Clinical Oral Implants Research

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CLINICAL ORAL IMPLANTS RESEARCH

ORIGINAL ARTICLE OPEN ACCESS

A 10-Year Follow-Up of Reconstructive Treatment of Peri-Implantitis Using Mineralized Dehydrated Allograft and Resorbable Membrane: A Retrospective Case Series

Gerardo La Monaca | Nicola Pranno | Susanna Annibali | Antonella Polimeni | Maria Paola Cristalli

Department of Oral and Maxillo-Facial Sciences, Sapienza, University of Rome, Rome, Italy

Correspondence: Nicola Pranno (nicola.pranno@uniroma1.it)

Received: 16 October 2023 | **Revised:** 1 August 2024 | **Accepted:** 13 November 2024

Funding: The authors received no specific funding for this work.

Keywords: bone graft | collagen membrane | decontamination | dental implant | guided bone regeneration | peri-implantitis | radiography | surgical reconstructive therapy

ABSTRACT

Objectives: To evaluate the 10-year clinical and radiographic outcomes of peri-implantitis intrabony defects treated with mineralized dehydrated bone allograft (MDBA) and resorbable membrane in patients undergoing a regular supportive peri-implant/periodontal therapy (STP).

Materials and Methods: The original study participants were 34 (34 defects). After mechanical debridement and chemical decontamination of implant surfaces, intrabony defects were filled with MDBA and covered by a resorbable membrane. Patients were enrolled in a maintenance program with a recall interval of 6 months. The primary outcome was the absence of additional marginal peri-implant bone loss ≥ 1.0 mm after surgery. The composite outcome was no additional marginal peri-implant bone loss ≥ 1.0 mm and the absence of probing depth (PD) ≥ 5 mm, bleeding on probing and suppuration.

Results: Of the original 34 implants, 20 completed the 10-year follow-up, and three failed. Related to the primary outcome, the mean peri-implant marginal bone level changed from 4.78 mm (SD 1.84) at baseline to 3.10 mm (SD 1.73) after surgery and 3.71 mm (SD 1.78) at the follow-up end point. According to the composite outcome for disease resolution, 19 of the 34 original implants were successfully treated at the 10-year follow-up with a statistically significant difference between 1 (31/34 implants) and 5 years (20/34 implants) ($p = 0.003$) and 1 and 10 years ($p = 0.001$) but not between 5 and 10 years ($p = 1.000$).

Conclusions: Ten years after the reconstructive treatment, followed by regular SPT, the cumulative successful treatment rate, according to the primary and the composite outcomes, was 58% (20/34 implants) and 53% (19/34) implants, respectively.

1 | Introduction

Peri-implantitis is a worldwide emerging disease in implant dentistry with an increasing prevalence well-documented in the literature. However, the real impact is challenging to estimate due to the wide range between 1.1% and 85.0% at the implant level reported by different studies showing a significant heterogeneity in case definitions and selection criteria (Derks and Tomasi 2015; Lee et al. 2017; Rakic et al. 2018; Dreyer et al. 2018; Doornewaard et al. 2018; Salvi, Cosgarea, and Sculean 2019).

Several nonsurgical and surgical clinical protocols have been proposed to determine the most effective approach to treat peri-implantitis (Heitz-Mayfield and Mombelli 2014; Ting et al. 2018; Herrera, et al. 2023; Berglundh et al. 2024).

Nonsurgical therapy aims to reduce the bacterial load and remove the biofilm from infected implant surfaces using various decontamination strategies, including mechanical, chemical, photodynamic, laser and electrolytic treatments either alone or in multiple combinations (Ting et al. 2018; Renvert et al. 2019; Monje et al. 2022).

In surgical therapy, access to contaminated implant surfaces is gained with full-thickness flaps. Interventions include open-flap debridement in conjunction with anti-infective agents, implantoplasty, resective peri-implant surgery and reconstructive procedures with different graft materials used alone or with different types of barrier membranes (Khoury et al. 2019; Ramanauskaite et al. 2022; Schwarz et al. 2022). Combined resective and reconstructive approaches have also been proposed (Monje and Schwarz 2022).

Nevertheless, despite treatments, resolution of peri-implantitis and no disease progression or recurrence are challenging to achieve (Renvert et al. 2019; Carcuac et al. 2020).

Based on the available scientific evidence, nonsurgical approaches have demonstrated limited efficacy in managing peri-implantitis due to inadequate implant surface access, which jeopardizes the complete removal of granulation tissue, biofilm, and hard deposits (Faggion Jr. et al. 2014; Karlsson et al. 2019; Ramanauskaite, Fretwurst, and Schwarz 2021; Joshi et al. 2022; Cosgarea et al. 2023).

In contrast, surgical protocols, such as access flaps, allowing debridement/degranulation of the lesion and decontamination of infected implant surfaces under direct visual inspection, and pocket elimination procedures, have proven to be more effective in reducing bleeding on probing (BOP) and probing depth (PD), especially in advanced forms of peri-implantitis (Keeve et al. 2019; Karlsson et al. 2023). Furthermore, surgical reconstructive approaches have been shown to achieve significant improvements in clinical parameters and radiographic bone level in cases of peri-implantitis recurrence after nonsurgical treatment and in the presence of intrabony three- or four-wall-contained defects with ≥ 3 mm depth and adequate keratinized mucosa (Jepsen et al. 2019; Ramanauskaite et al. 2019; Li et al. 2023). Nevertheless, despite the large variety of reconstructive protocols, which use autogenous bone or bone-substitute materials, with or without different barrier membranes and biologically active materials, the efficacy of reconstructive procedures in treating peri-implantitis lesions has limited evidence and is referred to short-time follow-up (Tomasi et al. 2019; Donos et al. 2023; Ramanauskaite et al. 2023; Monje et al. 2023a).

Data on long-term results are reported only by a few studies with limited sample sizes and a lack of control groups (Andersen, Aass, and Wohlfahrt 2017; Berglundh, Wennström, and Lindhe 2018; Roccuzzo et al. 2020; Parma-Benfenati et al. 2020; Froum and Kim 2022; Jia et al. 2023).

This study aimed to increase the evidence on the long-term effectiveness of reconstructive treatment of single peri-implantitis intrabony defects with a mineralized dehydrated bone allograft and resorbable membrane, previously described in a publication with a 5-year follow-up (La Monaca et al. 2018), by reporting the 10-year clinical and radiographic outcomes of patients who underwent a regular supportive therapy program.

