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REVIEW ARTICLE

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Do soft tissue augmentation techniques provide stable and favorable peri-implant conditions in the medium and long term? A systematic review

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Abstract

Objectives: To review the available literature on the medium- and long-term effects of soft tissue augmentation (STA) at implant sites and to explore the effects of the different approaches on clinical-, patient-reported, and health-related parameters.

Materials and Methods: A comprehensive electronic and manual search was performed to identify prospective clinical studies that assessed the medium- and long-term (≥36 months) outcomes following STA, including number of sites maintaining peri-implant health and number of sites developing peri-implant disease, incidence of complications, stability of the clinical, volumetric, and radiographic parameters, and patient-reported outcome measures (PROMs).

Results: Fifteen studies were included in the qualitative analysis. STA was performed with either a bilaminar- or an apically positioned flap (APF) approach, in combination with autogenous grafts (free gingival graft [FGG] and connective tissue graft [CTG]) or substitutes (acellular dermal matrix [ADM] and xenogeneic cross-linked collagen matrix [CCM]). An overall high survival rate was observed. Most of the augmented implant sites maintained peri-implant health in the medium and long term, with the incidence of peri-implant mucositis and peri-implantitis ranging from 0% to 50% and from 0% to 7.14%, respectively. The position of the soft tissue margin following APF + FGG and bilaminar approaches involving CTG or CCM was found to be stable over time. No substantial changes were reported for plaque score/index, bleeding on probing/bleeding index, and probing depth between early time points and following visits. CTG-based STA procedures resulted in a stable or increased dimension of keratinized mucosa width (KMW) and mucosal thickness (MT)/volumetric outcomes over time, when compared with early follow-ups. Most of the included studies described stable marginal bone levels at the grafted implant sites over time. No substantial changes for patient-reported outcomes and professionally assessed esthetic results were reported at different time points.

Conclusions: Implants that received STA showed overall high survival rate and relatively low incidence of peri-implantitis in the medium and long term. Augmented sites seem to maintain the level of soft tissue margin and marginal bone over time, while non-augmented implants may exhibit apical shift of the soft tissue margin. The overall favorable early outcomes obtained with STA are maintained in the medium and long term, with an increase in KMW and MT that may be expected over time at CTG-augmented sites.

KEYWORDS
connective tissue graft, dental implants, evidence-based dentistry, soft tissue augmentation, systematic review

1 | INTRODUCTION

Soft tissue augmentation (STA) is routinely performed at implants sites. Common indications for this procedure include treatment of implant esthetic complications, mucosal thickness augmentation, keratinized mucosa augmentation, and papilla reconstruction, among others (Avila-Ortiz et al., 2020; Zucchelli et al., 2020).

Studies investigating patient-reported outcome measures (PROMs) demonstrated that keratinized mucosa width (KMW) plays a key role on patient's comfort during brushing (Perussolo et al., 2018; Roccuzzo et al., 2016; Souza et al., 2016; Stefanini et al., 2021). In a 4-year longitudinal study, Perussolo et al. (2018) demonstrated that implants surrounded by an adequate KMW were associated with significantly less patient-reported discomfort during brushing and less marginal bone loss compared to implant sites characterized by <2 mm of KMW. In line with these findings, other authors advocated that an adequate band of keratinized and attached mucosa can have a protective effect on peri-implant health (Gharpure et al., 2021; Lin et al., 2013; Monje & Blasi, 2019; Sanz et al., 2022). Similarly, the role of mucosal thickness (MT) on implant-related outcomes has been extensively investigated (Gharpure et al., 2021; Jung et al., 2022; Puzio et al., 2020; Wang et al., 2021). It has been shown that MT can affect the color match of the peri-implant soft tissue with the adjacent natural gingiva and that it can also play a role on the stability of the marginal bone levels (Bhat et al., 2015; Garaicoa-Pazmino et al., 2021; Jung et al., 2008; Martinez-Rus et al., 2017; Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Thoma et al., 2018). In addition, in line with recent evidence from long-term studies on root coverage procedures in natural dentition (Barootchi et al., 2022; Tavelli et al., 2019), it has been advocated that an augmented MT can contribute to the stability of the peri-implant soft tissue margin in the long term (Wang et al., 2021; Zucchelli et al., 2020).

Soft tissue augmentation can be performed with autogenous grafts or substitutes. An apically positioned flap (APF) in combination with a FGG is considered the technique of choice for posterior sites lacking keratinized and attached mucosa (Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Zucchelli et al., 2020). MT augmentation, and overall STA at implant sites in the esthetic zone, is usually performed utilizing a bilaminar approach, with the flap that is coronally advanced to completely cover the graft, aiming for a healing by primary intention (Cosyn et al., 2016; Hosseini et al., 2020; Zucchelli, Felice, et al., 2018). Autogenous connective tissue graft (CTG), acellular dermal matrix (ADM), and xenogeneic collagen matrix (CCM) have been found effective in increasing MT at implant sites (Hutton et al., 2018; Schmitt et al., 2021; Thoma et al., 2016). When compared to CTG, soft tissue graft substitutes allow to avoid a second surgical site and to reduce the overall morbidity of the procedure (Stefanini et al., 2021; Tavelli, Barootchi, Stefanini, et al., 2022).

Nevertheless, comparisons among different STA procedures and graft materials have been mainly described in the short term, and their outcomes in the medium- and long-term periods need further investigation.

Therefore, the aim of this article was to conduct a systematic appraisal of the existing literature reporting the medium- and long-term results of peri-implant STA, exploring the effects of the different approaches on clinical-, patient-reported, and health-related parameters, together with the stability of these outcomes over time.

2 | MATERIALS AND METHODS

2.1 | Protocol registration and reporting format

The protocol for this review was designed according to the Cochrane guidelines (Higgins et al., 2021) and reported with the Preferred Reporting Items for Systematic reviews and Meta-Analysis Extension (PRISMA) (Page et al., 2021). The study protocol was registered in the PROSPERO database, hosted by the National Institute for Health Research, University of York, Center for Reviews and Dissemination.

