## Dimensional Influence of Epithelialized Tissue Graft Harvested From Palate on Postoperative Pain: a Systematic Review

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## ABSTRACT

**Objectives:** The aim of the present systematic review was to evaluate the dimensional influence of the epithelialized tissue graft harvested from the palate in the postoperative pain.

**Material and Methods:** Research was conducted in electronic databases Cochrane Library, Embase, LILACS, PubMed, Scopus, and Web of Science upwards May 15, 2022. Studies that reported the influence of graft dimensions of palatal epithelized harvesting on postoperative pain were eligible. The evaluation was made using the methodological quality assessment by Joanna Briggs Institute Critical Appraisal Checklist for randomized clinical trials and non-randomized studies and the level of evidence according to GRADE.

**Results:** Four studies were included. The clinical and methodological heterogeneity among studies led to an analysed narrative. The postoperative pain was assessed during the period of 1 to 28 postoperative days. It was determined by using visual analog scale in three studies, while the evaluation was performed indirectly based on analgesics intake in one study. According to three studies, bigger graft sizes were associated with higher postoperative pain. The methodological quality assessment categorized two study as high (one randomized control trial and one non-randomized), and two as moderate (one randomized control trial and one non-randomized).

**Conclusions:** Based on the moderate certainty level, bigger graft sizes of palatal epithelized harvesting appear to promote more postoperative pain. Understanding the postoperative pain as a response to a graft extension may assist some clinical decisions regarding the surgical periodontal and peri-implant planning.

Keywords: autografts; periodontal guided tissue regeneration; systematic review; wound healing.

Accepted for publication: 30 September 2022

To cite this article:

Escobar M, Scheeren Brum R, Apaza-Bedoya K, Pauletto P, Benfatti CAM, Cruz ACC, Henriques BAPC. Dimensional Influence of Epithelialized Tissue Graft Harvested From Palate on Postoperative Pain: a Systematic Review J Oral Maxillofac Res 2022;13(3):e1 URL: http://www.ejomr.org/JOMR/archives/2022/3/e1/v13n3e1.pdf doi: 10.5037/jomr.2022.13301

#### INTRODUCTION

Due to the periodontal and peri-implant plastic surgery demands, the harvesting of epithelialized tissue graft from the palate has continued to be performed either in free gingival graft (FGG) technique or in connective tissue graft (CTG) after graft de-epithelialization [1]. These soft tissue grafts hold several indications to benefit periodontal and peri-implant health, used for tissue thickness augmentation and mucogingival deformities correction [1-4]. Although soft tissue grafts can be procured from distinct parts of the oral cavity such as edentulous regions and maxillary tuberosity, the palatal gingival tissue is the most common donor site [5,6]. The palate area enables large graft dimensions harvesting and has similarity with keratinized attached mucosa of the alveolar ridge [7]. Nonetheless, it has been suggested that autogenous soft tissue graft techniques may be associated with increased surgical time, postoperative pain, swelling, and bleeding [<u>8,9</u>].

Therefore, strategies to reduce overall patient affliction are currently being investigated [10,11]. surgical harvesting They comprise different techniques and methods of wound closure [12,13]. Additionally, some randomized clinical trials (RCTs) have evaluated epithelialized graft tissue dimensions on patient ailment [11,14-17] and have been discussed how to harvest the graft from the palate to minimize patient soreness [9]. The palatal mucosal thickness varies from the anatomical conditions of each patient [18], site [19,20], gender [21], and age [22]. When a collagen-rich graft is devoided of adipose and glandular tissues, it is indicated a more superficial harvesting area, which seems to provide better outcomes [23]. Therefore, in these cases, the FGG harvesting technique may represent benefits since the CTG will be composed of the lamina propria only or with minor additional parts of the submucosal layer. However, the FGG harvesting process promoted a denuded wound area involving healing by secondary intention, which may be related to increased postoperative pain.

Since there is no consensus concerning

the dimensional effect on postoperative pain, the purpose of this systematic review was to critically appraise available evidence to answer the following tic focused question: "In patients who underwent surgical removal of palatal epithelized tissue for graft purposes, what is the influence of the graft dimensions G) concerning postoperative pain?"

