Increasing the width of the keratinized mucosa around implants with L-PRF: report of a case and systematic review.

Authors

Silvia D'Agostino[1,2 *]†, Marco Grieco[2]†, Giulia Valentini[2], Sorana Andreea Stoica[2], Marco Dolci[2]

[1]Department of Interdisciplinary Medicine, University A. Moro, Bari, Italy

[2]Department of Medical, Oral and Biotechnological Sciences, University G. d'Annunzio, Chieti, Italy

† These authors contributed equally to this work.

Corresponding author

Silvia D'Agostino

Correspondence: silviadagostino00@gmail.com

ABSTRACT

Peri-implant phenotypes is essential for long-term success because a thick biotype can lead to a better resistance against bacterial and mechanical damages. Plastic surgery of the peri-implant site is usually performed in order to gain a greater keratinized mucosa width. The purpose of this study was to evaluate the knowledge in literature about leucocytes platelet-rich fibrin (L-PRF) as an autologous solution to change peri-implant width. A case of L-PRF membranes around dental implants is also reported. The systematic review showed a lack of longitudinal long-term studies and a heterogeneity of protocol to produce L-PRF. At the best of our knowledge, L-PRF could represent a suitable soft tissue substitute to increase keratinized mucosa surrounding dental implants.

Keywords: L-PRF; keratinized mucosa; dental implants; per-implant phenotype.

INTRODUCTION

In the last two decades, the use of platelet concentrates has become very popular in dentistry, due to their regenerative properties. However, the various methods developed by different scientists and companies foresaw the obtaining of concentrates through the use of tubes containing anticoagulants. Only in 2001 with Choukroun et al. a second generation of platelet concentrates was born, the fibrin rich in leukocyte platelets (L-PRF), obtained by blood centrifugation using tubes without anticoagulants agents [1-2]. The first example of the use of blood-derived coagulating substances in the treatment of wounds and hemostasis was presented by Grey [3]. Subsequentially, Young and Medawar successfully achieved the union of animal peripheral nerves through the use of blood plasma [4]. Similar experiments were conducted by Tarlov, but with a significant percentage of failures [5]. In the early 1970s, Helene Matras tried to achieve a faster healing process by creating fibrin glue [6]. Since the various components of the two solutions were mixed, the fibrin glue revealed to be surrounded by the granulation tissue and finally to be completely reabsorbed. The benefits obtained over the years have expanded the use of Matras fibrin glue, reaching the

field of orthopedic surgery, plastic, neurology, ophthalmology, otolaryngology. As stated by Tayapongsak, the use of fibrin glue to hold bone graft fragments in place, had represented the largest application in oral and maxillofacial surgery [7]. Although new techniques for autologous fibrin glue had been proposed, its preparation did not receive the approval of the American Food and Drug Administration (FDA) due to a potential risk of viral infection [8;9]. Therefore, the fibrin glue was replaced by platelet-rich plasma (PRP), when Withman et al. increased the attention about its release of growth factors [10]. In L-PRF membranes secretoma, clathrin-mediated endocytosis is the most represented pathway, mainly due to the presence of growth factors such as platelet-derived growth factor (PDGF) and epidermal growth factor (EGF) [11]. This type of endocytosis allows to internalize tyrosine kinase receptors, which contribute to the response to EGF and PDGF that stimulate cell migration and proliferation. Furthermore, most of growth factors were found on the third day because of the increased degranulation of platelets and neutrophils at that time. Regarding the levels of fibrinogen, the absence of thrombin in the L-PRF secretoma and the decreasing levels of prothrombin and factor V of coagulation over time do not allow the fibrinogen transformation into fibrin, justifying its accumulation over the time. Thus contributes to the wound healing properties of L-PRF membranes [12].