2.2 | Objective

The goal of this review was to address the following focused question in regard to soft tissue augmentation at implant sites: "Which soft tissue augmentation techniques provide the most predictable and favorable clinical and health-related conditions in the medium-long term?"

2.3 | PICOT question

The following Population, Intervention, Comparison, Outcome, and Time (PICOT) framework (Stillwell et al., 2010) was used to guide the inclusion and exclusion of studies for the abovementioned focused question. In adult patients with one or more healthy dental implant(s), which soft tissue augmentation technique provides a better peri-implant health condition and stable outcomes over time as reported in RCTs or cohort studies (S) with at least a 36 months follow-up?

- Population (P): Adult patients (≥18 years old) who underwent soft tissue augmentation on at least one healthy dental implant.
- Intervention (I): Surgical treatment for soft tissue augmentation involving pedicle flaps or tunnel techniques in combination with autogenous grafts (free gingival graft [FGG] or connective tissue graft [CTG]) or substitutes (collagen matrices [CMs] or acellular dermal matrices [ADMs]) at healthy dental implants.
- Comparison (C): All possible comparisons among the eligible studies in terms of flap approaches and grafting materials, including non-treated sites (if available as a comparative arm) and non-grafted sites (such as the coronal advancement or apical positioning of flap alone).
- Outcome (O): The number of cases maintaining a condition of peri-implant health (Berglundh et al., 2018) and the number of cases developing biological complications ("as defined by the authors of the study" or as determined by the presence of bleeding on probing, an increase in probing depth, an increase in recession of the peri-implant soft tissue margin, and an increase in radiographic marginal bone loss) were set as the primary outcome. Changes in the position of the peri-implant soft tissue margin (defined as peri-implant soft tissue dehiscence [PSTD] depth when compared to the cemento-enamel junction [CEJ] of the homologous contralateral tooth, or midfacial recessions [Midf REC] when compared to the level of the soft tissue margin at crown delivery), changes in pocket depth, plaque index/score, bleeding on probing/bleeding index, changes in marginal bone levels (MBLs) assessed radiographically, professional esthetic assessment, and patient-reported outcome measures (PROMs) were also investigated.
- Time (T): Studies reporting outcomes in the medium (≥36 months) and long (≥60 months) term.

2.4 | Eligible studies

To specifically address the focused question, prospective interventional human studies were included in this systematic review's qualitative and quantitative assessment if they met the following criteria in at least one study arm: (i) soft tissue augmentation performed at healthy implant sites using FGG, CTG, or soft tissue graft substitutes; (ii) Evaluation and reporting of clinical outcomes of interest over a minimum of 36 months; (iii) Minimum of 10 participants at the first follow-up ≥36 months; and (iv) Eligible therapies included the use of apically positioned flap-based approach or bilaminar techniques.

Reasons for article exclusion included: (i) Retrospective studies, case reports, or animal studies; (ii) Inclusion of implants with a diagnosis of peri-implant disease (Berglundh et al., 2018); (iii) Soft tissue augmentation at edentulous areas or natural teeth; (iv) Simultaneous hard and soft tissue augmentation; and (v) Studies recruiting smokers only.

2.5 | Information sources and search strategy

To identify eligible articles, detailed search strategies were modelled for the following electronic databases: MEDLINE (via PubMed), EMBASE via OVID; the Cochrane Central Register of Controlled Trials; and Latin American & Caribbean Health Sciences Literature (LILACS), Web of Science, and Scopus. The grey literature, nonprofit reports, government research, or other materials were also electronically explored in ClinicalTrial.gov and OpenGrey. The search strategy was conducted to identify articles published up to September 1, 2022, and it was primarily designed for the MEDLINE database with a string of medical subject headings and free text terms, and then modified appropriately for other databases. No restrictions were set for date of publication, journal, or language. The search results were downloaded to a bibliographic database to facilitate duplicate removal and cross-reference checks. Details regarding the search strategy and the development of the search key terms for the databases, are displayed in the Appendix S1.

The reference lists of the retrieved studies for full-text screening and previous reviews in periodontal regeneration were screened. A manual search was also performed in the *Clinical Oral Implant Research*, *Journal of Periodontology*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *International Journal of Periodontics and Restorative Dentistry*, and *Clinical Implant Dentistry and Related Research*. Previous systematic reviews assessing medium and long-term outcomes of peri-implant soft tissue augmentations were also examined (Cairo et al., 2019; Fickl et al., 2021; Poskevicius et al., 2017; Rotundo et al., 2015; Sicilia et al., 2015; Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Thoma et al., 2018, 2021).

2.6 | Article selection process

Two independent reviewers (L.T. and S.B.) screened the titles and abstracts (if available) of the entries identified in the literature search in duplicate and independently. Next, the full-text version of all studies that potentially met the eligibility criteria or for which there was insufficient information in the title and abstract to make a decision were obtained. Any article considered potentially relevant by at least one of the reviewers was included in the next screening phase. Subsequently, the full-text publications were also evaluated in duplicate and independently by the same review examiners. Disagreements between the review authors were resolved by open discussion. If no consensus

could be reached, a third author (L.M.) was consulted. All articles that did not meet the eligibility criteria were excluded, and the reasons for exclusion were noted. Inter-examiner agreement following full-text assessment was calculated via kappa statistics. Any missing information that could contribute to this systematic review was requested to the corresponding author(s) via email communication. In the case of multiple publications reporting on the same study or investigating the same cohort at different follow-up intervals (or secondary analysis of the same data), it was decided to pool together all relevant details as a single report with the most comprehensive data for inclusion in the qualitative and quantitative analyses.

2.7 | Data extraction and outcome measures

Two examiners (L.T. and S.B.) independently retrieved all relevant information from the included articles using a data extraction sheet specifically designed for this review.