2 | Materials and Methods

2.1 | Study Design

The study was a retrospective case series to evaluate the 10-year outcomes of the surgical reconstructive approach in treating single intrabony peri-implantitis defects. The study protocol was based on the 1975 Declaration of Helsinki on medical protocols and ethics and its later amendments. The manuscript was drafted in accordance with the Joanna Briggs Institute Checklist for Case Series. Ethics approval was obtained from the Lazio Territorial Ethics Committee Area 1—Italy (Ref. 7229/Prot. 0789/2023).

2.2 | Study Population

The original study participants consisted of 34 consecutive patients with at least one implant with a peri-implantitis intrabony defect (implant in function for >12 months, progressive angular bone loss of ≥ 3 mm beyond crestal bone level changes resulting from initial bone remodeling detected on standard intraoral radiographs, bleeding on gentle probing and/or suppuration). In patients with more than one peri-implantitis lesion, only the implant with the most severe defect was included in the study for a total of 34 implants. The applied exclusion criteria were as follows: (a) uncontrolled medical condition, (b) systemic diseases that could influence the outcome of the therapy (i.e., diabetes with HbA1c $\geq 6.5\%$, osteoporosis, or bisphosphonate medication), (c) pregnant or nursing, (d) current smoker, (e) implants placed in the regenerated bone, (f) implant previously treated for peri-implantitis or with prosthetic supra-structure impossible to remove, (g) implant with consistent horizontal bone loss (Class II defects), or (h) implant mobility.

All patients had been previously rehabilitated with TiUnite surface implants (Brånemark System, Nobel Biocare, Göteborg, Sweden) and cemented fixed prosthesis (31 bridges and three single crowns) with good oral hygiene accessibility. The surgical reconstructive procedures with an allogenic bone substitute (Puros; Zimmer Dental, Treviso, Italy) and a resorbable membrane (Bio-Gide; Geistlich Biomaterials, Vicenza, Italy) were performed at the Oral Surgery Unit of Policlinico Umberto I, part of the "Sapienza" University of Rome, Italy, between January 2010 and December 2011.

Each patient signed up for informed consent after detailed treatment and study protocol descriptions, including the extended follow-up and the use of data for statistical analysis.

2.3 | Surgical and Postsurgical Treatment

Surgical and postsurgical treatment has been detailed in a previous publication reporting clinical and radiographic results at a 5-year follow-up (La Monaca et al. 2018).

Briefly, before surgery, all patients underwent mechanical debridement and polishing and received motivational reinforcement. All surgical procedures were performed by the same experienced surgeon (G.L.M.). Under local anesthesia with 2% mepivacaine and 1:100,000 adrenalin (Carbocaine, AstraZeneca, Milan, Italy), the prosthetic suprastructure was removed, and oral and buccal mucoperiosteal flaps were raised following intrasulcular incisions around the neck of the implant abutment (Figure 1a). After removing the granulation tissue, peri-implant defect characteristics were recorded. Configurations were determined based on the classification proposed by Schwarz et al. (2007). The extension (in millimetres) of vertical bone loss was also measured intraoperatively, from the implant platform to the deepest aspect's bottom. Supra- and intrabony implant surfaces were debrided using an ultrasound instrument and rotating titanium brush, polished with glycine and bicarbonate powders, and rinsed for 1 min with a sterile saline solution. Implant surfaces were decontaminated with 3% hydrogen peroxide for 1 min and 0.2% chlorhexidine solution for 1 min and treated for 3 min with a solution of tetracycline hydrochloride (Figure 1b). The bone defect was filled with mineralized dehydrated bone allograft (Puros; Zimmer Dental) moistened in sterile saline for 5 min and covered by a resorbable membrane (Bio-Gide; Geistlich Biomaterials) (Figure 1c). The mucoperiosteal flaps were repositioned coronally and stabilized with resorbable interrupted sutures (5-0 Vicryl; Johnson & Johnson Medical, Norderstedt, Germany), which were removed after 2 weeks (Figure 1d). At the end of the surgical procedure, the prosthetic suprastructure was cleaned and remounted in a non-submerged healing mode. The antibiotic protocol included administering 875 mg of amoxicillin plus 125 mg of clavulanic acid (Augmentin; GlaxoSmithKline, London, UK) twice-daily and 250 mg of metronidazole (Flagyl; Zambon, Milan, Italy) three times daily for 10 days, starting 1 h before surgery. Analgesia was achieved with 200 mg of ketoprofen (Ibifen; Aprilia, Latina, Italy) for a maximum of three times daily according to patients' needs.

Post-operative care for the first month included cleaning the surgical area with a soft toothbrush, avoiding floss, interdental brushes and toothpicks, and mouth rinsing with 0.12% chlorhexidine digluconate (Corsodyl; GlaxoSmithKline Consumer Healthcare) three times daily. For the first year after surgery, patients were recalled at 1, 3, 6, 9, and 12 months for re-evaluation, professional prophylaxis with supragingival debridement, and counselling to maintain high levels of oral hygiene. Afterwards, recall visits were scheduled every 6 months to monitor clinical parameters and perform supportive peri-implant/periodontal therapy (SPT) involving removal of supra- and submucosal biofilm and calcified deposits using titanium or carbon-fiber curettes, ultrasonic devices with titanium tips, rubber cup and polishing paste. Furthermore, motivational encouragement and tailored oral hygiene instructions were given. BoP/suppuration and increasing PD were treated with systemic antibiotics, antiseptics and open-flap debridement. No supplementary surgical reconstructive treatment was performed. Periapical radiographs were performed once yearly.