The advantages obtained by PRF in implant rehabilitations are multiple, its use seems to achieve an increased width of the keratinized mucosa (KM) [13]. However, a controversial scenario exists, because of the report of a reduction in peri-implant soft tissues and bone loss after PRF [14]. In a similar way, it was stated an absence of benefits in implants treated with PRF neither in increased keratinized tissue nor in bone tissue gain [15]. On the other hand, in cases of an initial deficit of KM (< 2mm), it was assessed an improvement of the patient's discomfort and a success in height and thickness of peri-implant keratinized gingiva associating the PRF to xenogeneic collagen matrix [16]. Many contrasts emerge in literature and there is an urgent need to develop uniform industry standards and clinical guidelines for PRF's clinical use [17]. The aim of this study is to report about a case of PRF membranes used during implant healing screws locations, evaluating an additional systematic literature review in order to establish the current knowledge about this specific management.

MATERIALS AND METHODS

A systematic review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18].

Literature Search

To identify relevant studies investigating the use of L-PRF in order to gain KM around implants, a comprehensive search of PubMed, Scopus, Web Of Sciences (WOS) and WHO databases using the Patient/Population/Problem, Intervention, Comparison and Outcome (PICO) format, was conducted from 2012 to 2022.

- Population: Adults.
- Intervention: Soft tissues augmentation around implants with L-PRF.
- Comparator: Free gingival grafts (FGG) OR xenogeneic collagen matrix.
- Outcome: KM width augmentation; lower pain; lower edema; better post-operative progress.

The following MeSH terms were used: L-PRF Mucosa Dental Implant. No language restrictions were applied.

Eligibility criteria

The inclusion criteria were as follows: all studies analyzing the effects of L-PRF membranes to gain KM around dental implants in adults.
The exclusion criteria were as follows: animal studies; other types of PRF or autologous blood compounds; L-PRF used in sinus membrane perforation.

Data extraction

Studies were screened by two reviewers independently, and a matrix of relevant data were produced. Disagreements were resolved by consensus with third reviewer. Data extraction included general details relating the characteristic of the study (e.g. authors, year of publication, source of funding) and the conclusion about the use of L-PRF to increase the KM.

Assessment of methodological quality

The methodological quality of included studies was assessed using the prediction model risk of bias assessment tool Newcastle – Ottawa Quality Assessment Scale [19] as showed in Table 2. A qualitative description of the characteristics of the included studies as well as a narrative data synthesis was performed.