Clinical outcomes of interest included probing depth (PD), PSTD depth, Midf REC, keratinized mucosa width (KMW), attached mucosa (AM), mucosal thickness (MT), bleeding on probing (BOP), plaque indices, inflammatory indices, presence/absence of bleeding on probing (BOP), and presence/absence of suppuration. Volumetric changes were considered if assessed through optical scanning (Tavelli, Barootchi, Majzoub, Siqueira, et al., 2021). Radiographic imaging outcomes included two-dimensional (using periapical radiographs) or three-dimensional (using cone-beam computed tomography [CBCT] or computed tomography [CT]) X-rays. Esthetic outcomes were evaluated through professional esthetic indices or a visual analog scale (VAS). PROMs involved quality-of-life assessments made by patients regarding different aspects of implant therapy, such as esthetic assessment, satisfaction, willingness for retreatment, etc., using standardized methods of assessment. Implant survival rate and incidence of peri-implant disease (mucositis and peri-implantitis) were assessed at the different time points.

Aside from the outcomes of interest, the following study characteristics were retrieved: (i) Year of publication, study design, geographic location, setting (university vs. private practice), and source of funding; (ii) Population characteristics, including age and gender of participants, number of participants and treated sites (baseline/follow-up), and inclusion of smokers; (iii) Timing of the STA procedure and type of surgical intervention (apically positioned flap [APF]-based procedure or bilaminar approaches), (iv) Soft tissue graft utilized; and (v) Follow-up time points. All values were extracted from the selected publications as mean ± standard deviations, when possible.

2.8 | Methodological quality and risk of bias assessment

The assessment of methodological quality and risk of bias (RoB) was independently evaluated by two authors (L.T. and S.B.). The recommendation of the Cochrane collaboration group was followed for assessing the RoB of randomized controlled clinical trials (RCTs) (RoB 2 tool) (Sterne et al., 2019). Risk of bias assessment for non-randomized case–control studies was performed using the ROBINS-I tool (Sterne et al., 2016), while the Joanna Briggs Institute Critical Appraisal tool (Moola et al., 2017) was utilized for quality assessment of case series. Any disagreement was discussed between the same authors. Another author (L.M.) was consulted in case no agreement was reached. No study was excluded based on the risk of bias within a study.

2.9 | Data analysis

When possible, weighted means (based on the treated sample size) with standard deviation were calculated for each outcome of interest based on the type of STA (bilaminar, APF-based approach, or non-augmented sites) and the type of graft utilized (FGG, CTG, or substitutes).

2.10 | Evidence quality rating and strength of recommendation

Evidence quality rating and strength of recommendation of STA procedures at implant sites were assessed in terms of levels of certainty in the body of evidence, net benefit rating (benefit-harm estimation), and strength of recommendation, as previously described (Avila-Ortiz et al., 2022; Tavelli, Chen, Barootchi, & Kim, 2022). Additional information are depicted in the Appendix S1.

3 | RESULTS

3.1 | Search results and study selection

The literature search flow diagram is shown in Figure 1. Following the removal of duplicates, 1329 records were identified based on titles and abstracts. A full-text assessment was performed for 47 articles. Based on our predetermined inclusion criteria, 15 studies were included in this review (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). The two included articles from Thoma et al. (2020, 2022), as well as the articles from Cosyn et al. (2016) and Seyssens et al. (2020), reported data on the same cohort at different time points. The reason for the exclusion of the other 32 articles is reported in Table S4 of the Appendix S1. The inter-examiner reliability in the screening and inclusion process based on title and abstract, as assessed with Cohen's κ, corresponded to 0.89, while the inter-examiner reliability for full-text evaluation was 0.96.

