Minimizing Patient Morbidity Following Palatal Gingival Harvesting: A Randomized Controlled Clinical Study

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This clinical study was conducted to evaluate the impact of different hemostatic treatments following palatal gingival harvesting on patient discomfort. Fifty patients who needed a mucogingival surgery requiring gingival graft harvesting were enrolled and randomly assigned to one of five groups: (1) a control group in which only sutures were applied; (2) a cyanoacrylate group; (3) a periodontal dressing material group; (4) a hemostatic gelatin sponge group; and (5) a group in which the gelatin sponge and cyanoacrylate were combined. In the 2 weeks following the procedures, perception of pain, healing, consumption of drugs, and willingness to repeat the procedure were recorded through visual analog scale (VAS) by patients. Over the 2 weeks, lower pain (VAS) was found in all test groups compared to the control group ($P < .01$, value for time-group interaction). Notably, the gelatin sponge combined with cyanoacrylate group had very low pain (VAS ≤ 0.5 points) throughout the 14 days. The lowest healing scores at day 10 were associated with the control group (6.8 VAS points) in contrast to the four test groups (8.2 to 9.0 VAS points, $P = .0001$). Pain was inversely correlated with age ($P < .05$). Pain also depended on the apicocoronal dimension of the graft: the higher the graft, the more pain was experienced by the participants (0.4 VAS points per 1 mm, $P < .05$). Within the limitations of this study, palatal coverage appears to result in better outcomes when compared to suture alone. In particular, a double-layered protection of the palatal wound with a gelatin sponge combined with cyanoacrylate appeared to be the best option in reducing pain and postoperative discomfort.
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Autogenous or de-epithelialized free gingival grafts have been adopted in several clinical scenarios, including not only recession coverage[1,2] but also increase of keratinized gingiva width and thickness,[3,4] treatment of recessions around dental implants,[5] lack of keratinized tissue around dental implants,[6] and soft tissue augmentation for other purposes.[7–9] Gingival grafts can be harvested from the maxillary tuberosity, from edentulous areas, or from the palate, which is the most common donor site because of its large tissue availability. Different harvesting techniques have been described for palatal gingival/connective tissue grafts: epithelialized gingival graft (EGG)[10,11] and subepithelial connective tissue grafts (SCTG) with several variations.[3,12–14] As SCTG harvesting techniques allow for primary intention healing of the palatal wound, they have been considered the gold standard in CTG harvesting for many years due to reduced postoperative morbidity.[15–17] More recently, EGG has become popular due to its ease of use and tissue availability. Moreover, EGG can be harvested even in thinner palatal mucosa, while CTG harvesting techniques require at least 3 to 4 mm of palatal thickness to avoid necrosis or dehiscence of the primary flap. The palatal wound resulting from the EGG harvesting technique

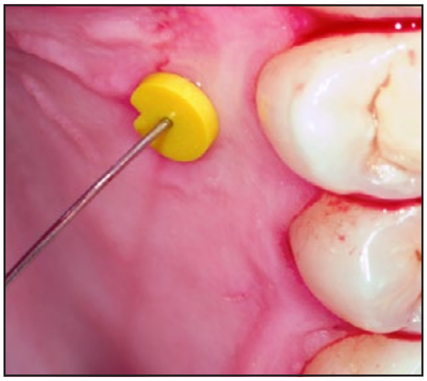

Fig 1 *Measurement of palatal thickness with needle penetration.*

heals by secondary intention, which may increase postoperative patient discomfort.[15–17] Different materials have been suggested to minimize postoperative bleeding and patient discomfort following gingival graft harvesting, such as periodontal dressings[18] and hemostatic absorbable gelatin sponges.[11,19] However, there is still limited information on which material would be best to minimize bleeding and postoperative pain, thus reducing the need for postsurgical analgesics. With this goal in mind, the authors conducted a clinical study to evaluate postoperative outcomes of the following different palatal covering materials after EGG harvesting: *(1)* simple suturing, *(2)* cyanoacrylate bioadhesives, *(3)* periodontal dressing, *(4)* hemostatic absorbable gelatin sponge, and *(5)* a double-layered protection (DLP) involving a hemostatic gelatin sponge in combination with a cyanoacrylate bioadhesive.

Materials and Methods

Fifty patients who needed a mucogingival surgery requiring gingival graft harvesting—either free gingival grafts or de-epithelialized gingival grafts (DGGs)—were enrolled in the study from a private dental practice in Milan, Italy. All patients were informed of and understood the objectives of the study and signed informed consent forms. The study was performed between January 2016 and December 2016.