## MATERIAL AND METHODS Protocol and registration

The current systematic review was performed agreeing to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) [24]. The PRISMA checklist was employed [24]. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO). Rregistration No. CRD42020194423.

The protocol can be assessed at:

https://www.crd.york.ac.uk/prospero/display\_record. php?ID=CRD42020194423

#### **Focus question**

The focused interrogation of this study "In patients who underwent surgical removal of palatal epithelized tissue for graft purposes, what is the influence of the graft dimensions concerning postoperative pain?" followed the abbreviation PICOS (Population, Intervention, Comparison, Outcomes, and Study design) [25] (Table 1). Since there is no consensus at literature to determine what is a small or a big graft, included articles must have at least two different groups differing on graft size, as specified at Inclusion criteria section.

#### **Information sources**

The procedures included denominating keywords and MeSH terms, developing electronic search strategies, and adjusting them for six databases: Embase, Cochrane, PubMed/Medline, Latin American and Caribbean Health Sciences (LILACS), Scopus, and Web of Science. The search was carried out until May 15, 2022.

Patient and population (P)	Patients who underwent surgical removal of palatal epithelialized tissue graft
Intervention (I)	Small dimension of palatal epithelialized tissue graft
Comparator or control group (C)	Big dimension of palatal epithelialized tissue graft
Outcomes (O)	Postoperative pain
Study design (S)	Randomized clinical trials and non-randomized prospective studies

Table 1. PICOS guidelines

## Search

The included papers references were selected by hand for possibly relevant articles by two authors (M.E.) and (R.S.B.). Duplicate articles were removed using reference manager software - Mendeley<sup>®</sup> (Elsevier; London, UK). More information concerning appropriate truncation and word combinations for each specific database is obtainable in Appendix 1.

## **Study selection**

Selecting the studies was accomplished by two selfgoverning reviewers (M.E. and R.S.B.). Initially, titles and abstracts were selected using an online software for systematic reviews Rayyan<sup>®</sup> (Qatar Computing Research Institute; HBKU, Doha, Qatar) [<u>26</u>].

Next, the same authors applied the eligibility to the full-text studies. Another author (K.A.B.) was accessed to make a final pronouncement in both phases if any disparity arose.

## **Types of publications**

The review included studies on humans published in international journals. Abstracts, case-control studies, PhD thesis and literature reviews were excluded.

## **Types of studies**

Randomized clinical trials and non-randomized prospective studies were considered eligible.

## Types of participants/population

Patients within 18 years of age or older, males or females, no restriction of ethnicity, who underwent surgical removal of epithelized graft from palate for periodontal or peri-implant surgery.

## Inclusion and exclusion criteria Inclusion criteria

Included studies should possess at least two groups that evaluate length, and/or thickness, and/or height of palatal epithelialized tissue harvesting employing patient postoperative pain through visual analog scale (VAS) or indirectly evaluated based on the mean of analgesics intake. There were no language and/or publication period restrictions included.

## Exclusion criteria

The exclusion criteria adopted were:

- Study does not evaluate graft dimension and its association with postoperative pain.
- Study does not employ a subgroup classification based on graft dimensions.
- Donor site distinct from palate.
- Book chapters, guidelines, reviews, letters, conference, abstracts, case series, personal opinions, animal studies, and technique description.
- Duplicate data (e.g. dissertations and/or thesis whichever equivalent published articles were available).

## **Data extraction**

Two authors (M.E. and R.S.B.) separately implemented the data assembly. Mistyping and mistakes were further checked for accuracy by the third reviewer (K.A.B.). Regarding the included studies, the ensuing information was collected: study characteristics (author, publication year, country, and study design); graft dimension groups (thickness, height, and/or width), graft measurement method, sample size, statistical analysis, postoperative pain, and main findings. If the required data was missing in the main text, four attempts to contact the corresponding authors of primary studies were made by e-mail in one-month period.

## Data items

Graft dimension groups, based on thickness, height, and width, were evaluated in included studies according to the postoperative pain through VAS or indirectly evaluated based on analgesics intake.

## **Risk of bias within studies**

The methodological quality assessment of the analysed studies was evaluated by two authors (M.E. and R.S.B.) using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for RCTs (Table 2) and the JBI Critical Appraisal Checklist for Quasi-Experimental Studies (non-randomized clinical trials) (Table 3) (https://joannabriggs.org/).

