One-Year Outcomes of a Piscine Soft Tissue Alternative Used in Mucogingival Procedures: A Clinical Case Series

The free gingival graft (FGG) has been used predictably for gingival procedures aimed to increase the width of keratinized tissue (KT). Several soft tissue alternatives, such as xenografts and allografts, have been studied and proven to be successful with varying degrees. This pilot clinical case series evaluated the efficacy, safety, and initial clinical outcomes (measuring KT width) of a piscine xenograft material (Omega3 Wound, Kerecis) compared to the FGG (harvested from the patient palate) in correcting mucogingival deformities around teeth. A convenience sample of six subjects with unilateral or bilateral lack of KT were enrolled in the study. The primary objective of this pilot study was to determine the gain in width of KT. Secondary objectives included investigating the probing depth, recession depth, bleeding on probing, and inflammation score. There were three FGG sites and six xenograft sites. In bilateral-site treatments, FGG or piscine xenograft were randomly assigned. For unilateral sites, the piscine xenograft was used. Postoperatively, the patients returned for follow-up at 1, 2, 4, 12, 24, 48, and 52 weeks. All six subjects completed the 12-month study and reported uneventful healing. On average, the xenograft sites had a 3.25-mm gain in KT width, and the FGG had an average gain of 3.67 mm. This pilot clinical series showed the piscine xenograft to be safe and efficacious during healing and to increase the width of KT. Future studies may include a more robust study design with a greater number of subjects. Int J Periodontics Restorative Dent 2020;40:603–609. doi: 10.11607/prd.4165

Due to its high predictability of success, the free gingival graft (FGG) is a procedure that is frequently used to correct mucogingival deformities and increase the width of keratinized tissue (KT) around teeth.\(^1,2\) Although this procedure is predictable, there are some limitations, including, morbidity, limited supply of the graft, possible complications during surgery, and esthetic concerns.\(^3\)

In order to overcome these limitations, soft tissue alternatives that lead to effective outcomes have been developed.\(^4\) In prosthesis cases, Nevins and Skurow reported that the minimum width of KT should be 3 mm.\(^5\) Clinicians also need to consider each specific clinical situation in order to plan treatment for increases in KT (eg, implant therapy and orthodontics). Although studies have demonstrated that the absence of attached KT still allows for the maintenance of periodontal health, the presence of a thin biotype may facilitate the development of a mucogingival defect.\(^6\)

In the present study, the authors used a new xenograft material derived of piscine origin (Omega3 Wound, Kerecis) to correct mucogingival deformities instead of the well-known soft tissue alternatives derived of porcine or bovine that were referenced previously.\(^1,7\) Omega3 Wound is a piscine acellular
dermal matrix and has been used as an effective tissue regenerating material in the medical field. One of the advantages is that it does not transmit any diseases to humans during the healing process. This material has been used successfully in the healing of acute and chronic wounds (diabetic foot ulcer and nonhealing leg wounds of other varieties). In addition, the piscine graft includes anti-inflammatory and antimicrobial factors (omega-3 polyunsaturated fatty acids, eicosapentaenoic acid, and docosahexaenoic acid) and creates an environment that allows the subject’s cells to repopulate. An additional benefit for populations in the Muslim and Hindu religious groups could be the source of the material compared to materials derived from bovine/porcine. Limited data reports that piscine acellular dermal matrix was used in previous cases to provide safe and effective wound healing and decreased the healthcare cost in the medical field. The use of piscine xenograft in oral applications needs to be explored as an alternative xenograft. The objective of this pilot clinical case series was to determine the 1-year safety and effectiveness outcomes of the piscine material in terms of increasing the width of KT compared to FGG. The primary outcome measure was the increase in KT width and the secondary outcome measures were the changes in probing depths, recession, and bleeding on probing at 6 and 12 months. The outcomes were compared to a limited sample of FGG procedures in some of the subjects recruited for this clinical case series.

Material and Methods

Study Participants

This clinical study received ethical approval from the Multidisciplinary Institute of Dental Specialties (Guadalajara, Jalisco, Mexico). All participants signed an informed consent form to participate in the 1-year study. To be included in the study, subjects had to be at least 18 but no more than 65 years of age and have at least two nonadjacent teeth in contralateral sides of the same arch (maxilla or mandible) with an insufficient zone (≤ 1 mm) of KT that required soft tissue grafting. If the adjacent teeth needed grafting, then only one tooth at each site was the test or control site. Subjects treated for medical conditions, hypersensitivity to fish, or any acute lesions in the areas of the intended surgery were excluded. In addition, subjects who were smokers were excluded.

Study Design

This pilot clinical case series included a convenience sample. Three subjects had bilateral mucogingival deformities, which allowed for the comparison of the test (piscine xenograft Omega3 Wound) and control (FGG harvested from the patient’s palate) treatment modalities. Three subjects had unilateral mucogingival deformities and were included for the test sites only. For the three subjects with bilateral defects, each subject had their two sites randomly assigned to receive either Omega3 Wound as the donor material or an FGG using donor tissue harvested from the same treatment side of the palate. The control and test sites for each subject were assigned by a predetermined computer-generated randomization scheme for the treatment assignments (test vs control). This information was contained in sealed envelopes to ensure there was no bias. The envelopes were marked with unique sequential subject identification numbers and contained the following items: treatment assignment for Study Site 1, treatment assignment for Study Site 2, and order of treatment administration (Omega3 Wound first or FGG first). The study teeth on the subject’s right side corresponded to Study Site 1. The study teeth on the subject’s left side corresponded to Study Site 2. For participants who had unilateral lesions, only Omega3 Wound was used. There were nine study sites in total, including three FGG sites and six piscine xenograft sites.