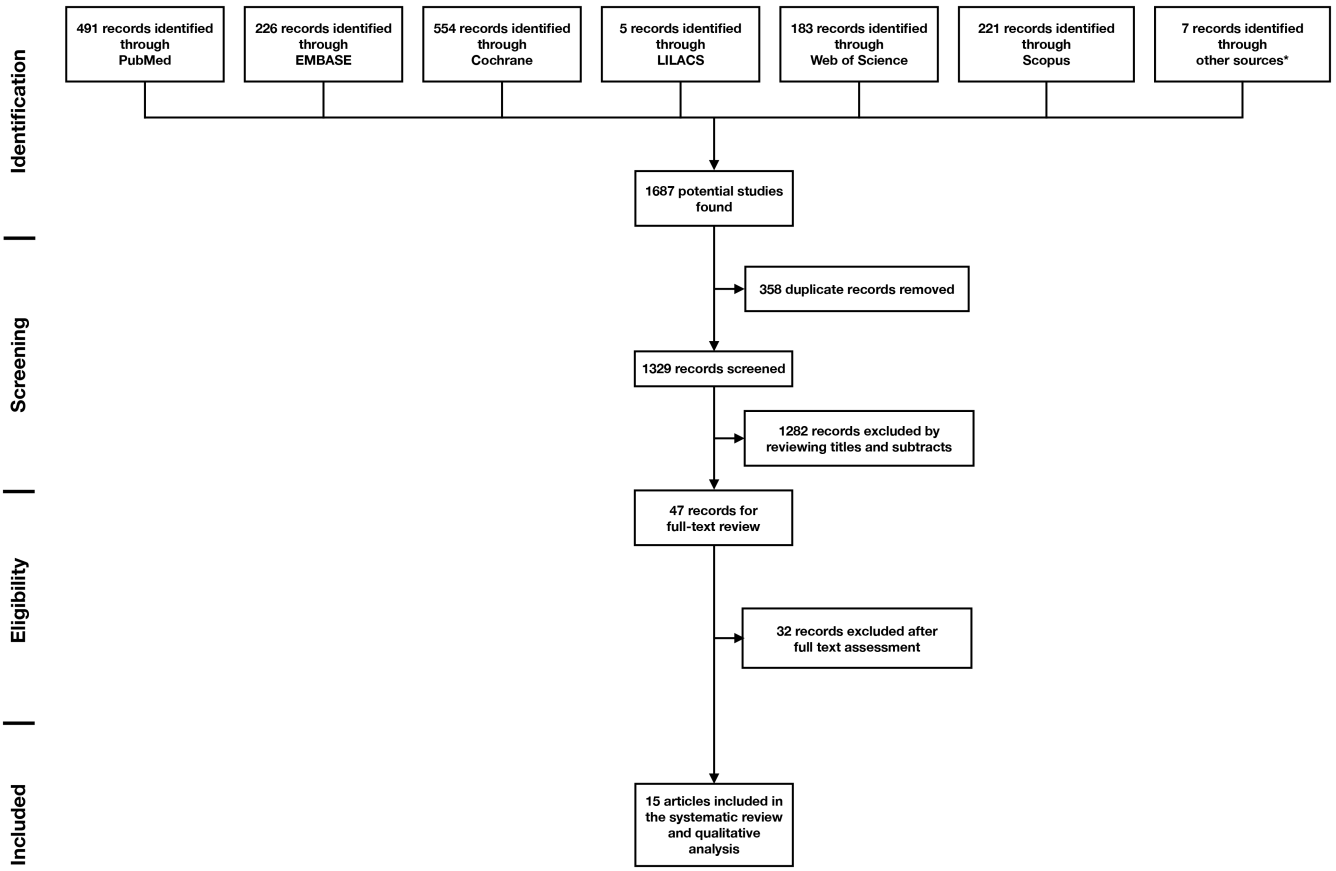

FIGURE 1 PRISMA flowchart.

3.2 | Characteristics of the included studies

Four of the included studies/publications (representing three cohorts) are RCTs (Bianchi & Sanfilippo, 2004; Oh et al., 2020; Thoma et al., 2020, 2022), five are non-randomized trials (Cosyn et al., 2016; Fenner et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2016; Seyssens et al., 2020), and the remaining six are case series (Eeckhout et al., 2020; Eghbali et al., 2018; Hanser & Khoury, 2016; Roccuzzo et al., 2019; Stefanini et al., 2016; Zucchelli, Felice, et al., 2018). All the studies were conducted in a single center. Five of them were performed in private practice (Cosyn et al., 2016; Hanser & Khoury, 2016; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020), while the other studies took place in a university setting (Bianchi & Sanfilippo, 2004; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hosseini et al., 2020; Oh et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018).

In terms of indications for treatment, STA procedures were performed as a part of immediate implant therapy (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eghbali et al., 2018; Seyssens et al., 2020), for MT augmentation (Eeckhout et al., 2020; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022), for KMW augmentation (Oh et al., 2020; Roccuzzo et al., 2016), and for addressing implant esthetic complications (PSTDs) (Cosyn et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Zucchelli, Felice, et al., 2018). STA was executed at implant placement in four studies (Bianchi & Sanfilippo, 2004; Eeckhout et al., 2020; Hanser & Khoury, 2016; Stefanini et al., 2016), at second stage in one article (Hosseini et al., 2020), and delayed in 10 studies (Cosyn et al., 2016; Eghbali et al., 2018; Fenner et al., 2016; Oh et al., 2020; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). Two studies performed soft tissue augmentation using APF + FGG (Oh et al., 2020; Roccuzzo et al., 2016), while in the other studies, STA was carried out using a bilaminar approach, involving a CTG, a porcine-derived acellular dermal matrix (PADM) or xenogeneic cross-linked collagen matrix (CCM) (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). Three studies (two cohorts) assessed the outcomes of STA using graft substitutes (Eeckhout et al., 2020; Thoma et al., 2020, 2022). In terms of follow-up, three studies had a maximum period of observation of 3 years (Eeckhout et al., 2020; Stefanini et al., 2016; Thoma et al., 2020), one study reported data up to 4 years (Oh et al., 2020), seven articles described outcomes up to 5 years following STA (Cosyn et al., 2016; Eghbali et al., 2018; Hanser & Khoury, 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Thoma et al., 2022; Zucchelli, Felice, et al., 2018), Fenner et al. (2016) followed the study participants for 5–9 years (mean 7.2 years), Bianchi and Sanfilippo (2004) reported outcomes up to the 9-year follow-up and two studies provided data at 10 years (Roccuzzo et al., 2016; Seyssens et al., 2020). Further details are reported in Tables 1 and 2.

TABLE 1 Characteristics of the included studies at baseline and their interventions.