2.4 | Clinical and Radiographic Assessment

The same examiner (M.P.C.) expert, unblinded and noncalibrated, recorded the following clinical parameters using a pressure-sensitive probe (Hawe Click probe, Kerr Dental, Bioggio, Switzerland) at a standardized probing force of 0.25 N. Probing depth (PD) from the mucosal margin to the bottom of the probeable pocket, presence/absence of bleeding on probing (BoP) within 30 s, presence/absence of suppuration on probing, and presence/absence of plaque (PI) were collected at the four sites (mesial, distal, buccal, and palatal/lingual) of each treated implant. The marginal peri-implant bone level (MPBL) was detected on periapical radiographs performed with the parallel long-cone technique and a standardized film holder (Rinn Centratore XCP Evolution 2003; Dentsply, Rome, Italy). All radiographs were scanned at 600 dpi and digitized

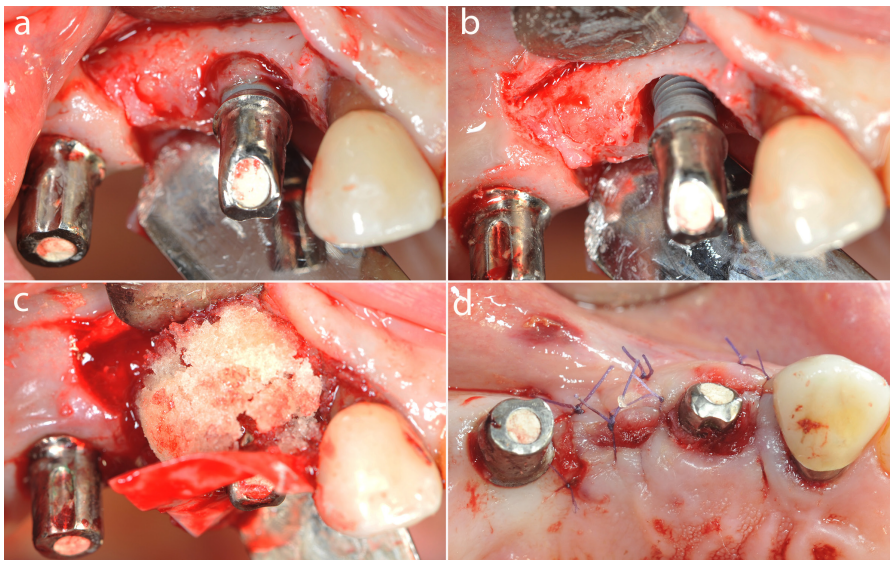

FIGURE 1 | Intraoperative views of surgical reconstructive treatment: (a) mobilization of the mucoperiosteal flaps; (b) intrabony defect after granulation tissue removal and implant surface debridement and decontamination; (c) defect filling with mineralized dehydrated bone allograft and the resorbable membrane fixed on palatal aspect, (d) mucoperiosteal flaps repositioned coronally and stabilized with resorbable interrupted sutures.

(Expression 10000 XL; Epson, Houston Texans, USA). Two expert investigators, blinded to other aspects of the study, measured in millimeters the distance from the implant shoulder to the bottom of the marginal bony defect on each implant's mesial and distal aspects, and the average value was calculated. Marginal peri-implant bone-level variations were estimated with DBSWIN 5 software (Durr Dental, Ludwigsburg, Germany), and the calibration was performed using known implant length and width as references. The 10-year clinical and radiographic findings were compared with baseline, 1-, 3-, and 5-year values (Figure 2).

2.5 | Statistical Analysis

Data included in the study referred to implant with the most severe peri-implant defect of each patient. Standard statistical analysis software (version 20.0, Statistical Package for the Social Sciences; IBM Corporation, Armonk, NY, USA) was used to evaluate data. Descriptive statistics, including mean and SD values, were calculated for each variable. Data outliers were analyzed with box plots, and data conformed to a normal distribution were determined with the Shapiro–Wilk test. The investigators' calibration was performed using 30 randomly selected periapical radiographs. The Intraclass Correlation Coefficient (ICC) was employed to evaluate inter- and intraoperator variability in assessing marginal peri-implant bone levels. When the ICC for inter- and intraoperators indicated good reliability (ICC > 0.75), the operators were considered calibrated and started the radiograph evaluations. During the study after the calibration, any disagreement was solved by consensus, and a third investigator was consulted when it was not initially possible to achieve complete agreement (defined as a difference between the measurements made by the two experts of > 0.1 mm). The primary outcome was the absence of additional marginal peri-implant bone loss ≥ 1.0 mm (two times the SD of the measurement error) after surgery compared with the baseline. The composite outcome included no additional bone loss ≥ 1.0 mm, and the absence of PD ≥ 5 mm, BoP, and suppuration. Survival analysis was used to evaluate treatment efficacy based on primary and secondary outcomes. Additionally, Kaplan–Meier analysis was conducted to examine the impact of defect configuration and severity over a 10-year period Cochran's Q test (Cochran 1950) was performed to determine whether the percentage of implants satisfying the primary and the composite outcome differed between 1, 3, 5, and 10 years of follow-up. To avoid overestimating the treatment effect due to the loss of more than 5% of patients to the last follow-up, the worst-case scenario was considered, where the treatment of dropouts was evaluated as a failure. Differences in the mean value of MPBL and PD were assessed with one-way repeated measures ANOVA. Pairwise comparisons with Bonferroni correction were performed for both Cochran's Q test and repeated measures ANOVA. The statistical significance cutoff for each test was set at $p \leq 0.05$.

3 | Results

Of the 34 original study participants, 23 completed the 10-year examination. Patient, implant, intrabony defect, and prosthesis characteristics were reported in Table 1.