All study participants fit the following inclusion criteria: *(1)* 18 years of age or older; *(2)* without any reported systemic diseases; *(3)* having a healthy periodontium or demonstrating a stable periodontal condition following conventional periodontal therapy; *(4)* showing full-mouth plaque and bleeding scores < 20%; and *(5)* clinical indication for periodontal plastic surgery utilizing DGGs was to treat either single or multiple recession defects (Miller Class I, II, or III). Free gingival grafts were used to increase keratinized tissues around implants. The exclusion criteria were the following: *(1)* pregnancy; *(2)* reported use of anticoagulant or antiplatelet drugs such as NSAIDs, heparin, warfarin, etc, or blood-thinning supplements; and *(3)* severe clinical attachment loss.

This study is a single-blind, randomized, controlled pilot clinical investigation with parallel, balanced groups: four test groups and a control group. The donor site was only sutured in the control group (group 1). In the test groups, the donor sites were protected using one of the following commercially available materials: *(1)* adhesive agent (PeriAcryl 90 HV, Glustitch; group 2); *(2)* hemostatic agent (Spongostan, Ethicon; group 3); *(3)* periodontal dressing (Peripac, Dentsply DeTrey; group 4); or *(4)* hemostatic agent combined with an adhesive agent (Spongostan + PeriAcryl; group 5). Patients were randomly assigned to one of the five groups (n = 10 per group) using a computer-generated randomization table. Each patient's assigned group was communicated to the operator through a sealed envelope that was opened during the surgery, immediately after the graft harvesting procedure was completed. On the day of the surgery, local anesthesia was administered (2% lidocaine with epinephrine 1:100,000), and the palatal tissue thickness was measured at the mesial, central, and distal parts of the designated graft-harvesting area by using the same anesthesia needle with an adjustable silicone disk stop (Fig 1). An EGG was harvested by applying the same surgical technique previously described by Zucchelli et al.[11] For bilaminar techniques, the harvested graft was extraorally de-epithelialized (DGG) (Fig 2), while the epithelium was maintained in cases utilizing free gingival graft techniques. A periodontal probe was used to measure the height, width, and thickness of the harvested graft before de-epithelialization

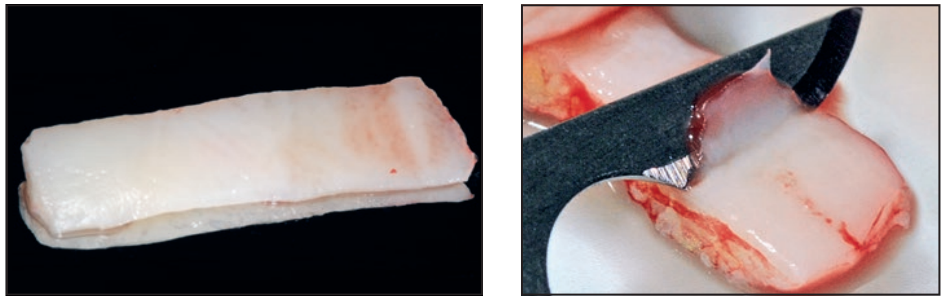

Fig 2 *Harvested free gingival graft followed by the de-epithelialization process for obtaining a connective tissue graft.*

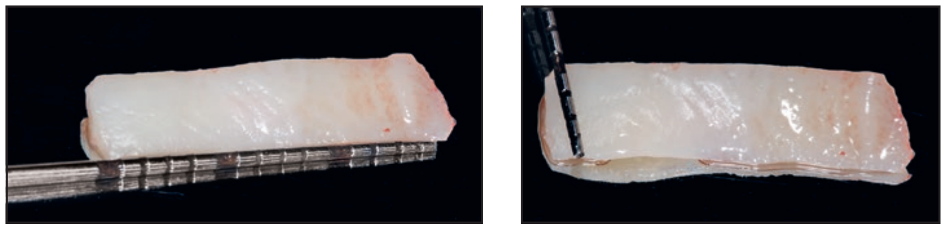

Fig 3 *Measurements of graft dimensions done with a periodontal probe.*

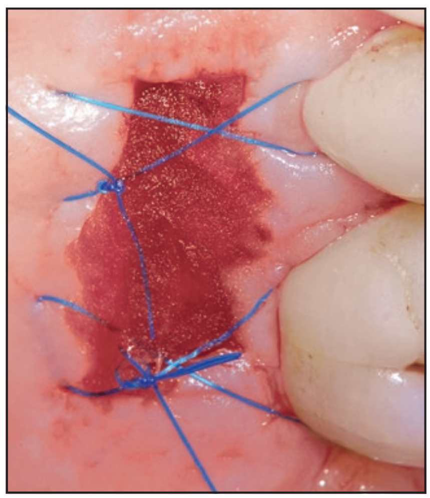

Fig 4 *Palatal donor site protected using a gelatin sponge.*

Fig 5 *Double-layered palatal protection using a gelatin sponge and cyanoacrylate.*