Divergences were deciphered by a third reviewer (K.A.B.). The possible answers to each question were: "yes (Y)", "no (N)", or "unclear (UN)". The operational quality was considered as low when the paper extends to 49% score "yes", moderate when the article encompassed 50% to 69% score "yes", and high when the study went as more than 70% score "yes".

#### Table 2. The Joanna Briggs Institute Critical Appraisal Checklist for randomized clinical trials

Q1	Was true randomization used for assignment of participants to treatment groups?
Q2	Was allocation to treatment groups concealed?
Q3	Were treatment groups similar at the baseline?
Q4	Were participants blind to treatment assignment?
Q5	Were those delivering treatment blind to treatment assignment?
Q6	Were outcomes assessors blind to treatment assignment?
Q7	Were treatment groups treated identically other than the intervention of interest?
Q8	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?
Q9	Were participants analysed in the groups to which they were randomized?
Q10	Were outcomes measured in the same way for treatment groups?
Q11	Were outcomes measured in a reliable way?
Q12	Was appropriate statistical analysis used?
Q13	Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) ac- counted for in the conduct and analysis of the trial?

Table 3. The Joanna Briggs Institute Critical Appraisal Checklist for non-randomized studies

Q1	Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?
Q2	Were the participants included in any comparisons similar?
Q3	Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?
Q4	Was there a control group?
Q5	Were there multiple measurements of the outcome both pre and post the intervention/exposure?
Q6	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?
Q7	Were the outcomes of participants included in any comparisons measured in the same way?
Q8	Were outcomes measured in a reliable way?
Q9	Was appropriate statistical analysis used?

#### Synthesis of results

A qualitative analysis of results was performed based on postoperative pain. Statistical pooling of data using meta-analysis was planned if studies were considered sufficiently homogeneous with regards to methodology and data availability.

#### **Risk of bias across studies**

An outline of the strength of evidence available was performed based on the "Grading of Recommendations Assessment, Development, and Evaluation" (GRADE). Summary of findings tables was produced on GRADE online software (GRADEpro GTD; Copenhagen, Denmark) [27].

## **RESULTS** Study selection

The search in the 6 main databases identified 1515 references (May 6, 2021). After removing the duplicates the number was 1101. Overall 1032 not relevant titles and abstracts was removed through

screening. The eligibility criteria were applied to 69 papers for full-text reading. After thorough analysis, 4 articles were embodied in qualitative synthesis [16,17,23,28]. A flowchart summarizing this systematically selection process is shown in Figure 1.

#### **Study characteristics**

The included studies [16,17,23,28] were conducted in Italy, Poland, and Switzerland, those being published between the years of 2014 to 2018. Sample sizes ranged from 45 to 90 patients, resulting in a total of 254 participants.

With exception of one study, that did not specify participants' gender [23], all studies included both males and females. Two studies allowed smokers as participants [16,28], while for two studies smoking was considered an exclusion criterion [17,23]. Exceptionally in one study [28], analgesics were prescribed. Additional intervention to haemostasis and/ or pain management applying haemostatic sponge [17] or haemostatic sponge-associated with cyanoacrylate [16] was performed. Three studies determined the postoperative pain through VAS [16,17,28], while one manuscript indirectly evaluated the pain based on

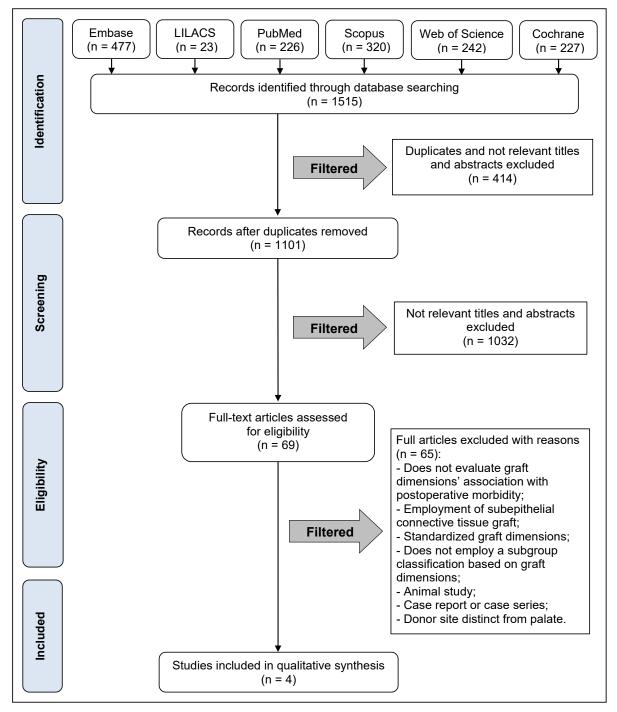


Figure 1. Flow diagram of literature search and selection criteria (adapted from PRISMA).