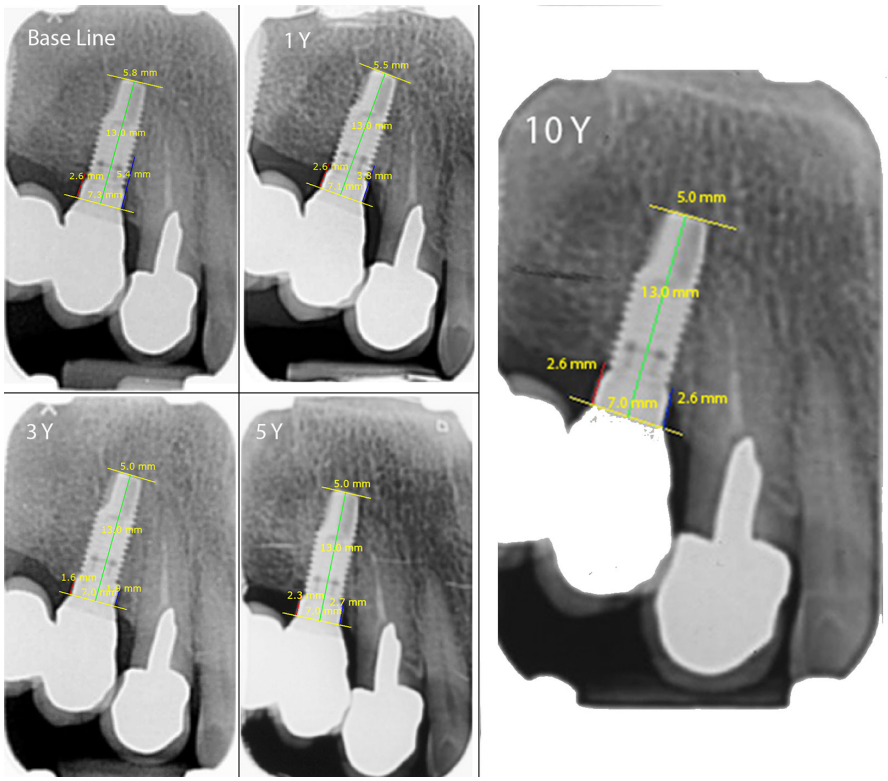

FIGURE 2 | Radiographic assessments at baseline, 1-, 3-, 5- and 10-year follow-up using implant length as reference for calibration of measurements (green line). The distance in millimeters from the implant shoulder to the bottom of the defect, both at mesial (blue line) and distal (red line), measures marginal bone height to estimate bone level variations over time.

TABLE 1 | Data on patients, defect location and morphology, implant and prosthesis, adjunctive therapy and implant survival of 34 original study participants.

N	Sex	Age	History of periodontal treatment	Former smokers	Months of function	Implant site/ configuration/severity	Implant	Prosthesis/ n°units	Adjunctive therapy
1	F	50			18	14/1e/s	Ø 4×13 mm	S/4	
2	F	52			36	37/1d/m	Ø 5×10 mm	S/2	
3	F	28			18	25/1c/m	Ø 4×11.5 mm	S/3	Yes
4	F	62			38	12/1c/m	Ø 4×10 mm	S/3	
5	M	64		Yes	34	25/1c/m	Ø 3.5×10 mm	S/3	
6	M	65			85	34/1e/s	Ø 4×13 mm[a]	NS	
7	F	44	Yes		72	16/1c/m	Ø 5×11.5 mm[b]	S/3	
8	M	37	Unknown		39	44/1c/m	Ø 4×13 mm[b]	S/3	
9	F	69	Yes	Yes	73	26/1d/s	Ø 5×13 mm[b]	S/3	
10	F	54			63	32/1c/s	Ø 3.5×13 mm[b]	S/3	
11	M	51			56	46/1d/s	Ø 5×10 mm[b]	S/3	
12	F	43	Unknown	Yes	62	35/1d/s	Ø 4×11.5 mm[b]	S/3	
13	M	49	Yes	Yes	70	44/1c/m	Ø 4×13 mm	S/2	Yes
14	M	64			70	14/1e/s	Ø 4×13 mm	S/2	
15	F	62			54	15/1e/m	Ø 4×13 mm	S/4	
16	F	55			24	16/1e/s	Ø 5×13 mm[b]	S/2	
17	F	63	Yes		42	12/1e/s	Ø 3.5×10 mm[b]	S/2	
18	M	53			89	26/1d/s	Ø 5×13 mm	S/3	
19	F	38	Yes		46	16/1c/m	Ø 5×13 mm	S/3	
20	F	56	Yes	Yes	37	24/1c//m	Ø 3.5×13 mm[b]	S/3	
21	M	39			48	42/1d/m	Ø 3.5×13 mm	S/3	
22	M	69			29	44/1d/m	Ø 4×10 mm[a]	NS	
23	M	60	Yes	Yes	83	16/1e/m	Ø 5×10 mm	S/2	
24	F	52	Unknown		50	46/1d/m	Ø 5×10 mm	S/2	
25	F	67		Yes	63	14/1c/s	Ø 4×13 mm[a]	S/3	

(Continues)

TABLE 1 | (Continued)

N	Sex	Age	History of periodontal treatment	Former smokers	Months of function	Implant site/ configuration/severity	Implant	Prosthesis/ n°units	Adjunctive therapy
26	F	63	Yes	Yes	49	35/1c/s	Ø 4×13 mm	S/3	
27	M	47	Yes		29	45/1c/m	Ø 4×13 mm	S/3	Yes
28	F	50			89	34/1e/m	Ø 4×11.5 mm	NS	
29	M	55	Yes		41	42/1c/m	Ø 3.5×13 mm	S/3	
30	F	66			62	25/1c/m	Ø 3.5×13 mm[b]	S/3	
31	M	68			119	45/1d/m	Ø 4×10 mm[b]	S/3	
32	F	53	Yes	Yes	26	32/1c/s	Ø 3.5×13 mm	S/3	
33	M	33			24	36/1d/m	Ø 5×8 mm	S/3	
34	M	57	Yes		39	47/1d/s	Ø 5×10 mm	S/3	

Abbreviations: Ic = buccal dehiscence and circumferential bony defect; Id = oral and buccal dehiscence and circumferential bony defect; Ie = circumferential bony defect with maintaining oral and buccal cortical; s = slight (3–4 mm/< 25% of the implant length); m = moderate (4-5 mm/≥ 25% of the implant length); S = splinted (bridge); NS = non splinted (single crown); Adjunctive therapy = systemic antibiotics, antiseptics and open-flap debridement.
[a]Failed.
[b]Lost to follow-up.

Of the 23 remaining patients, the male-to-female ratio was 12:11, and the mean age was 53.57 (SD 11.04) years (range: 28–69). Nine subjects had previous periodontal treatment, and six were former smokers. All patients received cemented restorations, including three individual crowns and 20 partial fixed prostheses. The partial fixed prostheses consisted of three splinted units in 13 cases, two splinted units in five cases, and four splinted units in two cases. Intrabony defects involved the lower more than the upper jaw and were located at premolar (six mandibular and six maxillary), molar (four mandibular and three maxillary) and incisor (three mandibular and one maxillary) sites. Based on the configuration, 10 defects were allocated in class Ic (buccal dehiscence plus circumferential defect), seven in class Id (buccal and oral dehiscences plus circumferential defect) and six in class Ie (circumferential defect without buccal and oral dehiscences). According to the severity classification based on the ratio of vertical bone loss and the implant length (Monje et al. 2019), eight defects were considered slight (3–4 mm/< 25% of the implant length) and 15 moderate (4–5 mm/= 25%–50% of the implant length). Over a period of 5 to 10 years, three implants (all in class Ic and moderate severity) presenting BoP/suppuration and increasing PD required additional treatments, and three implants had to be removed due to disease progression. Implant loss, more than to the defect severity (slight in two implants in class Ic and Ie and moderate in one implant in class Id), was attributed to the patient's advanced age and medical conditions (stroke, Alzheimer's, and Parkinson's disease). These conditions made it challenging to comply with recall visits and adhere to oral hygiene regimes, thus preventing the maintenance of healthy peri-implant conditions.