Publication	Study design	No. of centers, country, setting, funding	Clinical condition, treatment	Timing of intervention, flap approach	Age (years), male/female (*N*), inclusion of smokers	Patients at BL (*N*), implants at BL (*N*), implant type	Follow-up (months), patients at the last visit (*N*)
Bianchi and Sanfilippo (2004)	RCT	Single center, Italy, University, NA	Immediate implant therapy, CTG (bilaminar)	At implant placement	45.4, 58/58, yes	96, 96, Straumann Tissue Level (Straumann)	36–108 (19)
			No soft tissue augmentation	N/A		20, 20, Straumann Tissue Level (Straumann)	
Cosyn et al. (2016)	Non-RCT	Single center, Belgium, Private Practice, self-supported	Immediate implant therapy (esthetic complications), CTG (bilaminar)	Delayed	50, 12/10, no	7, 7, NobelActive (Nobel)	60 (17)
			Immediate implant therapy, no soft tissue augmentation	N/A		15, 15, NobelActive (Nobel)	
Eeckhout et al. (2020)	Case series	Single center, Belgium, University, self-supported	MT augmentation, Porcine-derived ADM (bilaminar)	At implant placement	51.4, 10/5, no	15, 15, NobelActive (Nobel)	36 (14)
Eghbali et al. (2018)	Case series	Single center, Belgium, University, self-supported	Immediate implant therapy, CTG (bilaminar)	Delayed	38, 19/18, no	37, 37, NobelActive (Nobel)	60 (32)
Fenner et al. (2016)	Non-RCT	Single center, Switzerland, University, self-supported	MT augmentation, CTG (bilaminar)	Delayed	48, N/A, yes	14, 14, Straumann Tissue Level (Straumann)	86.4[a] (28)
			No soft tissue augmentation	N/A		22, 22, Straumann Tissue Level (Straumann)	
Hanser and Khoury (2016)	Non-RCT	Single center, Germany, Private Practice, self-supported	MT augmentation, CTG (bilaminar)	At implant placement	37.8, 19/27, no	46, 52, Ankylos and XiVE (Dentsply Sirona)	60 (N/A)
Hosseini et al. (2020)	Non-RCT	Single center, Denmark, University, self-supported	MT augmentation and/or PSTD treatment, CTG (bilaminar)	At second stage	19, 8/11, yes	10, 10, Astra (Dentsply Sirona)	36, 60 (17)
			No soft tissue augmentation			15, 15, Astra (Dentsply Sirona)	
Oh et al. (2020)	RCT	Single center, USA, University, self-supported	KMW augmentation, FGG (APF)	Delayed	65.3, 2/9, no	15, 23, N/A	48 (11)
			KMW augmentation, FGG (APF) (delayed)[b]	Delayed	65, 2/3, no	5, 8, N/A	27[a] (5)
			No soft tissue augmentation	N/A	66, 3/4, no	15, 22, N/A	48 (7)
Roccuzzo et al. (2016)	Non-RCT	Single center, Italy, Private practice, self-supported	KMW augmentation, FGG (APF)	Delayed	52.4, 52/76, yes	N/A, 11, Straumann Tissue Level (Straumann)	120 (98)
			No soft tissue augmentation (implants with KM)	N/A		N/A, 63, Straumann Tissue Level (Straumann)	
			No soft tissue augmentation (implants without KM)	N/A		N/A, 24, Straumann Tissue Level (Straumann)	

(Continues)

TABLE 1 (Continued)

Publication	Study design	No. of centers, country, setting, funding	Clinical condition, treatment	Timing of intervention, flap approach	Age (years), male/female (*N*), inclusion of smokers	Patients at BL (*N*), implants at BL (*N*), implant type	Follow-up (months), patients at the last visit (*N*)
Roccuzzo et al. (2019)	Case series	Single center, Italy, Private Practice, self-supported	PSTD treatment, CTG (bilaminar)	Delayed	53.1, 3/13, yes	16, 16, Straumann Tissue Level (Straumann)	60 (13)
Seyssens et al. (2020)	Non-RCT	Single center, Belgium, Private Practice, self-supported	Immediate implant therapy (esthetic complications), CTG (bilaminar)	Delayed	50, 12/10, no	7, 7, NobelActive (Nobel)	120 (18)
			Immediate implant therapy, No soft tissue augmentation	N/A		15, 15, NobelActive (Nobel)	
Stefanini et al. (2016)	Case series	Single center, Italy, University, self-supported	MT augmentation, CTG (bilaminar)	At implant placement	NA, 8/12, no	20, 20, Straumann Tissue Level (Straumann)	36 (20)
Thoma et al. (2020)	RCT	Single center, Switzerland, University, sponsored	MT augmentation, CTG (bilaminar)	Delayed	43.4, N/A, yes	10, 10, N/A	36 (17)
			MT augmentation, CCM (bilaminar)	Delayed	44.1, N/A, yes	10, 10, N/A	
Thoma et al. (2022)	RCT	Single center, Switzerland, University, sponsored	MT augmentation, CTG (bilaminar)	Delayed	N/A, N/A, yes	10, 10, N/A	60 (15)
			MT augmentation, CCM (bilaminar)	Delayed	N/A, N/A, yes	10, 10, N/A	
Zucchelli, Felice, et al. (2018)	Case series	Single center, Italy, University, self-supported	PSTD treatment, CTG (bilaminar)	Delayed	N/A, N/A, yes	20, 20, N/A	60 (19)

Abbreviations: ADM, acellular dermal matrix (Mucoderm, Botiss); APF, apically positioned flap; BL, baseline; CCM, cross-linked collagen matrix (Geistlich Fibrogide, Geistlich Pharma); CTG, connective tissue graft; FGG, free gingival graft; KM/AM, keratinized and attached mucosa; KMW, keratinized mucosa width; MT, mucosal thickness; N/A, not available/not assessed; non-RCT, prospective non-randomized controlled clinical study; PSTD, peri-implant soft tissue dehiscence; RCT, Randomized controlled trial.

[a]Median observation period.

[b]Treatment arm not considered in the qualitative analysis (follow-up <36 months).

TABLE 2 Outcomes of interest of the included studies.

Publication	Clinical outcomes	Level of the soft tissue margin	Volumetric outcomes	Radiographic outcomes	Esthetic outcomes	PROMs	Complications
Bianchi and Sanfilippo (2004)	BOP, KMW, PAL, PD, and plaque score	EL alignment	N/A	DIB, bone peaks stability	Based on KMW and EL	Patient satisfaction with the esthetic outcomes	Survival rate
Cosyn et al. (2016)	BOP, PD, and plaque score	Midf REC	N/A	MBL	Mesial and distal papillary recession, PES	N/A	Survival rate, incidence of peri-implant diseases, biological, and prosthetic complications
Eeckhout et al. (2020)	BOP, PD, and plaque score	N/A	ΔD from 3D analysis	MBL	N/A	N/A	Survival rate, biological, and prosthetic complications
Eghbali et al. (2018)	BOP, PD, and plaque score	Midf REC	UMT	MBL	Mesial and distal papillary recession, PES	N/A	Survival rate, biological, and prosthetic complications
Fenner et al. (2016)	BOP, KMW, PD, and plaque index	Midf REC	N/A	MBL	Papilla index	Satisfaction (VAS)	Survival rate, biological, and prosthetic complications
Hanser and Khoury (2016)	PD	N/A	cMT	DIB	N/A	N/A	Survival rate
Hosseini et al. (2020)	Bleeding index, KMW, PD, and plaque score	Midf REC	cMT. LD changes at 1, 3, and 5 mm ΔD from 3D analysis	MBL	CIS, discoloration scores and papilla index	N/A	Survival rate, incidence of peri-implant diseases, biological, and prosthetic complications
Oh et al. (2020)	KMW	Midf REC	N/A	MBL	N/A	N/A	N/A
Roccuzzo et al. (2016)	BOP, PD, plaque score, and presence of plaque	Midf REC	N/A	MBL	N/A	Discomfort during brushing (yes/no), soreness upon hygiene maintenance (yes/no)	Survival rate, biological, and prosthetic complications
Roccuzzo et al. (2019)	BOP, PD, and presence of plaque	Midf REC	N/A	N/A	VAS	Satisfaction (VAS)	Survival rate, biological, and prosthetic complications
Seyssens et al. (2020)	BOP, papillary recession, PD, and plaque score	Midf REC	N/A	MBL BBT (from CBCT)	PES	N/A	Survival rate, incidence of peri-implant diseases, biological, and prosthetic complications
Stefanini et al. (2016)	KMW, PD	Vertical soft tissue level (Midf REC)	cMT	MBL	N/A	N/A	Incidence of peri-implant diseases