the mean of analgesics intake [9] (Table 4).

## **Risk of bias within studies**

According to JBI Critical Appraisal Checklist for RCTs tool, the methodological quality of RCTs studies was classified as high by one study [11] and moderate by one manuscript [23] (Table 5). Considering non-randomized studies, the methodological quality was judge as high by one study [28] and moderate by one manuscript [17] (Table 6). The most concerning points regarding the

non-randomized studies were: lack of a control group for both studies (there was just different groups, but it was not settled which was considered as control) [17,28]; just one measurement of postoperative discomfort [17].

## **Results of individual studies**

Burkhardt et al. [28] in a prospective non randomized clinical trial described 90 patients for different periodontal and peri-implant plastic surgeries requiring palatal epithelized graft harvesting.

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**Table 4**. Summary of descriptive characteristics of included studies (n = 4)

Study	Year of	Type of	Country	Gra	ft dimension gro (n)	oups	Graft	Donor site	Outcome	Main findings	
·	publication	study		Thickness	Height	Width	measurement	treatment	measurements		
Tavelli et al. [11]	2018	Randomized clinical trial	Italy	≤ 1.5 mm; > 1.5 mm	≤ 4 mm; > 4 mm	< 14 mm; ≥ 14 mm	Periodontal probe	Haemostatic porcine absorbable sponge alone or associated with tissue adhesive	Visual analog scale analysis on days 1, 2, 3, 4, 5, 6, 7, 10, and 14 postoperative	Graft width minor than 14 mm was related to less visual analog scale pain (days 3, 4, 6, 7, 10, and 14, $P < 0.05$ ). Height and thickness did not show significant difference for perceived pain (P = 0.05)	
				≤ 2 mm		$\leq 10 \text{ mm} \\ (n = 20)$			Pain visual analog scale analysis on day 7 postoperative		
Wyrębek et al. [17]	2018	Prospective non- randomized	Poland	(n = 30); > 2 mm (n = 30)	Not evaluated	10  to  20  mm (n = 20)	Periodontal probe	Haemostatic sponge		Graft length and thickness did not influence the VAS pain	
						$\geq 20 \text{ mm}$ $(n = 20)$					
Zucchelli et al. [23]	2014	Randomized clinical trial	Italy	$\geq 2 \text{ mm}$ (n = 30); < 2 mm (n = 30)	Equal to bone dehiscence (n = 30); 4  mm (n = 30)	Not evaluated	Periodontal probe	Equine-derived collagen and suture	Postoperative pain indirectly evaluated, on day 7, based on the mean analgesic intake	Pain killer consumption was higher for bigger grafts group (P < 0.01)	
Burkhardt et al. [28]	2015	Prospective non- randomized	Switzerland	$\leq 1 \text{ mm}$ (n = 16); 1.01 to 2 mm (n = 49); > 2 mm (n = 25)	Not evaluated	Not evaluated	Ultrasonic device and periodontal probe	Gauze soaked in saline and a 15% ferric sulphate solution in case of bleeding	Visual analog scale analysis on days 1, 3, 7, 14, 21, and 28 postoperative	From day 1 until day 7 the visual analog scale pain values were directly related to the increase of the graft thickness. The reduction of the graft thickness to less than 2 mm reduced the visual analog scale pain values by more than a half at the postoperative days 1, 3, and 7 (P < 0.05)	

N = number of group population, VAS = visual analog scale.

Table 5. Methodological quality assessment summary of author's judgments for each included study, assessed by the Joanna Briggs Institute
Critical Appraisal Checklist for randomized clinical trials

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total (% score yes)	Methodological quality
Tavelli et al. [11]	Y	Y	Y	U	Y	Y	N	Y	Y	Y	Y	Y	Y	84.61%	High
Zucchelli et al. [23]	Y	Y	Y	U	U	U	Y	U	Y	Y	Y	Y	Y	69.23%	Moderate

Y = yes; N = no; U = unclear.