3.1 | Primary Outcome

According to the primary outcome, none of all 34 implants included in the baseline analysis had additional marginal peri-implant bone loss ≥ 1.0 mm 1 year after surgery. The successful treatment rate decreased progressively to 94% (32 out of 34) at 3 years and 76% (26 out of 34) at 5 years. At 10 years, after excluding three failures, all 20 remaining implants satisfied the primary outcome with a cumulative success rate of 58% (20 out of 34) (Table 2). Post hoc analysis with Bonferroni adjustment revealed a statistically significant difference between 1 and 5 years ($p = 0.028$) and 1 and 10 years ($p < 0.001$) but not between 5 and 10 years ($p = 0.203$).

Furthermore, the success over time was not significantly influenced by the configuration ($p = 0.460$) and severity ($p = 0.095$) of intrabony defects (Tables 3 and 4).

3.2 | Composite Outcome

According to the composite outcome of disease resolution (absence of PD ≥ 5 mm, BoP, and suppuration and no additional bone loss ≥ 1.0 mm at the follow-up end point), 31 of 34 baseline implants (91%) were successfully treated 1 year after surgery. The cumulative success rate decreased over time to 79% (27 out of 34) at 3 years, 59% (20 out of 34) at 5 years, and 53% (19 out of 34) at 10 years, as only one of the 20 remaining implants, after

TABLE 2 | Cumulative successful treatment rates according to the primary and composite outcomes.

Time (years)	Number of implants entering interval	Number of implants withdrawing	Number of implant terminal events	Proportion terminating (%)	Proportion surviving (%)	Cumulative successful treatment rate at the end of interval
Primary outcome						
0	34	0	0	0	100	100
1	34	0	0	0	100	100
3	34	0	2	6	94	94
5	32	3	6	20	80	76
10	23	20	3	23	77	58
Composite outcome						
0	34	0	0	0	100	100
1	34	0	3	9	91	91
3	31	0	4	13	87	79
5	27	0	7	26	74	59
10	20	19	1	10	90	53

Note: Number of implants withdrawing: the number of implants that left the study before an event occurred.
Number of implant terminal events: the number of implants did not meet primary and composite outcomes.
Proportion terminating: the ratio of terminal events to the number exposed to risk.

TABLE 3 | Cumulative success rate for primary and composite outcomes based on defect configuration.

Defect configuration	Censored (%)	Event (%)	Total
Primary outcome			
1c	11 (73.3)	4 (26.7)	15
1d	6 (54.5)	5 (45.5)	11
1e	6 (75)	2 (25)	8
Total	23	11	34
Composite outcome			
1c	9 (60)	6 (40)	15
1d	6 (54.5)	5 (45.5)	11
1e	4 (50)	4 (50)	8
Total	19	15	34

Note: Censored: The implants who left the study before its conclusion.
Event: implants not meeting primary and composite outcomes.

TABLE 4 | Cumulative success rate for the primary and composite outcomes based on defect severity.

Defect severity	Censored (%)	Event (%)	Total
Primary outcome			
Slight	12 (85.7)	2 (14.3)	14
Moderate	11 (55)	9 (45)	20
Total	23	11	34
Composite outcome			
Slight	7 (50)	7 (50)	14
Moderate	12 (60)	8 (40)	20
Total	19	15	34

Note: Event: implants not meeting primary and composite outcomes.

excluding three failures, showed PD ≥ 5 mm (Table 2). A statistically significant difference was found between 1 and 5 years ($p = 0.003$) and 1 and 10 years ($p = 0.001$) but not between 5 and 10 years ($p = 1.000$).

Furthermore, the composite outcome success rate over time was not significantly influenced by the configuration ($p = 0.924$) and severity ($p = 0.0668$) of intrabony defects (Tables 3 and 4).

3.3 | Radiographic and Clinical Assessment

Radiographic and clinical parameters assessed around the 20 implants reaching the 10-year follow-up were presented as means ± SD in Table 5. Compared to 4.78 mm (SD 1.84) at the baseline, the marginal peri-implant bone level (MPBL) improved by 1.68 mm (SD 0.25) at 1 year after surgery. This value decreased slowly and progressively to 1.52 mm (SD 0.21) at 3 years, to 1.28 mm (SD 0.25) at 5 years, and to 1.07 mm (SD 0.25) at 10 years, which was the lowest reduction over time (Figure 3). MPBL showed a statistically significant improvement at 1 ($p < 0.001$), 3 ($p < 0.001$), 5 ($p = 0.001$), and 10 years ($p = 0.005$) after surgery (Table S1).

The overall mean PD of 6.32 mm (SD 1.85) at the baseline decreased significantly ($p < 0.001$) at 1, 3, 5, and 10 years after surgical treatment (Table 5; Table S2). At the end of the follow-up, the mean PD of 2.95 mm (SD 0.98) represented a more remarkable improvement (3.380 mm, SD 0.489) over time compared with the baseline (Figure 4).

4 | Discussion

The present retrospective observational study investigated clinical and radiographic parameters at a 10-year follow-up of a previous case series (La Monaca et al. 2018) of patients with peri-implantitis intrabony defects treated with mineralized dehydrated bone allograft and resorbable membrane and enrolled in a regular supportive therapy program.

According to the composite outcome for disease resolution (no additional bone loss ≥ 1.0 mm and the absence of PD ≥ 5 mm, BoP, and suppuration), 19 implants out of the 34 included in the baseline investigation were successfully treated at the follow-up endpoint with a statistically significant difference between 1 and 5 years and 1 and 10 years but not between 5 and 10 years.