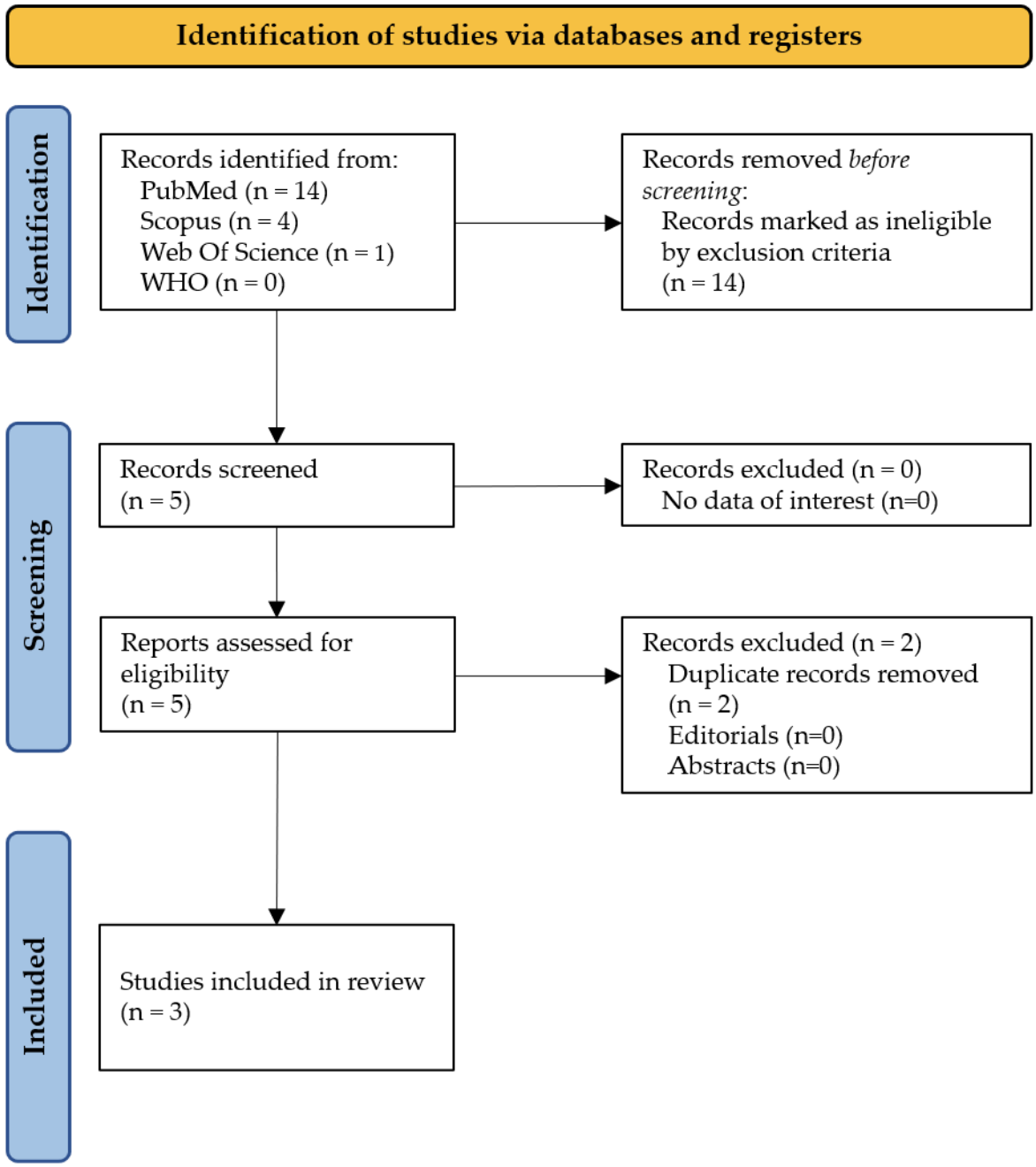


Fig 1 – PRISMA flowchart.

Table 1. Articles matching inclusion criteria.

Authors/Year	Kind of study	Conclusion
Rajan SA et al. 2022	Cohort study; 21 sites.	PRF membranes are equal to buccally advanced flap and to connective tissue graft for the closure of immediate implant sites.
Temmerman A. et al. 2018	Clinical trial; 8 patients.	L-PRF can increase the width of KM around implants and had lower surgical time with less postoperative discomfort and pain for the patients in comparison to the FGG.
Shah R. et al. 2017	Case report.	L-PRF membranes transformed think to thick peri-implant mucosa.

Table 2. New Castle – Ottawa Quality Assessment Scale. Possible total points were 4 points for selection; 2 points for comparability, and 3 points for exposures.

Authors	Year	Selection	Comparability	Exposure	Total
Rajan SA. et al.	2022	3	2	3	8
Temmerman A. et al.	2018	2	2	3	7
Shah R. et al.	2017	2	1	2	5

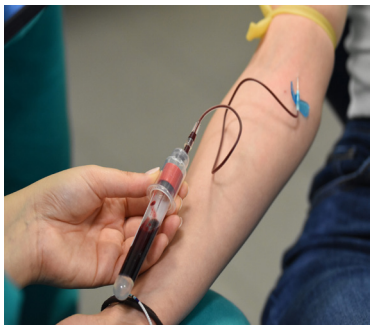
RESULTS

The initial website search provided a total of 14 articles; in detail 14 from PubMed, 4 from Scopus, 1 from WOS and 0 from WHO International Clinical Trial Registry Platform. Fourteen articles were excluded because ineligible by exclusion criteria. Five items accessed the screening phase and two was excluded because they were a duplicate. Just three studies were finally included in review (Figure 1). A table was drawn up including each eligible article, authors, year, kind of study, numbers of sites/patients treated and a brief conclusion (Table 1).