Total =  $\Sigma Y$ /applicable items (the not applicable (NA) items were excluded from the sum).

Methodological quality was categorized as low when the study reaches up to 49% score "yes", moderate when the study reached 50% to 69% score "yes", and high when the study reached more than 70% score "yes".

**Table 6.** Methodological quality assessment summary of author's judgments for each included study, assessed by the Joanna Briggs Institute

 Critical Appraisal Checklist for non-randomized clinical trials

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total (% score yes)	Methodological quality
Wyrębek et al. [17]	Y	Y	N	N	N	Y	Y	Y	Y	66.66%	Moderate
Burkhardt et al. [28]	Y	Y	N	N	Y	Y	Y	Y	Y	77.77%	High

Y = yes; N = no; U = unclear.

Total =  $\Sigma Y$ /applicable items (the not applicable (NA) items were excluded from the sum).

Methodological quality was categorized as low when the study reaches up to 49% score "yes", moderate when the study reached 50% to 69% score "yes", and high when the study reached more than 70% score "yes".

The authors organized the graft thickness in  $\leq 1$  mm, 1.01 to 2 mm, and > 2 mm groups. The VAS pain was collected after the intervention on days 1, 3, 7, and 14. The highest pain perception was observed on the first postsurgical day and decreased over time. On day 1, for each millimeter of graft thickness increase, the VAS pain value increased by 15.6 units. A one-millimeter increase in graft thickness increased the VAS value by 17.66 units on day 3. On day 7, an increase of the VAS pain values of 11.29 units by each additional millimeter of graft thickness was observed. Therefore, graft thickness was directly correlated with the amount of pain perceived (P < 0.001) after 1-, 3-, and 7-days following graft harvesting.

Tavelli et al. [16] included 44 patients randomly distributed into the following groups: suture + haemostatic sponge (Spongostan); and suture + haemostatic sponge + cyanoacrylate tissue adhesive + PeryAcryl). (Spongostan Regarding graft dimensions, grafts with less than 14 mm of width demonstrated less pain perception (P < 0.05) for both groups on days 3, 4, 6, 7, 10, and 14. Furthermore, in general, no correlation was observed between the height, or the thickness of the harvested graft, and the VAS pain results (P > 0.05). However, when the height was  $\leq 4$  mm, less VAS pain was observed on day 3, while graft thickness  $\leq 1.5$  mm promoted less pain on days 6 and 7.

Wyrebęk et al. [17], in a prospective non randomized clinical trial, assessed data from 60 patients divided

into 3 groups according to the graft length (group L1:  $\leq 10$  mm, group L2: 10 to 20 mm, and group L3:  $\geq 20$  mm) and into 2 groups depending on the graft thickness (group T1:  $\leq 2$  mm, and group T2: > 2 mm). Pain at the donor site was evaluated using a VAS scale 7 days postoperatively. No differences were demonstrated in the postoperative pain concerning the graft length or thickness (P > 0.05).

Zucchelli et al. [9], in this randomized clinical trial, included 60 patients with aesthetic and/or hypersensitivity complaints due to the presence of single type gingival recession. Miller class I and II ( $\geq$  3 mm in depth) and divided into 2 groups according to the length of the graft: G1 thickness of  $\geq$  2 mm and the height equal to bone dehiscence (Big graft group); and G2 thickness < 2 mm and 4 mm height (small graft group). The pain was indirectly evaluated on day 7, based on the mean of analgesics intake. The greater analgesic assumption was observed in patients treated with bigger grafts (P < 0.01).

## Synthesis of results

The postoperative pain was determined using VAS in three studies [16,17,28], while the evaluation was performed indirectly based on the mean of analgesics intake in one study [9].

Burkhardt et al. [28] evaluated the postoperative pain on days 1, 2, 3, 7, 14, 21, and 28, while Tavelli et al. [16] performed the evaluations on days 1, 2, 3, 4, 5, 6, 7, 10, and 14. The evaluations were performed after 7 days postoperative by Zucchelli et al. [9] and Wyrębek et al. [17]. In summary, three of the four included studies [16,23,28] found that bigger grafts, evaluated by its thickness (> 2 mm) [23,28] or by its width ( $\geq$  14 mm) [16] were related to more postoperative pain than smaller grafts [9,16,17].