The lack of statistically significant difference in successful treatment rates at 5 and 10 years of observation might be justified by the trend in clinical and radiographic parameters of implants reaching the 10-year follow-up. When comparing MPBL, the decrease in bone-filling gain (0.21 mm) between 5 and 10 years was lower than that (0.24 mm) between 3 and 5 years. The decrease in bone-filling gain during the additional 5-year observation period was in line with progressive level changes in marginal peri-implant bone that should not exceed 0.2 mm/year after the initial phase of remodeling (usually 1 year of function) (Albrektsson et al. 2022). Furthermore, the mean PD at the 10-year follow-up showed a significant improvement (3.38 mm, SD 0.49) compared to the baseline,

TABLE 5 | Radiographic and clinical parameters of 20 implants reaching the 10-year follow-up.

Parameter	Baseline	1-year	3-year	5-year	10-years
MPBL (mm)	4.78 ± 1.84	3.10 ± 1.73[a]	3.26 ± 1.98[a]	3.50 ± 2.02[a]	3.71 ± 1.79[a]
PD (mm)	6.33 ± 1.86	3.65 ± 1.46[a]	3.74 ± 1.38[a]	3.88 ± 1.63[a]	2.95 ± 0.98[a]

Note: Data were presented as means ± SD.
Abbreviations: MPBL, means of mesial and distal marginal peri-implant bone level; PD, probing depth index out of four sites per implant.
[a]Significant difference compared to the baseline.

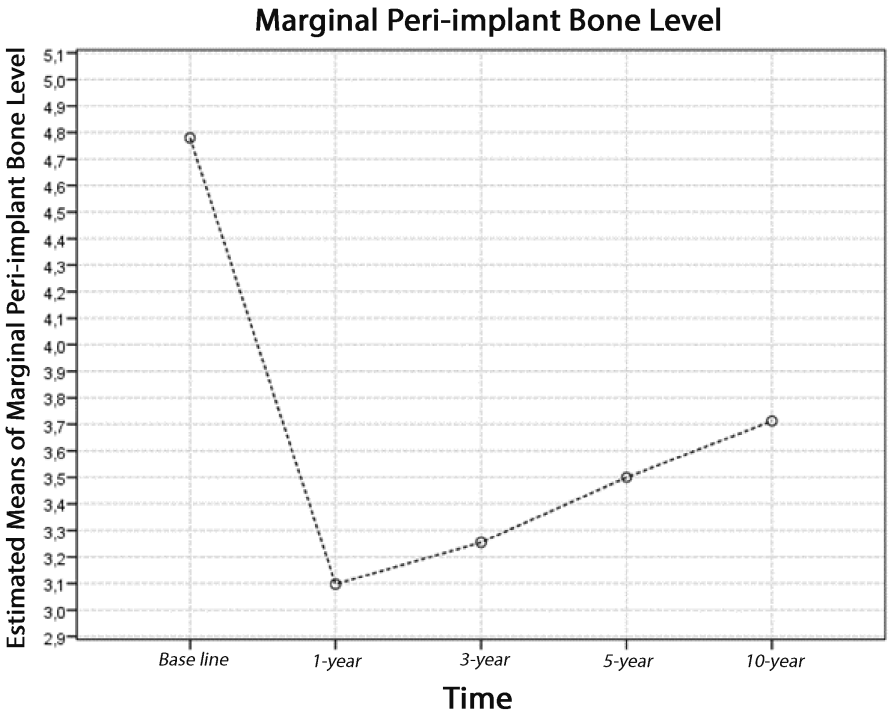

FIGURE 3 | Estimated means of marginal peri-implant bone level from baseline to 10-year follow-up.

instead of the slight and progressive increase recorded up to 5 years after surgery. This improvement might be justified by more oral hygiene accessibility and the consequent best inflammation control due to mucosal recessions frequently observed after 5 years of reconstructive surgical therapy (Roos-Jansåker et al. 2014; Sanz-Martín et al. 2021). The stability of the clinical and radiographic parameters observed after the first 5 years from the adopted surgical reconstructive approach might be affected by the limited number of patients, the loss at follow-up of subjects with a less favorable therapeutic outcome, and above all by the strict adherence to a regular maintenance care protocol.

To our knowledge, this is the only longitudinal trial reporting 10-year outcomes following a surgical reconstructive approach with MDBA and resorbable membrane in treating peri-implantitis. In the literature, only two papers refer to the 10-year follow-up data on the results of peri-implantitis surgical approaches (Roccuzzo et al. 2020; Serino et al. 2021).

Recently, Roccuzzo and colleagues, in a prospective study, published long-term clinical and radiographic outcomes of a regenerative surgical procedure to treat peri-implantitis crater-like defects using deproteinized bovine bone mineral with 10% collagen. The authors, excluding dropouts, reported an overall implant survival rate at 10 years of 55% of titanium plasma-sprayed surface (TPS) implants (6/14) and 80% for the sandblasted large grit and acid-etched surface (SLA) implants (8/12). Furthermore, the overall successful therapy, defined as PD ≤ 5 mm, absence of bleeding/suppuration on probing, and no further bone loss, was found in 35% of implants (9/26), while 7 implants (5 TPS and 2 SLA) had to be removed due to recurrent infections. More in detail, out of the implants still in function at 10 years, the overall mean distance between the base of the implant shoulder and the most coronal visible bone-to-implant contact (BL) decreased from 3.2 mm (SD 1.1) to 0.9 mm (SD 1.0), and the overall PD decreased from 6.9 mm (SD 1.3) to 3.7 mm (SD 1.5) at 1-year, to 3.2 mm (SD 0.7) at 7-year and to 3.3 mm (SD 0.5) at 10-year of follow-up. Mean peri-implant pocket depths markedly decreased at the 1-year evaluation and remained stable during the following years of observation. Regarding interproximal bone levels, a significant improvement was found at 1-year after treatment, while a slight tendency to relapse was detected at the 7- and 10-year analyses.