and fatty tissue removal (Fig 3). After covering the palatal wound with sterile gauze for a few seconds, the wound was treated according to the patient's randomized assigned procedure. In the control group (suturing), several simple interrupted sutures were performed with a 5-0 nonresorbable monofilament suture (Seralon, Serag Wiessner). No further sealing materials were applied. In group 2 (PeriAcryl), one or more 5-0 nonresorbable sling sutures (Seralon, Serag Wiessner) were anchored to the soft tissues apical to the palatal wound area, followed by some drops of high viscosity cyanoacrylate. In group 3 (Spongostan), the palatal wound was protected with a porcine-derived hemostatic absorbable gelatin sponge, which was stabilized by one or more 5-0 nonresorbable sling sutures (Seralon, Serag Wiessner) anchored to the soft tissues apical to the palatal wound area (Fig 4). In group 4 (Peripac), the wound was protected with a periodontal dressing that covered the entire palate and was pressed into interdental spaces, enhancing physical retention of the dressing. In group 5 (Spongostan + PeriAcryl; DLP), palatal protection was initially similar to that described for group 3: Spongostan was stabilized with a sling suture (Seralon, Serag Wiessner) and high-viscosity cyanoacrylate was then applied along the wound borders and throughout the whole wound surface, over the Spongostan, in order to have a uniform superficial layer of the acrylic adhesive (Fig 5). All surgeries were performed by the same experienced periodontist (R.A.). Each patient was given 600 mg of ibuprofen immediately before the surgery and was instructed to continue the same dose at 6 hours post-operation, then taken as needed.