#### **Risk of bias across studies**

The certainty of evidence was considered moderate according to the GRADE criteria for postoperative pain. Inconsistency was judged to be serious due clinical and methodological heterogeneity among studies for both study design. The assessment of certainty of evidence is presented in Table 7.

#### DISCUSSION

Autogenous soft tissue grafts are undeniably beneficial at periodontal and peri-implant clinical practice. However, the patient pain management is a major concern since the palatal graft harvesting may affect daily and work routines, causing stress, discomfort, and concerns. The present systematic review aimed to critically appraise available literature concerning the dimensional influence of the epithelialized tissue graft harvested from the palate in the postoperative pain. Herein, in summary, the tendency that bigger grafts increase the postoperative pain was observed. Therefore, understanding and anticipating the postoperative pain as a response to a graft extension may assist some clinical decisions regarding the surgical periodontal and peri-implant planning and the postoperative guidelines.

When considering the philosophy of minimally invasive dentistry [29], it could be postulated that the necessity of soft tissue graft should be prevented always when possible. Whereas, identifying susceptible patients for gingival recessions and the evaluation of modifiable risk exposures are mandatory to develop adequate action plans [ $\underline{30}$ ]. Complementary, for dental implant placement, when anatomic conditions are favourable (e.g. enough keratinized mucosa and bone dimensions), proper treatment planning and precise surgical execution can avoid the necessity of soft tissue grafting procedures [ $\underline{31,32}$ ]. However, when prevention is not possible and major periodontal defects and complex anatomic deficiencies are found, soft tissue grafts are mandatory [ $\underline{33}$ ].

Within this context, several strategies have been investigated to reduce postoperative morbidity. Positive results have been demonstrated when palatal wound coverage is performed with platelet-rich fibrin [15], ozonated oils [34], topical erythropoietin [35], oral flurbiprofen spray [36], hyaluronic acid [37], and cyanoacrylate [13], among others. Techniques have also been described as alternatives to reduce patient postoperative morbidity. For example, in order to remove subepithelial connective tissue graft, the single incision technique has been demonstrated to significantly reduce early healing, compared to trap-door approach [38]. On the other hand, Zucchelli et al. [9] compared the employment of CTG harvesting through the trap door technique with the de-epithelialization of FGG and no differences were observed on postoperative pain between the techniques.

Alternatively, the employment of non-autogenous materials has been proposed, such as allografts, xenografts, and synthetic soft tissue substitutes. Those major advances on bioengineering would be not just morbidity reduction, but also the unlimited graft availability [33]. In this regard, collagen matrices have been employed to substitute soft periodontal and peri-implant tissues [39,40]. Although favourable results have been demonstrated, the volume gain is usually lower than when conventional matrices are employed, compared to autogenous soft tissue graft [39]. On the other hand, a randomized clinical trial demonstrated comparable results between autogenous CTG and volume-stable collagen matrix on crestal and buccal volume at dental implants [40].

Table 7. GRADE summary of finding	gs
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Certainty assessment									
Number of studies	Outcome	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Certainty	
2	Postoperative pain	Randomized clinical trials	Not serious	Serious <sup>a</sup>	Not serious	Not Serious	None	Moderate	
2	Postoperative pain	Non-randomized clinical studies	Not serious	Serious <sup>a</sup>	Not serious	Not Serious	None	Moderate	

<sup>a</sup>Presence of clinical and methodological heterogeneity.

GRADE = grading of recommendations assessment, development, and evaluation.

It is important to highlight that even though postoperative morbidity reduction is desired, the results obtained on the present systematic review are based on studies that showed a big heterogeneity among each other, not allowing the performance of a meta-analysis. Suggesting the classification standardization of graft dimensions, taking in consideration thickness, height and width for future researches (Table 2) [16]. Moreover, risk of bias was considered moderate to high on some investigations included. Methodological issues such as groups randomization should be further improved on future research about this theme. It is important to highlight that the only study that has not found statistical influence of graft dimensions on pain perception was a non-randomized study that employed just one postoperative measurement (after one week) [17].