CASE – REPORT

A 57-years old female patient came to our attention for implants placement after a previous left hemimaxillectomy due to a squamous cell carcinoma on the adherent gingiva and later reconstructed with iliac crest bone graft covered with a cheek flap. Two submerged dental implants were placed in position 2.4 and 2.5 after a routinary crestal flap. Because of previous oncological resection, a shallow vestibular depth and a lack of KM were observed (< 2mm). During the implants uncovering surgery two L-PRF membranes were created, placed under the flap and fixed with the healing screws (Figure 3 a,b). After the peripheral venous blood sampling (Figure 2a) using blood tubes with clot activator (Figure 2b), they were put into the centrifugation machine for 10 minutes at 3000 rpm (Figure 2c). Once L-PRF clots were extracted (Figure 2d), L-PRF membranes were achieved after compression in the PRF Box (Figure 2e). Finally the site was closed with 3/0 silk wire (Figure 3c) and covered with a periodontal dressing (Coe-Pak ™) (Figure 3d).

The lady came back regularly for the check of the surgical site referring a minimum pain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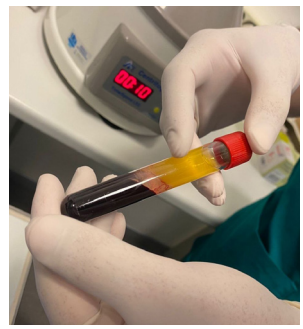
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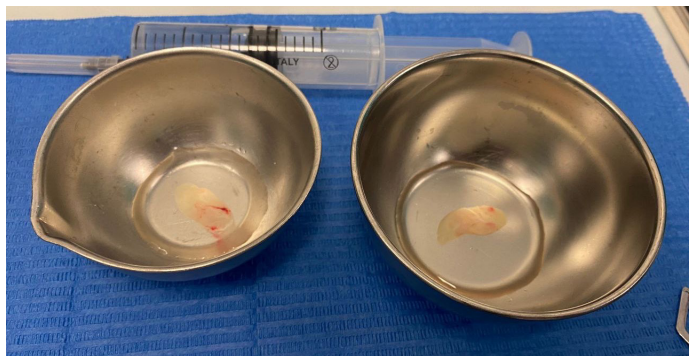
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Figure 2 – L-PRF membranes procedures: **a**. Peripheral venous blood sampling. **b**. Blood tubes with clot activator. **c.** Tube after centrifugation for 10 minutes at 3000 rpm. **d.** L-PRF clot extraction. **e.** L-PRF membranes achieved after compression in the PRF Box.

just in the first two postoperative days. Sutures were removed after 10 days. The patient is still in follow-up waiting for the prosthetic phase, soft tissues are settling around healing screws and the width of the KM is qualitative increased, even if a regular probing is not recommended before the complete recovery of the surgical wound. A one-month follow-up image is visible in Figure 4.

DISCUSSION

A systematic review following the PRISMA flowchart was conducted in order to assess the state-of-the-art about the possibility to gain KM width with L-PRF membranes around dental implants. Due to a considerable heterogeneity in the study population, design, and outcome measures a formal meta-analysis was not carried out. A case-report is also presented. This case showed a huge area without keratinized tissue and a reduced width of the non-keratinized mucosa due to several surgeries on the site, because of the oncological history of the patient. In light of this, it seems clear that this case is far from the cases treated in the articles cited for the review part. The authors suggest to consider this report as an infrequent case and to evaluate it as a starting point for further surgical managements, such as deepening of vestibular depth. The long-term success of dental implants is made up of several factors such as good plaque control, absence of occlusal overload and healthy peri-implant soft tissues, in order to achieve esthetics and long-term stability [20]. The most used method to increase thickness and width of the KM is the FGG. By the way, this procedure implies some critical aspects as pain, surgical skills to avoid injuries to nerves and vessels, long surgical time and healing time for the donor site, these are factors discouraging the patient to accept the surgery plan [21]. For this reason, options that can reduce these side effects have to be explored. L-PRF is widely used in dentistry especially for its growth factors release and its easy way to produce it [22]. Our review was referred to a 10-year period of time and at the