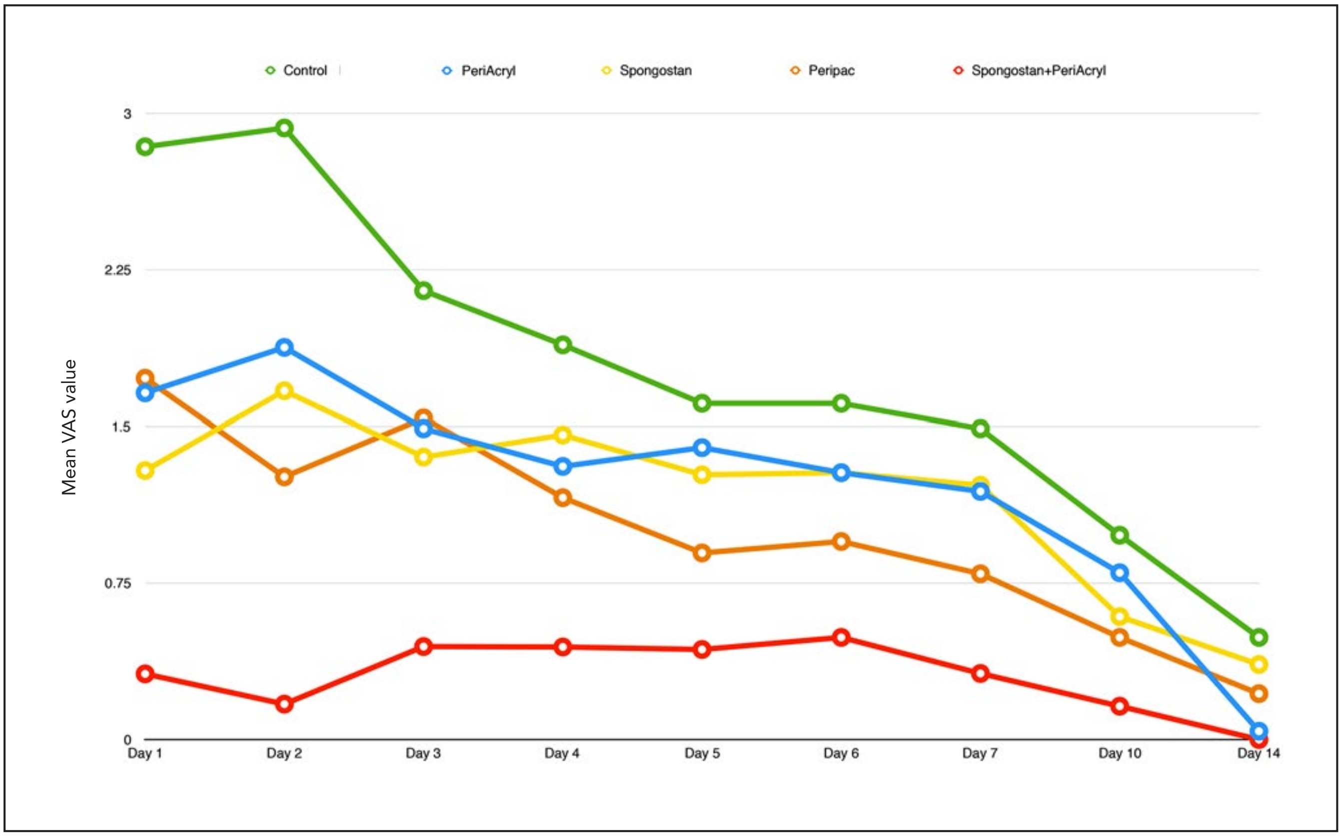

Fig 6 *Mean visual analog scale (VAS) value changes for each group during the follow-up period.*

No antibiotics were prescribed. Patients were asked to refrain from brushing the palatal surface of the maxillary teeth until the protective material and sutures were removed. Ten days after surgery, a blinded examiner (L.T.) visually evaluated the healing of the palatal wound by comparing the operated palate site to its contralateral counterpart using a visual analog scale (VAS), as previously described in literature.[18] Sutures and covering materials were removed 10 days postsurgery.

Based on the perceived postoperative pain, patients were instructed to mark a 100-mm VAS[20] at 1, 2, 3, 4, 5, 6, 7, 10, and 14 days postoperative, preferably at the same time of the day. Patients also answered to the following questions: *(a)* "Did you take any painkillers due to the palatal pain, other than what was given on the day of surgery?" and *(b)* "If necessary, would you repeat the palatal harvesting procedure?"

The primary outcome was the postoperative palatal pain score measured with the VAS scale. Secondary outcomes were painkiller consumption, palatal healing score, and willingness to repeat the treatment. Moreover, correlations between postoperative pain and graft thickness, width, height, palatal thickness, and age were investigated.

Statistical Analysis

The authors used Kruskal-Wallis (continuous variables) or chi-square (categorical variables) test to analyze characteristics across the treatment groups. Multiple random effects regression models were applied to evaluate VAS changes across the five groups over time. The authors adjusted for gender, age (years), and clinical characteristics (graft height, width, and thickness). Group-time interaction was tested using a global Wald test. Statistical analyses were performed with Stata 14 (StataCorp. 2015).

Table 1 Demographic Characteristics of Study Participants

Demographic characteristic	Control group (n = 10)	PeriAcryl (n = 10)	Spongostan (n = 10)	Peripac (n = 10)	Spongostan + PeriAcryl (n = 10)
Age, y (mean ± SD)	46.4 ± 14.4	45.3 ± 11.5	54.7 ± 10.3	52.8 ± 7.1	50.9 ± 11.5
Gender, n (%)					
Female	5 (50)	7 (70)	4 (40)	8 (80)	9 (90)
Smokers, n (%)					
Yes	2 (20)	1 (10)	2 (20)	1 (10)	1 (10)

Table 2 Dimensions of Harvested Grafts in the Five Treatment Groups

Clinical characteristic	Control group (n = 10)	PeriAcryl (n = 10)	Spongostan (n = 10)	Peripac (n = 10)	Spongostan + PeriAcryl (n = 10)	*P* value
Graft height (mean ± SD)	5 ± 1	5.4 ± 1.8	5.2 ± 1.1	4.6 ± 1.6	4.9 ± 0.7	.94
Graft width (mean ± SD)	18.2 ± 5	13.0 ± 4.9	14.8 ± 5.4	13.2 ± 4.5	11.9 ± 4.4	.08
Graft thickness (mean ± SD)	1.6 ± 0.4	1.3 ± 0.4	1.8 ± 0.4	1.6 ± 0.4	1.7 ± 0.4	.08