Zuchelli et al. [9] have been shown that the height of the graft may positively affect patient discomfort, however not all the articles included in the present systematic review confirm this correlation [<u>11,16</u>]. A possible explanation may be the differences of the graft harvested dimensions. Nevertheless, no matter the dimensions of the harvested area, the palatal donor area seems to create postoperative pain [9]. However, as demonstrated by Zucchelli et al. [9], patient suffering and discomfort following EGG harvesting techniques can be successfully controlled if properly managed, improving wound healing, decreasing patient distress and in consequence patients are more willing to receive treatment [9,11,16,17,28].

Regarding the limitations of this systematic review,

it should be highlighted the lack of graft measurement standardization observed in included studies. Additionally, it is important to mention that not all the included studies prescribed analgesic, as well as some studies evaluated the postoperative pain in smoker patients. Also, some studies performed additional procedures to promote haemostasis and pain control. Therefore, further RCTs shall be performed evaluating the dimensional influence of palatal epithelized tissue graft increasing the methodological quality.

## **CONCLUSIONS**

Based on the moderate certainty level, bigger graft sizes of palatal epithelized harvesting appear to promote more postoperative pain. Further randomized clinical trials shall be performed evaluating the dimensional influence of palatal epithelized tissue graft increasing the methodological quality.

## ACKNOWLEDGMENTS AND DISCLOSURE STATEMENTS

This study was not supporter by any funding. Mário Escobar, Renata Scheeren Brum, Karin Apaza Bedoya, and Patrícia Pauletto were supported with scholarship by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) (Coordination for the Improvement of Higher Education Personnel), Brazil.

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#### To cite this article:

Escobar M, Scheeren Brum R, Apaza-Bedoya K, Pauletto P, Benfatti CAM, Cruz ACC, Henriques BAPC. Dimensional Influence of Epithelialized Tissue Graft Harvested From Palate on Postoperative Pain: a Systematic Review J Oral Maxillofac Res 2022;13(3):e1 URL: <u>http://www.ejomr.org/JOMR/archives/2022/3/e1/v13n3e1.pdf</u>

doi: <u>10.5037/jomr.2022.13301</u>

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#### Appendix 1. Database search strategy, May 15<sup>th</sup>, 2022

