly accompanied with mechanical debridement. The agents used were chlorhexidine,[18,44,48,52] cetylpyridinium chloride (CPC),[44] citric acid,[48] tetracycline,[46,51] hydrogen peroxide,[43,48,53-55] and EDTA.[19,52] Compared with the placebos, chlorhexidine and CPC did not result in significantly better clinical outcomes,[44] although they had the ability to suppress growth of anaerobic bacteria. Implantoplasty with resective surgery was associated with a higher implant survival rate, more PD reduction, and reduced bone loss compared with resective surgery alone.[16,17] Precaution should be exercised when performing implantoplasty on narrower implants because of weakening the implant structure, which could potentially lead to fracture of the fixture.[58] The CO_2, diode, and Er:YAG lasers were applied in some studies.[20-23,45,47] Comparative studies were conducted by Deppe et al.[45] and Schwarz et al.[21] to evaluate the effects of using CO_2 and Er:YAG lasers, respectively. No statistically significant differences in all assessed parameters could be found. Therefore, the limited evidence suggested that these lasers generated similar treatment outcomes as hand curets.

Results of the Meta-Analyses

The results and forest plots of the meta-analyses for PD reduction and RBF are demonstrated in Figures 1 through 3; the outcomes of various parameters for each surgical intervention are presented in Table 3.

Implants treated with access flap and debridement had a WM PD reduction of 2.38 mm (95% CI: 1.86 to 2.91 mm; Fig. 1A) or 37.9% (95% CI: 29.1% to 47.6%; Fig 2A). Only one article[19] reported RBF (0.1 ± 1.9 mm). The WM CAL gain was 1.20 mm (95% CI: –0.91 to 3.31 mm)[45,50] or 2.22%.[45] Two articles[18,50] reported the percentages of BOP at baseline and the last follow-up, which yielded 41.1% BOP reduction. The WM MR was 1.31 ± 0.61 mm.[18,45]

Implants treated with the resective surgery had a WM PD reduction of 2.04 mm (95% CI: 1.87 to 2.91 mm; Fig. 1B) or 33.4% (95% CI: 21.5% to 47.9%; Fig. 2B).[16,44] Only one article[16] reported CAL gain (–0.28 ± 0.88 mm, equivalent to –4.3%). The BOP reduction was 21.2%, reported in one article.[44] The WM MR was 1.44 ± 0.39 mm.[16] The amount of RBF was not reported.

Five articles[19,48,52,55,56] evaluated the effect of bone grafting on treating peri-implantitis. The WM PD was 2.32 mm (95% CI: 1.04 to 3.61 mm; Fig. 1C) or 37.1% (95% CI: 21.1% to 56.5%; Fig. 2C). The WM RBF was 2.10 mm (95% CI: 1.47 to 2.72 mm; Fig. 3A).[19,48,51-53,56] Only one article[55] reported the amount of CAL gain (0.6 ± 0.5 mm, equivalent to 8.2%). The percentage of BOP reduction was 39.6%.[52,55,56] The WM MR was 0.87 ± 0.88 mm.[55,56]

Implants treated with GBR had WM PD reduction of 3.16 mm (95% CI: 2.54 to 3.78 mm; Fig. 1D) or 48.2% (95% CI: 38.6% to 57.9%;