Table 3 Outcome Variables of the Five Treatment Groups

Variable	Control group (n = 10)	PeriAcryl (n = 10)	Spongostan (n = 10)	Peripac (n = 10)	Spongostan + PeriAcryl (n = 10)
Pain (VAS) day 1	2.8	1.7	1.3	1.7	0.3
Pain (VAS) day 2	2.9	1.9	1.7	1.3	0.2
Pain (VAS) day 3	2.2	1.5	1.4	1.5	0.4
Pain (VAS) day 4	1.9	1.3	1.5	1.2	0.4
Pain (VAS) day 5	1.6	1.4	1.3	0.9	0.5
Pain (VAS) day 6	1.6	1.3	1.3	1	0.3
Pain (VAS) day 7	1.5	1.2	1.2	0.8	0.2
Pain (VAS) day 10	1	0.8	0.6	0.5	0
Pain (VAS) day 14	0.5	0	0.4	0.2	0
Pain vs control group (*P* value)*		.063	.625	.328	.01
Healing (day 10)	6.8 ± 1	8.4 ± 0.5	8.2 ± 1.2	8.9 ± 0.6	9.0 ± 0.7
Patients who consumed additional pain-relief drugs, n (%)	5 (50)	2 (20)	4 (40)	5 (50)	1 (10)
Patients who would repeat the procedure if necessary, n (%)	6 (60)	9 (90)	9 (90)	8 (80)	10 (100)

*From a random-effects linear regression model adjusted for gender, age, and graft height, width, and thickness.

Results

Fifty patients were randomly distributed to the five groups. Study participants comprised of 33 females and 17 males between 26 and 73 years old (mean = 50.02 ± 11.36 years). There was no statistical difference in the mean age of participants between groups ($P > .05$). Demographic data of study participants are shown in Table 1. There were no statistically significant differences between groups regarding graft dimensions ($P > .05$) (Table 2). Hemostasis was achieved in all 50 patients, regardless of the palatal wound protection method. No palatal protection was lost prior to its removal on the 10th day. Each group's outcome variables, as reported by the patients and blinded examiner, are presented in Table 3. Participants in the test groups showed lower pain scores than patients in the control group. The overall difference in postoperative palatal pain was statistically significant between the DLP and the control group (*P* < .01). In particular, during the first and second days after the harvesting, this difference between the DLP group and the control group was statistically significant (*P* < .05). In the following days, the DLP group was associated with lower VAS scores compared to the control group. Compared to the other test groups, the DLP group (group 5) reported the lowest VAS values throughout the entire 2-week follow-up period (*P* > .05). Changes in VAS over time are demonstrated in Fig 6. The apicocoronal dimension of the graft (graft height) contributed to the perception of pain during the first 7 days following the surgery: the higher the graft, the more pain was experienced by the patients (0.4 VAS points per 1 mm on average; *P* < .05). On the other hand, the age was inversely correlated with pain, with statistically significant differences during postoperative days 3 through 7 (–0.03 VAS points per 10 years on average, *P* < .05). As for the healing of the palatal surface, the least optimal healing was associated with the control group when compared to the mean values of the four test groups (*P* < .001). When postoperative drug consumption was evaluated, 50% of study participants who did not receive any palatal protection reported taking additional doses of pain-relief medication beyond what was initially administered. The lowest drug consumption was reported for the DLP group. Sixty percent of patients in the control group were willing to repeat treatment if needed in comparison to 100% of patients in the DLP group. Random intercept regression models were used to assess the joint effect of age, palatal thickness, and graft width, height, and thickness on patients' self-perceived pain. In this study, neither palatal thickness, graft width, nor graft thickness seemed to have any correlation with pain. However, pain was correlated with age and graft height, as previously described (*P* < .05).

Discussion

Connective tissue graft harvested from the palate is commonly applied in periodontal practice.[4,6,20,21] Although the best connective tissue harvesting technique is still a subject of debate,[11,14,17] minimizing postoperative morbidity following palatal harvesting should be one of the primary aims. In general, CTG harvesting techniques allow for healing by primary intention, which reduces postoperative bleeding, burning sensation, and wound infection compared to healing by secondary intention.[15–17] However, CTG harvesting techniques might be associated with higher levels of pain due to necrosis or dehiscence of the primary flap, a complication that could occur when the primary flap is too thin or if sutures fail to secure the palatal flap over the wound.[11] Another disadvantage of the CTG harvesting techniques might be the poorer quality of the obtained graft, as denser tissues that are less prone to shrinkage are left in the primary flap to prevent necrosis.[11,22]