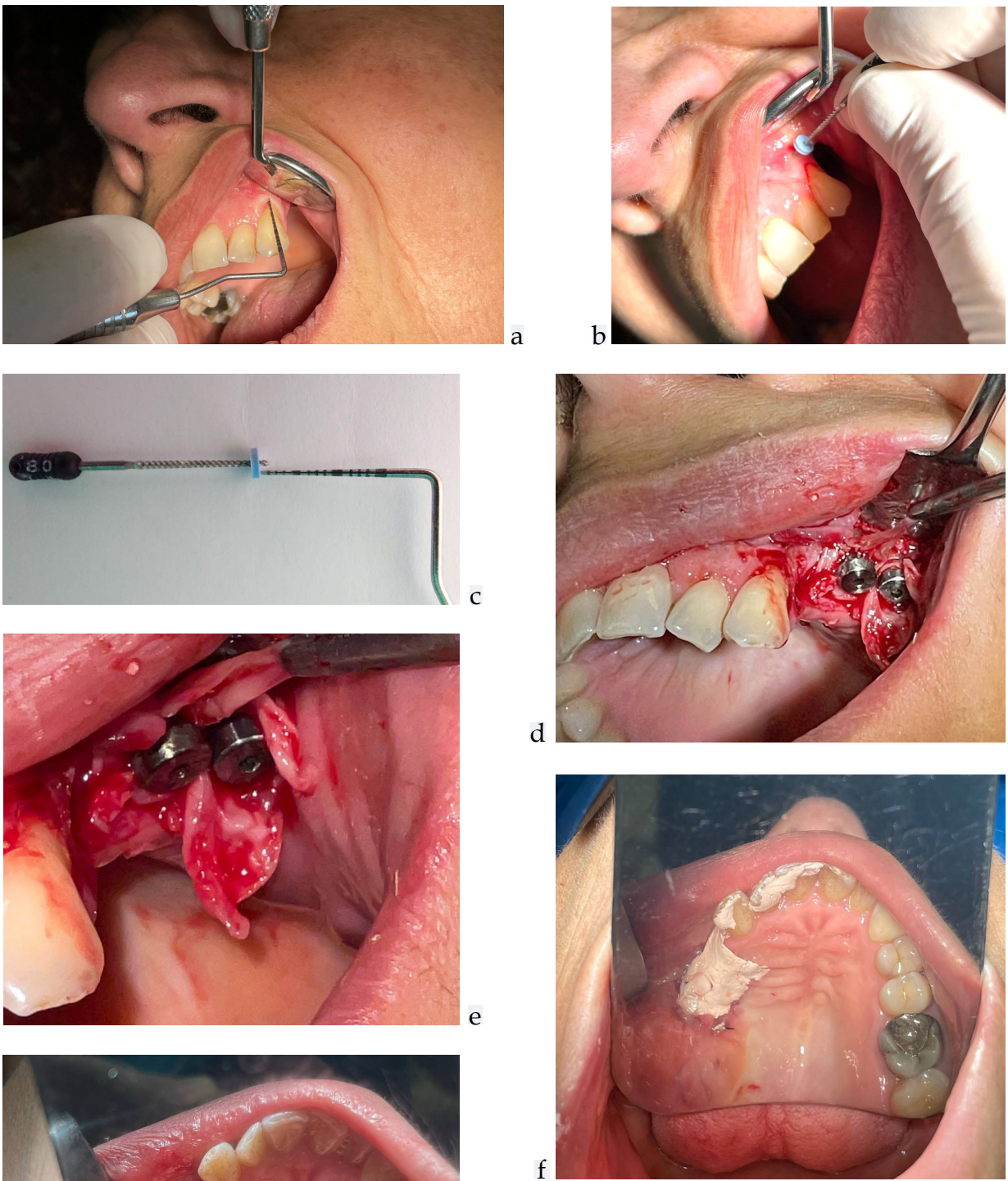

Fig. 3 – L-PRF membranes placements: **a.** Probing. The probe is visible in transparency under the gingiva. **b.** Bone probing with endodontic file: the gum stop was pushed against the gingiva. **c.** The endodontic file showed 1mm of keratinized tissue. **d.** L-PRF membranes fixed with healing screws. **e.** Detail of fixed L-PRF membranes **f.** Sutures. **g.** Coe-Pak.

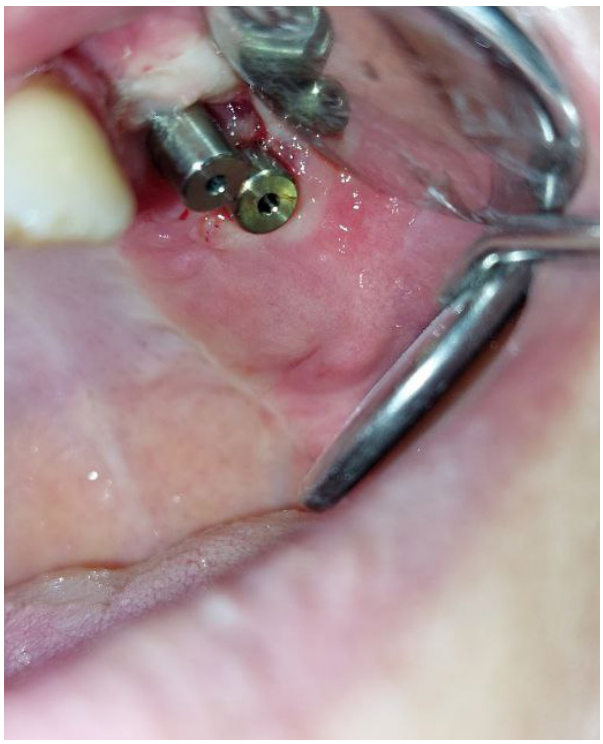

Figure 4 – One-month follow-up. The scar line between the hard palate and the previous cheek graft is clearly identifiable.

best of our knowledge this specific field has to be still extensively investigated. The valuable work of Temmerman et al. [13] proposed a randomized split-mouth trial evaluating L-PRF and FGG with the result that L-PRF membranes are able to enhance the peri-implant KM with a lower surgical time, lower pain and lower postoperative discomfort than FGG. Consequences of a thicker mucosal phenotype at implant sites could lead to a long-term failure of the rehabilitation as stated by Rajan SA et al. [23]. Finally, Shah R. et al [24] reported a successful case of biotype transformation of peri-implant soft tissues after L-PRF membranes application. The choice of L-PRF in peri-implant plastic surgery has only just begun. The potential clinical benefits of this autologous, biomimetic, affordable material are encouraging. The creation of a soft tissue substitute and the elimination of the donor site morbidity should be the main goals. An under-representation of long-term longitudinal studies was found, in conjunction with the lack of an evidence-based protocol about the choice of centrifugal pumps, tubes, times and rotation frequency.

CONCLUSION

Peri-implant phenotype modification is crucial in patients with reduced KM width around dental implants. The most used solution is FGG, despite several side effects. L-PRF can be considered a suitable substitute to gain KM surrounding implants. The selection of the technique to meet the purpose of gain keratinized soft tissue along with implant platform is a prerogative of the clinician according to his skills and to the history of the patient.

AUTHOR CONTRIBUTION

Conceptualization, S.D., M.G. and M.D.; methodology, S.D.; formal analysis, S.D.; investigation, S.D. and M.G.; data curation, S.D.; writing—original draft preparation, S.D.; writing—review and editing, S.D., M.G.; supervision, G.V., S.A.S. and M.D. All authors have read and agreed to the published version of the manuscript.

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