(Continues)

TABLE 2 (Continued)

Publication	Clinical outcomes	Level of the soft tissue margin	Volumetric outcomes	Radiographic outcomes	Esthetic outcomes	PROMs	Complications
Thoma et al. (2020)	BOP, KMW, PD, and plaque index	N/A	cMT and ΔD from 3D analysis	MBL	Papilla index and PES	OHIP-G14	N/A
Thoma et al. (2022)	BOP, KMW, PD, and plaque index	Midf REC	cMT and ΔD from 3D analysis	MBL	PES	OHIP-G14	Incidence of peri-implant diseases
Zucchelli, Felice, et al. (2018)	BOP, CAL, KMW, PD, and plaque score	PSTD depth, mean PSTD coverage, and complete PSTD coverage	cMT	N/A	PES/WES	Patient satisfaction with the esthetic outcomes (VAS)	Incidence of peri-implant diseases

Abbreviations: CAL, clinical attachment level; cMT, clinically assessed mucosal thickness using the transmucosal piercing method; DIB, distance from the implant shoulder to the first implant bone contact; EL, emergence line of the prosthetic crown from the soft tissue in relation to the EL of the mesial and distal adjacent teeth; KMW, keratinized mucosa width; LD changes, linear dimensional changes in the facial contour assessed with optical scanners; MBL, marginal bone loss; Midf REC, midfacial recession, defined as the apical shift of the peri-implant soft tissue margin from the prosthetic crown margin; N/A, not available/not assessed; OHIP-G14, oral health impact profile-G14; PAL, probing attachment level; PES, pink esthetic score; PSTD depth, depth of the peri-implant soft tissue dehiscence, measured as the distance between the peri-implant soft tissue margin and the cemento-enamel junction of the homologous contralateral tooth; UMT, mucosal thickness evaluated with an ultrasonic device; ΔD, mean distance between the surface/mean thickness of the reconstructed volume following superimposition of the digital models obtained with optical scanners.

3.3 | Risk of bias assessment

Among the RCTs, three studies were considered with a moderate risk of bias (Bianchi & Sanfilippo, 2004; Thoma et al., 2020, 2022) and one with a low risk of bias (Oh et al., 2020). Four non-RCTs were considered having a low risk of bias (Cosyn et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2016; Seyssens et al., 2020), with one case–control study that was rated with moderate risk of bias (Fenner et al., 2016). Four case series were judged with a low risk of bias (Eghbali et al., 2018; Roccuzzo et al., 2019; Stefanini et al., 2016; Zucchelli, Felice, et al., 2018), with the remaining two studies that were considered having moderate risk of bias (Eeckhout et al., 2020; Hanser & Khoury, 2016) (Tables S5–S7 of the Appendix S1).

3.4 | Qualitative analysis

The low number of RCTs and their heterogenous approaches and outcome measures did not allow to perform quantitative analyses.

Qualitative analyses on peri-implant health and biological complications, stability of the soft tissue margin, plaque score, BOP, PD, KMW, volumetric outcomes, MBLs, esthetic outcomes, and PROMs are depicted in detail in the Appendix S1.

3.4.1 | Implant survival rate and peri-implant health/disease

Overall, a high survival rate (ranging from 90.9% to 100%) was reported at augmented implant sites (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2022; Zucchelli, Felice, et al., 2018) (Table 3). The incidence of peri-implant mucositis ranged from 0% to 50%, while the incidence of peri-implantitis was from 0% to 7.14% (Eghbali et al., 2018; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Thoma et al., 2022; Zucchelli, Felice, et al., 2018). Statistical comparison among different STA procedures, as well as augmented versus non-augmented sites, was not feasible.

3.4.2 | Stability of the soft tissue margin

Twelve studies assessed the changes within the level of the soft tissue margin (Cosyn et al., 2016; Eghbali et al., 2018; Fenner et al., 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). The weighted mean the apical shift of the soft tissue margin following bilaminar augmentation with CTG was −0.06 mm on a mean observational period of 4.8 years (Cosyn et al., 2016; Eghbali et al., 2018; Fenner et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Stefanini

TABLE 3 Qualitative analysis on implant survival rate and stability of the soft tissue margin and marginal bone levels.

Outcome of interest	Group	Weighted mean	*N* cohort/sites
Implant survival rate (%)	BL+CTG	99.4	11/274
	NAS	100	4/75
Soft tissue margin (mm)	BL+CTG	−0.06	10/135
	BL+CCM	0.58	1/15
	APF+FGG	−0.54	1/18
	NAS	0.96	5/87
Marginal bone levels (mm)	BL+CTG	0.63	5/71
	BL+CTG[a]	0.18	4/57
	BL+CCM	0.71	1/15
	APF+FGG	0.28	2/22
	NAS	0.88	4/74
	NAS[a]	0.33	3/52

Note: Note that a negative value for soft tissue margin indicates an average trend toward coronal migration of the soft tissue margin.