Some authors reported healing by secondary intention of the palatal donor site to be associated with higher morbidity,[14,16,17] but a randomized clinical trial demonstrated no differences regarding the experienced postoperative pain between CTG and EGG harvesting techniques when the palatal wound resulting from the latter harvesting technique was protected with a collagen layer and maintained in situ with a sling mattress suture.[11] In this context, it is reasonable to assume that if local protection of the donor site following EGG is effective, the EGG technique might be considered the new palatal harvesting technique of choice. Indeed, this approach is relatively fast, easy to perform, can be applied in the presence of thin palatal mucosa,[11,15] and allows for de-epithelialization to obtain a high-quality CTG.[11,22] Ozcelik et al[23] suggested that irradiating the palatal wound with a laser might be more effective in decreasing postoperative morbidity than using a collagen matrix. However, high postoperative pain scores (VAS) were reported in both groups, with VAS peaks of 5.1 in the diode laser group and 7.6 in the collagen matrix group. The authors of the present study investigated the outcome of different hemostatic treatments on postoperative pain, and the results showed that protecting the palatal donor site has a positive impact on postoperative pain and discomfort. According to VAS values, DLP with a collagen sponge and cyanoacrylate seems to be effective in minimizing postoperative pain following graft harvesting in comparison to the control group

($P < .01$). Moreover, the DLP group was associated with the lowest mean VAS scores during the follow-up period. Patients of all study groups, except the DLP group, reported VAS pain peaks during the first and the second postoperative days, but these values started to decline after the first postoperative week, in accordance with previously published results.[24] All patients receiving double-layered wound coverage were willing to undergo another palatal harvesting procedure if needed. In general, all test groups showed better outcomes compared to the control group, but worse than the DLP group, even if these findings were not statistically significant.

Palatal healing was also better in all test groups compared to the control group ($P < .001$). Although palatal wound protection with a hemostatic agent has been advocated by different authors,[11,19] applying an adhesive agent over a hemostatic one might reinforce wound coverage, which could minimize postoperative morbidity that was thought to be associated with wound healing by secondary intention. It can be speculated that cyanoacrylate might enhance palatal wound healing due to its strong sealing, bacteriostatic, and hemostatic properties.[25] A previous study reported a positive correlation between graft thickness and the patient's perception of pain,[24] but the present study's results did not confirm such a correlation. This discrepancy might be attributed to the variations in graft thickness between both studies; Burkhardt et al[24] reported that grafts of more than 2 mm in thickness were associated with a higher morbidity, but no graft was thicker than 2 mm in the present study. Minimal graft thickness for root coverage was suggested in a previously published study: Zucchelli et al[21] demonstrated that a coronally advanced flap (CAF) combined with DGG of reduced thickness (< 1 mm) and height (< 4 mm) had similar root coverage outcomes as CAF with thicker and bigger DGG, but with lower patient morbidity. The present clinical study confirmed that reduced height of the graft plays an important role in decreasing patient's perception of pain (0.4 VAS points per 1 mm; $P < .05$). In particular, the apicocoronal dimension of the graft was important for pain perception during the first postoperative days, which, according to Burkhardt et al,[24] are the least comfortable for patients following a palatal harvesting procedure. It has been reported that age may influence the perception of pain,[26] and the present results showed that pain was inversely correlated with age: this might be attributed to the higher vascularization in younger individuals and more anastomosis of the vessels, which might play a role in increased perception of pain.

Several studies compared postoperative discomfort between CTG and EGG harvesting techniques[11,15–17] but did not explore ways to reduce patient morbidity following the EGG harvesting technique. Findings of the present study suggest that palatal coverage might result in better palatal wound healing and reduced patient morbidity. In particular, DLP with cyanoacrylate adhesive applied over a hemostatic collagen sponge seemed to be the most effective method in palatal wound management. This approach may be beneficial in minimizing palatal pain, which is thought to be a major drawback of the EGG harvesting technique.

A limitation of this study is the small sample size for each group, resulting in low statistical power to detect differences between groups. Future research will focus on comparing CTG and EGG tissue harvesting combined with the DLP technique, which appeared to be the most promising technique among those tested hereby.

Conclusions

The results of this study suggest that the adoption of different hemostatic agents for the protection of the palatal donor site following gingival harvesting procedures may provide better comfort to the patient compared to suturing only. In particular, a DLP of the palatal wound that includes the use of a gelatin sponge and cyanoacrylate might reduce pain and postoperative discomfort. Pain was correlated with graft height and inversely correlated with age. Future clinical studies are needed to confirm these preliminary findings.

Acknowledgments

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