Results reported by Roccuzzo and colleagues are consistent with those of the present study, even if an accurate comparison

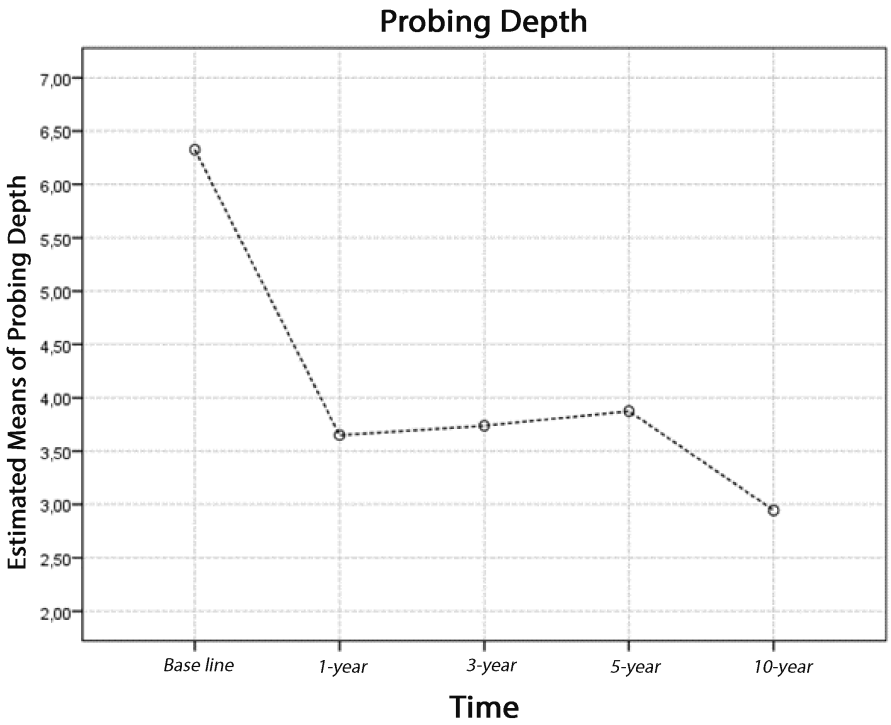

FIGURE 4 | Estimated means of probing depth from baseline to 10-year follow-up.

is difficult to make. However, it is important to highlight the same trend that emerged from both studies resulting in stable clinical parameters during the 10 years of examination when a regular supportive therapy program followed the surgical reconstructive approach.

Even more challenging is a comparison with the retrospective clinical trial at a 10-year follow-up of Serino and colleagues, who evaluated patients treated for peri-implantitis with a surgical anti-infective and resective approach and enrolled in a supportive peri-implant therapy program. At the 2-year follow-up, two groups of patients were identified: responding, with all implants healthy following treatment, and non-responding, presenting at least one implant with signs of peri-implant disease with or without radiographical signs of progression of bone loss (≥ 2 mm RX bone loss). Eighteen patients (85 implants) in the non-responding group were followed for further 8 years. At the 10-year examination, in the non-responding group, 84% of the implants that regained health following surgery (PPD ≤ 4 mm, and without BoP and/or Sup) remained healthy during the entire observation period; 66% of the implants with residual pockets following surgery (PD ≥ 5 mm with BoP and/or Sup in at least one site) maintained stable peri-implant conditions, and 29% of all treated implants showed disease progression evidenced by an increasing PPD and BoP/Sup and ≥ 2 mm RX bone loss, and 11 of those were extracted. The authors concluded that for most of the implants, the peri-implant health regained following surgical therapy for peri-implantitis could be maintained during the follow-up period in patients with a high standard of oral hygiene and enrolled in a 6-month recall program.

Outcomes of the present case series cannot be directly compared with those of other long-term studies published in the literature reporting results of reconstructive therapy for peri-implantitis due to high heterogeneity in definitions of peri-implantitis, implant surfaces, regenerative materials, use or not of membranes, follow-up (Parma-Benfenati et al. 2020; Froum and Kim 2022; Jia et al. 2023).

Current findings were not congruent with the rate of 70.2% for successfully treated implants, 15.8% for surviving implants, and 14.0% for explanted implants as reported by Parma-Benfenati and colleagues. The retrospective study involved 57 implants with different surfaces (seven turned and 38 modified), which were treated based on peri-implantitis defects with different regenerative approaches, including intraoral autogenous bone grafts, mineralized freeze-dried human bone allografts and/or xenografts, resorbable or non-resorbable membranes and submerged and non-submerged healing In addition, the latest follow-up after surgical therapy showed a high degree of variability from 8.1 years (SD 3.3, range 3–21 years) for the successfully treated implants (40/57) to 5.6 years (SD 1.8, range 3–8 years) for the surviving implants (9/57) and 4.9 years (SD 2.7, range 2–10 years) for the explanted implants (8/57). Likewise, the clinical and radiographic results of the present study were not comparable with those reported by Froum and Kin due to the differences in reconstructive treatment and follow-up period. The authors observed an average PD reduction of 6.7 mm (SD 1.6 mm, range 3–11) mm compared to preoperative of 9.7 mm (SD 1.6 mm, range 7–15) and a mean bone level gain of 3.6 mm (SD 2.4) compared to preoperative 5.2 mm (SD 2.4), and postoperative 1.6 mm (SD1.4). These findings referred to 46 implants with advanced peri-implantitis (> 50% intrabony bone loss), which were treated using recombinant human platelet-derived growth factor or enamel matrix derivative and a mineralized freeze-dried bone allograft and bovine xenograft in

3:1 ratio covered with a collagen membrane and followed from 3 to 15 years with the mean of 4.2 years (SD 1.6). It is challenging to make a comparison also with the average bone gain of 2.51 mm (SD 1.34) and the mean PD reduction of 2.93 mm (SD 1.20) reported in the study conducted by Jia and colleagues to evaluate the effect of a combined surgery approach to treat peri-implantitis. A total of 72 implants were treated with a combination of implantoplasty and guided bone regeneration with Bio-Oss Collagen covered by a concentrated growth factor membrane followed from 2 to 11 years. The effect of therapy was assessed at 2–5 for 61 implants and 5–10 years for 10 implants, with only one implant followed over 10 years.

However, the main differences were detected in retrospective observational studies that used resective methods to manage peri-implantitis (Berglundh, Wennström, and Lindhe 2018; Romandini et al. 2023).

The average PD reduction of 2.2 mm (SD 2.8) and bone level change of −0.3 (SD 2.1) mm were found by Berglund and colleagues around 25 turned and 25 implants with modified surfaces treated for peri-implantitis with mechanical anti-infective measures and pocket elimination. These results were recorded at a follow-up between 2 and 10.8 years, with a mean of 3.6 years (SD 1.4, range 2.0–8.1) for modified implants.