Abbreviations: APF, apically positioned flap; BL, bilaminar technique; CCM, cross-linked collagen matrix; CTG, connective tissue graft; FGG, free gingival graft; NAS, non-augmented sites.

[a]Non considering the outlier study (Fenner et al., 2016).

et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). Based on two studies from the same cohort (Thoma et al., 2020, 2022), the weighted mean of the apical shift of the soft tissue margin following bilaminar augmentation with XCM was 0.58 mm over 3–5 years. Non-augmented sites exhibited a weighted mean apical displacement of the soft tissue margin of 0.96 mm over a mean period of observation of 6.2 years (Cosyn et al., 2016; Fenner et al., 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016). The only study reporting this outcome for APF-based STA procedures, observed a mean coronal migration of the soft tissue margin of 0.54 mm within 4 years at sites augmented with APF+FGG (Oh et al., 2020) (Table 3).

3.4.3 | Stability of MBLs

Marginal bone level changes after STA were assessed and reported in 13 studies (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022). Except for one study reporting mean marginal bone loss of 2.2–2.5 mm after a follow-up of ≥5 years (Fenner et al., 2016), the other studies observed a marginal bone loss within 0.6 mm at augmented implant sites. The weighted mean marginal bone loss following STA with CTG-based bilaminar techniques was 0.63 mm over a mean period of 5 years, that dropped down to 0.18 mm over a mean period of 4.5 years if the abovementioned outlier study is not considered. The weighted mean marginal bone loss at non-augmented sites was 0.88 mm (mean follow-up of 6.6 years) considering the outlier study, and 0.33 mm (mean follow-up of 6.3 years) when excluding the study from Fenner et al. (2016). Sites augmented with APF+FGG showed a weighted mean marginal bone loss of 0.28 mm on a mean period of 7 years (Oh et al., 2020; Roccuzzo et al., 2016) (Table 3).

Clinical, esthetics, and volumetric outcomes, as well as PROMs of the individual studies are described in detail in the Appendix S1.

3.5 | Evidence quality rating

No serious complications or adverse reactions were reported following STA at implant sites. Clinical benefits of these procedures may include enhanced esthetic outcomes, stability of the soft tissue margin, and mucosal thickness over time, stability of marginal bone levels and improved PROMs. Therefore, the net benefit rating supporting soft tissue augmentation at implant sites should be considered strong, as the clinical benefits overweight the potential harms.

Based on the predetermined criteria recommended for rating the level of certainty, it can be stated that the body of evidence (and level of certainty) supporting the treatment effects of bilaminar STA with CTG in the medium and long term is moderate. Other approaches, such as APF+FGG and bilaminar techniques with PADM or CCM, are characterized by a low level of certainty when assessing their medium/long-term effect estimates.

Based on the net benefit rating and level of certainty rating, the strength of recommendation for STA at implant sites with the goal of promoting favorable and stable outcomes in the medium and long term, was deemed in favor.

4 | DISCUSSION

Modern periodontology and implantology aim for minimally invasive therapies with long-term stable outcomes. There are no doubts that biomaterials, together with advancements of surgical techniques and instruments, have had a major impact on STA at implant sites. Nevertheless, while long-term data of different approaches and graft materials following periodontal regeneration and root coverage in natural dentition are currently available, little is known on the medium- and long-term effects of STA at implant sites.

4.1 | Main findings

Based on 15 prospective studies from 13 cohorts, we observed that most of the dental implants that received STA were able to maintain peri-implant health over time. While isolated cases with peri-implant disease have been described, readers should bear in mind that peri-implant mucositis and peri-implantitis can be triggered by several factors, including but not limited to, history of periodontal disease, lack of compliance with supportive therapy, inadequate

design of the implant-supported crown, implant malpositioning not facilitating oral hygiene procedures, etc. (Berglundh et al., 2018; Heitz-Mayfield & Salvi, 2018). Nevertheless, it seems that an adequate soft tissue phenotype can contribute to reduce peri-implant inflammation and plaque accumulation, together with brushing discomfort (Oh et al., 2017; Roccuzzo et al., 2016; Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Thoma et al., 2018). A recent network meta-analysis demonstrated that STA procedures were effective in promoting an improvement of the clinical and radiographic parameters related to peri-implant health in the short term (Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021). Due to the lack of RCTs reporting medium- and long-term outcomes of STA, a quantitative analysis could not be performed in the present review. Findings from the individual studies showed that the early clinical and esthetic outcomes of STA observed at 6/12 months are maintained over time. These findings are of interest, as concerns could be raised on the long-term outcomes (e.g., PD, peri-implant health, stability of the soft tissue margin, etc) of STA procedures at implants exhibiting buccal bone dehiscence. When treating peri-implant soft tissue dehiscences, which are often characterized by deficient/lack of buccal bone (Tavelli, Barootchi, Majzoub, et al., 2022), a split-thickness flap elevation to facilitate graft nutrition and adhesion to the implant surface has been advocated (Stefanini et al., 2020; Zucchelli et al., 2013; Zucchelli, Tavelli, et al., 2021).