Database	Search	Results
Cochrane Library	(Palate OR Palates OR palatal) AND ("Connective Tissue" OR "Connective Tissues" OR "Gingival Recession" OR harvest OR "connective tissue graft" OR "free gingival graft" OR mucogingival OR "soft tissue graft" OR CTG OR FGG OR "peri-implant" OR periodontal OR "masticatory mucosa" OR "Gingival Retraction Techniques" OR Gingiva OR Gums OR Gum) in Title Abstract Keyword AND dimension OR dimensions OR length OR measurement OR thickness OR height OR thin OR thick OR width in Title Abstract Keyword AND Pain OR comfort OR discomfort OR Morbidities OR Bleeding OR Hemostasis OR Hemorrhage OR healing OR epithelization OR "re-epithelization" OR "non-healing" OR wound in Title Abstract Keyword - in Trials (Word variations have been searched)	
Embase	(('palate'/exp OR palate OR palates OR palatal) AND ('connective tissue' OR 'connective tissues' OR 'gingival recession' OR harvest OR 'connective tissue graft' OR or 'free gingival graft' OR mucogingival OR 'soft tissue graft' OR ctg OR fgg OR 'peri-implant' OR periodontal OR 'masticatory mucosa' OR 'gingival retraction techniques' OR gingiva OR gums OR gum)) AND ('dimension'/exp OR dimension OR dimensions OR 'length'/exp OR length OR 'measurement'/exp OR measurement OR 'thickness'/exp OR thickness OR 'height'/exp OR height OR thin OR thick OR 'width'/exp OR width) AND ('pain'/exp OR pain OR 'comfort'/exp OR comfort OR 'discomfort'/exp OR discomfort OR 'morbidity'/exp OR morbidities OR 'bleeding'/exp OR bleeding OR 'hemostasis'/exp OR hemostasis OR 'hemostasis OR 'hemostasis' OR 'hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis'/exp OR hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis'/exp OR hemostasis OR 'hemostasis'/exp OR hemostasis'/exp OR he	
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PubMed	(("Palate"[Mesh Terms] OR "Palate"[Title/Abstract] OR "Palates"[Title/Abstract] OR "palata"[Title/Abstract]) AND ("Connective Tissue"[Mesh Terms] OR "Connective Tissue"[Title/Abstract] OR "Gingival Recession"[Title/Abstract] OR "Gingival Recession"[Mesh Terms] OR "harvest"[Title/Abstract] OR "connective tissue graft"[Title/Abstract] OR "free gingival graft"[Title/Abstract] OR "mucogingival"[Title/Abstract] OR "soft tissue graft"[Title/Abstract] OR "CTG"[Title/Abstract] OR "FGG"[Title/Abstract] OR "peri-implant"[Title/Abstract] OR "periodontal"[Title/Abstract] OR "masticatory mucosa"[Title/Abstract] OR "Gingival Retraction Techniques"[Mesh Terms] OR "harvest"[Title/Abstract] OR "FGG"[Title/Abstract] OR "Gingiva"[Mesh Terms] OR "Gingival Retraction Techniques"[Mesh Terms] OR "Gingiva"[Mesh Terms] OR "Gingival Retraction Techniques"[Mesh Terms] OR "Gingiva"[Mesh Terms] OR "Gingival Retraction Techniques"[Mesh Terms] OR "Gingival Retraction Techniques"[Title/Abstract] OR "Gingival"[Title/Abstract] OR "Gingival Retraction Techniques"[Mesh Terms] OR "Gingival Retraction Techniques"[Title/Abstract] OR "Gingival Retraction Techniques"[Title/Abstract] OR "height"[Title/Abstract] OR "heigh	
Scopus	(TITLE-ABS-KEY(Palate OR Palates OR palatal) AND TITLE-ABS-KEY("Connective Tissue" OR "Connective Tissues" OR "Gingival Recession" OR harvest OR "connective tissue graft" OR "free gingival graft" OR mucogingival OR "soft tissue graft" OR CTG OR FGG OR "peri-implant" OR periodontal OR "masticatory mucosa" OR "Gingival Retraction Tech- niques" OR Gingiva OR Gums OR Gum)) AND TITLE-ABS-KEY(dimension OR dimensions OR length OR measurement OR thickness OR height OR thin OR thick OR width) AND TITLE-ABS-KEY(Pain OR comfort OR discomfort OR Morbidities OR Bleeding OR Hemostasis OR Hemorrhage OR healing OR epithelization OR "re-epithelization" OR "non-healing" OR wound)	
Web of Science	TS=("root canal therapiy" OR "root canal therapies" OR "root canal treatment" OR "root canal treatments" OR "endodontic treatment" OR "endodontic therapy" OR "root canal filling" OR "root canal obturation" OR "root canal obturations" OR "Endodontic Obturation" OR "root canal filling" OR "root canal filling" OR "root canal obturation" OR "periapical healing" OR "periapical health" OR "tooth survival" OR "nonsurgical root canal treatment") AND TS=("tomography" OR "tomographies" OR "cone beam" OR "cone beams" OR "periapical radiography" OR "periapical radiography" OR "radiographies" OR "X-Ray" OR "X-Rays" OR "radiologic exam" OR "radiologic exams" OR "radiographic") AND TS=("success" OR "successful" OR "Clinical Effectiveness" OR "Clinical Efficacy" OR "Treatment Effectiveness" OR "Gingival Recession" OR harvest OR "connective tissue graft" OR "free gingival graft" OR mucogingival OR "soft tissue graft" OR CTG OR FGG OR "peri-implant" OR periodontal OR "masticatory mucosa" OR "Gingival Retraction Techniques" OR Gingiva OR Gums) AND TOPIC: (dimension OR dimensions OR length OR measurement OR thickness OR height OR thin OR thick OR width) AND TOPIC: (Pain OR comfort OR discomfort OR discomfort OR dimensions OR length OR measurement OR thickness OR height OR thin OR thick OR width) AND TOPIC: (Pain OR comfort OR discomfort OR discomfort OR Morbidities OR Bleeding OR Hemostasis OR Hemorrhage OR healing OR epithelization OR "re-epithelization" OR "non-healing" OR wound)	•