Table 3.
Summary of the Outcomes of Meta-Analyses

Interventions		PD Reduction (mm)	PD Reduction (%)	RBF (mm)	CAL Gain (mm)	CAL Gain (%)	BOP Reduction (%)	MR (mm)
Access flap and debridement	No. of pooled studies	4	4	1	2	1	2	2
	Meta-analyzed results*	2.38 ± 0.53	37.9	0.1 ± 1.9	1.20 ± 2.11	2.22	41.1	1.31 ± 0.61
	Heterogeneity†	18.7/0.30	0/0.56	NA	0/0.32	NA	0/0.47	0/0.32
Resective approach	No. of pooled studies	2	2	NA	1	1	1	1
	Meta-analyzed results*	2.04 ± 0.15	33.4	NA	–0.28 ± 0.88	–4.3	21.2	1.44 ± 0.39
	Heterogeneity†	0/0.65	0/0.94	NA	NA	NA	NA	NA
Bone grafts or substitutes	No. of pooled studies	5	4	6	1	1	3	2
	Meta-analyzed results*	2.32 ± 1.29	37.1	2.10 ± 0.56	0.6 ± 0.5	8.2	39.6	0.87 ± 0.88
	Heterogeneity†	0/0.67	11.3/0.34	5.5/0.38	NA	NA	0/0.68	0/0.32
Grafts + barrier materials	No. of pooled studies	11	11	7	7	6	6	6
	Meta-analyzed results*	3.16 ± 0.62	48.2	2.16 ± 0.80	1.99 ± 0.46	28.1	50.2	0.39 ± 0.28
	Heterogeneity†	23.8/0.22	5.9/0.39	0/0.68	4.6/0.39	0/0.59	22.1/0.27	38.9/0.15

NA = not applicable.
* Meta-analyzed results are given as mean ± SD for linear measurements (mm).
† Heterogeneity represents I^2 test value (%)/P value for χ^2 test.

Fig. 2D).[20-23,43,45,46,48,49,54,55] Seven articles[43,46-49,53,54] reported a WM RBF of 2.16 mm (95% CI: 1.36 to 2.96 mm; Fig. 3B). The WM CAL was 1.99 ± 0.46 mm[21-23,45,49,54,55] or 28.1%. The WM BOP reduction was 50.2%.[21-23,43,49,55] The WM MR was 0.39 ± 0.28 mm.[21-23,45,49,55]

The results of the heterogeneity test are shown in Table 3. All P values for the χ^2 test were >0.1, and I^2 test values were <50%, representing a low to moderate heterogeneity among included studies. Because of the small number of selected studies, comparisons among different bone grafting materials, membrane types, and healing protocols were not performed.

Risk of Bias Assessment

The risk of bias assessment for the included RCTs is summarized in supplementary Table 2 in online *Journal of Periodontology*. One study[19] was considered to have a low risk of bias, and another three studies[21,43,44] were considered to have a moderate risk of bias; however, the one other study[16] was considered to have a high risk of bias.

DISCUSSION

Summary of Main Findings

PD reduction after surgical procedures comprised MR, resolution of inflammation, and formation of new attachment. This study showed that the amount and percentage of PD reduction for each surgical intervention was 2.38 ± 0.53 mm and 37.9% for the access flap and debridement (mean follow-up time of 22.5 months), 2.04 ± 0.15 mm and 33.4% for resective approach (mean follow-up time of 21 months), 2.32 ± 1.29 mm and 37.1% for using bone grafting materials (mean follow-up time of 14 months), and 3.16 ± 0.62 mm and 48.2% for GBR (mean follow-up time of 14.1 months). A 2 to 3 mm PD decrease could be expected as a result of a surgical procedure. The highest reported PD reduction was ≈5.4 mm, achieved by regenerative procedures.[46,48] The meticulous surface decontamination methods as well as the use of biologic agents might have accounted for the favorable outcome. Nevertheless, the outcomes of the regenerative approach are less predictable. Systemic conditions of the patients, defect features,[23] implant surfaces,[52] and materials used[43] were confounding factors that should be considered.

The results showed ≈2 mm RBF for surgical procedures using bone substitutes without and with barrier materials. The highest amount of bone fill was reported by Wiltfang et al.[56] (3.5 ± 2.4 mm) and Froum et al.[46] (3.8 ± 1.5 mm). The former study, with a follow-up period of 1 year, used autologous bone grafts in combination with demineralized

xenogenic bone grafts and bone morphogenetic proteins. The satisfactory outcomes might be attributable to the bone-forming and reosseointegration potential of the growth factors.[59] The latter study, with a follow-up period of 3 to 7.5 years, introduced a series of sophisticated protocols for implant surface decontamination, including use of air-abrasive devices, tetracycline and chlorhexidine gluconate applications, and enamel matrix derivatives in combination with xenografts or allografts. These surgical protocols were based on the authors' clinical experiences; more controlled clinical trials are thus needed to validate the proposed treatment approach.