The esthetic outcomes of dental implants are strongly affected by the position of the soft tissue margin (Furhauser et al., 2005; Zucchelli et al., 2019; Zucchelli, Barootchi, et al., 2021). Therefore, it is not surprising that this parameter was often reported as the primary outcomes in the included studies. Eleven studies assessed the changes within the position of the soft tissue margin compared to baseline (Midf REC). Although this outcome provides a valuable information of the changes within the soft tissue level at implant sites, the stability of Midf REC does not necessarily correlate with satisfying esthetic outcomes, since the goal of implant therapy and STA at implant sites in the esthetic region should be obtaining the peri-implant soft tissue margin at the same level of the CEJ of the homologous contralateral tooth (Zucchelli et al., 2019; Zucchelli, Barootchi, et al., 2021; Zucchelli, Sharma, & Mounssif, 2018). The weighted average of Midf REC at implant sites augmented with CTG was 0.006 on a mean observational period of approximately 5 years. When compared the stability of the soft tissue margin at CTG-augmented versus non-augmented implant sites over 5 years, Hosseini et al. (2020) reported better results for the grafted dental implants. The benefits of STA with CTG for maintaining the level of the soft tissue margin in the long term was further demonstrated by Seyssens et al. (2020) that showed that all the implant placed without STA developed a Midf REC of at least 1 mm over 10 years. The authors advocated that lack of STA at immediately placed implants should be considered among the putative risk factors for Midf REC in the long term (Seyssens et al., 2020). Interestingly, it appears that sites augmented with autogenous grafts may also exhibit creeping attachment, increased KM, and greater MT over time (Oh et al., 2020; Stefanini et al., 2016; Zucchelli, Felice, et al., 2018). Zucchelli, Felice, et al. (2018) observed that an improvement in the level of the soft tissue margin (PSTD depth) from 1 to 5 years at implant sites previously treated for esthetic complications. When it comes to KMW, STA procedures were found to maintain the early outcomes over time (Thoma et al., 2020, 2022), or even resulting in an increased KMW (Stefanini et al., 2016; Zucchelli, Felice, et al., 2018). It can be assumed that the type of harvesting technique and CTG composition, together with local characteristics of the augmented implants and adjacent sites, may affect the initial and long-term KMW change/gain (Tavelli, Barootchi, Majzoub, Chan, et al., 2021; Zucchelli et al., 2020). In line with this speculation, Rojo et al. (2018) demonstrated that STA with a fibrous CTG from the tuberosity resulted in significantly higher KMW than STA using a subepithelial CTG obtained from the deepest layers of the palate.

Findings from this review also support the stability of early MT/volumetric gain up to 3–5 years following STA with CTG or graft substitutes. Nevertheless, readers should bear in mind that these conclusions are more robust for CTG than for graft substitutes, that have been described in two cohorts only (Eeckhout et al., 2020; Thoma et al., 2020, 2022), and therefore, more evidence is needed for ADM and CCM. Two studies utilizing a CTG obtained from the most superficial layer of the palate—as a FGG and then de-epithelialized—showed a progressively increased in MT compared to early time points (Stefanini et al., 2016; Zucchelli, Felice, et al., 2018), that can be once again explain with the nature of this type of CTG, mainly composed by lamina propria with minimal amount of adipose and glandular tissue (Bertl et al., 2015; Zucchelli et al., 2020). Interestingly, when assessing dimensional changes with optical scanning, Hosseini et al. (2020) reported that while CTG-augmented implants progressively gained volume up to 5 years, non-augmented sites exhibited volume loss at 3 and 5 years. The use of 3D digital optical scanning for assessing outcomes of STA has rapidly become popular among clinicians and researchers, replacing traditional transmucosal piercing in several instances (Tavelli, Barootchi, Majzoub, Siqueira, et al., 2021). Optical scanning has the advantage of being noninvasive and better tolerated by patients compared to transmucosal piercing that requires local anesthesia. Nevertheless, the superimposition of digital impression obtained with optical scanning describe the overall changes occurred within the facial contour only, without discriminating between hard and soft tissue, and without being able to provide information at single time points. In this view, ultrasonography has been shown to be a promising and noninvasive tool for assessing soft tissue thickness and buccal bone dimensions at natural teeth and dental implants, and may become the method of choice for the assessment of these parameters in clinical research (Tavelli, Barootchi, Majzoub, et al., 2022).

In terms of radiographic outcomes, it has been previously advocated that STA can have beneficial effects on the stability of MBLs. Most of the studies included in this review showed that previously augmented implant sites have stable marginal bone levels over time, with a mean marginal bone loss within 0.6 mm—except for one study (Fenner et al., 2016). Few studies also reported marginal bone gain over time (Eeckhout et al., 2020; Oh et al., 2020). Oh et al. (2020)

demonstrated that implant sites augmented with APF + FGG obtained significantly higher MBL stability over 4 years compared to non-augmented sites. The advocated positive effects of STA on the stability of MBLs may be related to facilitate oral hygiene procedures and the reduction of patient discomfort, that can result in less plaque accumulation and inflammation (Perussolo et al., 2018; Sanz et al., 2022; Souza et al., 2016).

Among the limitations of this review, the relatively limited number of available studies, their design, and lack of information on implant location have to be mentioned. Readers should be aware that the results of the present reviews are qualitative only, and therefore, strong conclusions cannot be drawn at the present time. Several medium/long-term RCTs describing STA with APF/bilaminar approaches with autogenous grafts and substitutes are needed to perform robust statistical analyses (e.g., mixed-modeling approach to network meta-analysis) comparing different techniques and graft materials and their impact on the medium/long-term peri-implant health.

5 | CONCLUSIONS

Based on the current available evidence, and within the limitations of this study, it can be concluded that implants that received STA procedures exhibited overall high survival rate and relatively low incidence of peri-implantitis in the medium and long term. Implant sites following STA displayed stable soft tissue margin over time, while non-augmented implants tend to exhibit an apical shift of the soft tissue margin in the medium and long term. The overall favorable outcomes of STA observed at early time points are maintained in the medium and long term, with sites augmented with CTG that may also show a progressive increase in KMW and MT. More evidence from medium- and long-term RCTs is needed to compare different surgical approaches and graft materials.

AUTHOR CONTRIBUTIONS

M. Stefanini: Design of the study, interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. S. Barootchi: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. M. Sangiorgi: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. A. Pispero: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. M.G. Grusovin: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work L. Mancini: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. G. Zucchelli: Design of the study, critical review of the draft, and contribution to the writing of the article. Final approval of the version to be published and accountable to the accuracy or integrity of the work. L. Tavelli: Design of the study, study registration, literature search, acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the Appendix S1 and Tables S1–S3.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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