Likewise, it was not consistent the rate of 59.5% for implant lost/ retreated/bone loss > 1 mm, reported by Romandini and colleagues, who evaluated two cohorts of patients (267 implants) surgically treated for peri-implantitis with access flap and pocket elimination over a mean period of 7.0 years (SD 3.6, range 1–18).

Anyway, all studies, regardless of the approach, recognized that the adherence of patients to an active periodontal/ peri-implant supportive therapy program was essential for maintaining long-term outcomes of peri-implantitis surgical treatments (Roos-Jansåker et al. 2014; Serino, Turri, and Lang 2015; Heitz-Mayfield et al. 2018; Roccuzzo et al. 2018; Ravidà et al. 2022).

Lastly, it is worth noting that in the present case series, the success rate over time was not affected by the intrabony defects configuration and severity, even if the data should be interpreted with caution due to the limited number of evaluated defects. Nevertheless, conflicting opinions have been reported in the literature regarding the impact of defect morphology on outcomes of peri-implantitis surgical therapy, mainly due to variations in the sample size, resective or reconstructive treatments, and follow-up period.

In a prospective study, Schwarz and colleagues showed that partially edentulous patients who underwent regenerative therapy using a natural bone mineral and collagen membrane had significantly better results in clinical parameters (PD and CAL) at 6 months for Class Ie defects than for Class Ib or Class Ic sites, but not at 12 months (Schwarz et al. 2010). Defects filling greater at four-wall lesions than at two- and three-wall lesions with the best reconstructive potential in the deep defects was also found by Aghazadeh and colleagues in a prospective trial on 74 implants treated with autogenous bone or bovine-derived xenograft and a resorbable membrane (Aghazadeh, Persson, and Renvert 2020).

More recently, Ravidà and colleagues showed that implant failure risk was 20 and 15 times greater, respectively, when relative bone loss (%) was above 50% or between 25% and 50%, compared to below 25%.

(Ravidà et al. 2022). The study involved 121 implants with a mean follow-up of 42.6 months (SD 26.3, range 12–106). Among these, 77 implants with horizontal bone loss underwent a resective approach, while 44 with infrabony defects were treated with particulate bone allograft and xenograft, covered with a collagen membrane, and combined with implantoplasty in the presence of the suprabony exposed surface.

Conversely, Ichioka and colleagues, analyzing data from 129 patients (136 implants) of a previously published randomized controlled study, found no critical effect of defect configuration on outcomes of peri-implantitis treatments with or without a bone replacement graft (Ichioka et al. 2023).

Monje and colleagues shared the same observation in a secondary analysis of data from 48 implants (33 patients) with peri-implant intrabony defects treated using a demineralized (fiber) and mineralized (particulate) cortical allograft with or without collagen barrier membrane (Monje et al. 2023b). In the study, the influence of bone defect characteristics and severity on disease resolution and bone gain did not reach statistical significance, except for the narrow defect angle that was considered a predictor of radiographic bone gain.

Similar conclusions were reached by Roccuzzo and colleagues in a prospective investigation evaluating the results of reconstructive procedures using deproteinized bovine bone mineral with 10% collagen in 75 patients with peri-implantitis Class I defects (Roccuzzo et al. 2016). When clinical results of the same case series were re-evaluated after 5 years of follow-up, no statistically significant difference was detected ($p = 0.123$) in the percentages of implant survival rates among the different peri-implant defect configuration (Roccuzzo et al. 2021).

The present study presents several shortcomings. First, the small sample size (23 of 34 initial study participants) and the high number of dropouts (11 patients/implants). Nevertheless, these limitations are common to long-term studies assessing the treatment of peri-implantitis due to the length of follow-ups and the old age of patients (Roos-Jansåker et al. 2014; Andersen, Aass, and Wohlfahrt 2017; Schwarz et al. 2017; Heitz-Mayfield et al. 2018; Roccuzzo et al. 2020; Aghazadeh et al. 2022). Second, clinical parameters were recorded without calibration and unblinded even if by the same expert examiner (M.P.C.) because they were performed during scheduled routine recall visits over 10 years. Third, the supportive peri-implant/periodontal therapy was standardized (every 6 months) and not tailored to individual risk profiles and home care compliance and ability of patients. Nevertheless, in many studies, it has been demonstrated that different supportive care intervals maintained the stability of clinical improvements following surgical treatments of peri-implantitis (Roos-Jansåker et al. 2014; Schwarz et al. 2018; Roccuzzo et al. 2020; Stiesch et al. 2023). The last limitation is in common with the other studies

and involves the radiographic method that would not distinguish between bone regeneration and simple defect filling due to the differences in reabsorbability and opacity of different graft materials (Tomasi et al. 2019; Li et al. 2023; Aghazadeh et al. 2022; Almohandes et al. 2022). However, although newly formed bone can be demonstrated only histologically, the long-term PD reduction and MPBL stability seemed to support the efficacy of MDBA in the reconstructive treatment of peri-implantitis lesions.

Nevertheless, some points of strength are also present (a) the long-term follow-up, (b) surgical procedures carried out by the same experienced surgeon, (c) the same implant design and surface characteristics (TiUnite—Nobel Biocare, Göteborg, Sweden). Lastly, it should also be highlighted that the present investigation, reporting a clear surgical design, a proven method of implant surface decontamination, appropriate means of infection control, and a composite outcome of disease resolution, was conducted according to the recommendations about clinical research on peri-implantitis of Working Group 4 of the VIII European Workshop on Periodontology (Sanz and Chapple 2012).

5 | Conclusions

Within the limits of the present study, a reconstructive surgical approach with MDBA and resorbable membrane may be a medium to long-term effective therapeutic option for treating intrabony peri-implantitis defects in patients enrolled in regular supportive therapy.

Author Contributions

Gerardo La Monaca: formal analysis, data curation, investigation, writing – original draft, methodology. **Nicola Pranno:** investigation, methodology, formal analysis, data curation, writing – original draft. **Susanna Annibali:** conceptualization, writing – review and editing, supervision. **Antonella Polimeni:** conceptualization, writing – review and editing, supervision. **Maria Paola Cristalli:** investigation, writing – original draft, methodology, formal analysis, data curation, writing – review and editing.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Research data are not shared.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.