Barrier membranes were designed to exclude epithelial cells and fibroblasts, thus favoring the population of bone cells in a bony defect. Benefits of using barrier membranes are not clear. In one study,[55] the combination of grafting materials and a membrane appeared to yield a better clinical outcome compared with the use of grafting material alone. However, in another 3-year follow-up study,[48] it was concluded that the additional application of barrier membranes had no significant influence on bone level changes. Roos-Jansåker et al.[53] concurred that the use of barrier membranes did not significantly improved RBF. When a membrane is exposed, the regeneration potential of the site is diminished. This is especially true in the early stages of healing.[60] Evidence showed that membrane exposure rates were high: 13% to 38% in animal studies[14,61,62] and 18%[49] to 87.6%[53] in human clinical trials. Additionally, a well-contained defect might not require a membrane. Because application of a membrane is costly, time consuming, and technique sensitive, its potential benefits and costs should be carefully weighed before its use.

Four studies[20,21,45,47] applied lasers during the surgery. In a CS study,[20] CO_2 laser was used in combination with either autografts or xenografts and absorbable membranes with favorable outcomes. In contrast, Deppe et al.[45] concluded that no difference could be detected for regenerative procedures with or without CO_2 laser treatment on a long-term basis. More information is required to assess the benefit of using lasers for treating peri-implantitis.

Comparison With Other Relevant Systematic Reviews

Other systematic reviews[25,26,63] that investigated the clinical outcomes of treating peri-implantitis were available in the literature. A direct comparison of their results to this current analysis is not possible because of different selection criteria for the articles, surgical approaches, and methods of computing data. Nevertheless, the reported mean amount of PD reduction was generally compatible among the reviews. One study[26] concluded that the estimated PD reduction was 1.53 mm at 6 months with both non-surgical and surgical treatments. Another study[25] comparing PD reduction and CAL gain between non-surgical and various surgical procedures showed that using bone grafts and non-resorbable membranes resulted in the greatest PD reduction, with 3.52-mm greater reduction than non-surgical therapy.

Potential Biases Related to the Review Process

Several limitations were present in the current meta-analysis. First, the number of included papers for each surgical procedure is low, and only some studies compared treatment effects of different surgical approaches. Second, there are various degrees of heterogeneity in the study design, case selection, and treatment provided among studies. Third, the current review only includes studies written in English, which could introduce a publication bias. Last, the patient-centered outcome measurements,[26] such as changes of quality of life or esthetic improvements, are not analyzed in the current review.

CONCLUSIONS

Four main surgical procedures were identified for treating peri-implantitis: 1) access flap and debridement; 2) surgical resection; 3) regeneration with bone grafts; and 4) GBR. In short-term follow-ups, these procedures yielded an estimated 2- to 3-mm PD reduction, equivalent to 30% to 50% of the initial PD. A mean 2-mm RBF was achieved with regenerative procedures. The regenerative procedures using bone graft materials in combination with barrier membranes might be more effective; however, the outcomes of the regenerative procedures were also the most varied. Limited evidence suggested that implantoplasty could improve clinical outcomes, and lasers might provide equivalent effects to other commonly used methods for surface decontamination.

Implications for Practice

Currently available surgical approaches execute some clinical benefits, measured with surrogate endpoints in a short term. The treatment effects on implant survival and patient-centered outcomes are not known. The results provided an estimated PD reduction, among other parameters, that might be used to project treatment outcomes. Regenerative procedures using bone grafts and membranes seemed to generate greater PD reduction; however, comparative studies with low risk of bias that can substantiate this statement were lacking. The systemic condition of the patients, defect features, and types of materials could influence outcomes and should be assessed prudently.

Implications for Research

There is an urgent need for well-designed, studies with larger sample sizes, e.g., multicenter studies. The potential sources of bias should be reported for the purpose of quality assessment. Treatment outcomes should be evaluated at a multivariable level to identify the sources of heterogeneity. Studies on patient-centered outcomes and implant survival rate should be pursued. The clinical efficacy of biologic agents and lasers deserves additional investigation.

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