Study Outcomes

Patients were seen at 1, 2, 4, 12, 24, 48, and 52 weeks postoperatively. The change in KT width from time zero (day of surgery) to the final postoperative visit (12 months postoperative) was the primary outcome measure. The clinical examination at 6 months included the use of iodine solution to determine the location of the mucogingival junction. The secondary measures included changes in the clinical attachment level, probing depths, recession, and bleeding on probing.
Fig 1  Overview of the unilateral surgical procedure (piscine xeno-graft treatment) within a 24-week follow-up. (a) Initial presentation. (b) Periosteal bed preparation. (c) Soft tissue alternative adapted to the recipient bed. (d) Soft tissue alternative sutured. Follow-ups at (e) 1 week; (f) 4 weeks; and (g and h) 24 weeks, (g) without and (h) with iodine solution to highlight mucogingival and KT changes.
Surgical Procedures

For the piscine xenograft material, standard of care was used with specific recommendations for the material preparation and placement on the periosteal bed as instructed by the manufacturer (Figs 1 and 2). The FGG followed the standard of care procedure protocol (Fig 3). Resorbable sutures were used for the stabilization of the gingival grafts, and a periodontal dressing was applied. Postoperatively, patients were given instructions and prescriptions for antimicrobial rinse (chlorhexidine gluconate 0.12%), antibiotics (500 mg amoxicillin tid for 8 days), and analgesics (1 g acetaminophen or 400 mg ibuprofen). The sutures were removed 1 week after the procedure.

Results

All six participants who entered the study completed the 12-month follow-up visits. Three participants were treated for unilateral deformities and three participants for bilateral deformities. The average age of the participants was 54 years. All participants were Hispanic, non-smoking women. The nine sites treated for mucogingival deformities were located in the mandible. All participants attended the scheduled postoperative visits and reported having followed the provided instructions.

The healing reported was within normal limits, with no complications or adverse reactions. In addition, there were no symptoms of acute or chronic infection. The participants in the FGG group reported minor discomfort for the palatal surgical site. The FGG and piscine xenograft materials remained in place in all cases. The exposed piscine xenograft was replaced by KT within the first few postoperative weeks and maintained its stability through the 12-month follow-up. From the 2-week visit to the 12-month follow-up, an increase in the width...
of KT was noticed for all treated sites. FGG had an average gain of 3.67 mm for KT width, and piscine xenograft sites had an average gain of 3.25 mm (Table 1). As noticed in Fig 2, the piscine xenograft material presented with an esthetic outcome, overcoming one of the limitations of the FGG group.

**Discussion**

In this pilot case series study, the use of a new piscine xenograft successfully resulted in an average gain in KT width of 3.25 mm with no complications or adverse reactions. This amount has been reported adequate by the literature to maintain long-term periodontal health around natural dentition.\(^5\) Within the first postoperative weeks, KT slowly replaced the exposed piscine xenograft and maintained its stability throughout the 12-month follow-up.

Xenograft as a soft tissue alternative has been shown to successfully increase the width of KT to varying degrees. A previous study by McGuire et al (2008) successfully investigated how to enhance the width of KT using tissue-engineered bilayer cell therapy. Their study had a 6-month follow-up period instead of a 12-month follow-up period as seen in the present study.\(^11\) McGuire and Nunn (2005)\(^12\) conducted a study that investigated another soft tissue alternative: human fibroblast-derived dermal substitute (HF-DDS). That study had a similar 12-month follow-up period like that of the present study. However, a 3.25-mm increase in the width of KT was reported in the current study, whereas a 2.4-mm gain was reported when using HF-DDS. McGuire et al (2014 and 2011)\(^13,14\) completed two other studies investigating the use of a collagen matrix material compared

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**Fig 3** Overview of the bilateral surgical procedure (control site) within a 52-week follow-up of the FGG procedure. (a) Initial presentation. (b) The FGG adapted to the recipient bed. Follow-ups at (c) 1 week, (d) 12 weeks, (e) 24 weeks, and (f) 52 weeks.
to the FGG, similar to the current study. The outcomes showed that both treatments were tolerated by the patients, but there existed a preference towards the test treatment compared to the standard graft treatment, similar to the current study.

Harris completed a study that resulted in an increase in KT width using three different techniques. Patients reported more postoperative pain at the palatal donor site, which is similar to the results of pain at the donor surgical site reported by subjects in the current study. The follow-up period was also shorter, so that must be taken into consideration when comparing the results. The current study was able to determine outcome stability over a 1-year period vs the shorter 3-month period in Harris’s study.

A study by Nevins et al (2010) used an extracellular matrix membrane as an alternative material to FGG. That material is obtained from the small intestine of pigs. There may be advantages and disadvantages to the various xenograft materials that are available for clinicians. Disease transmission can be a general concern for xenografts (eg, bovine spongiform encephalopathy and porcine endogenous retroviruses). The piscine xenograft has no chance of disease transmission, is safe and efficacious, and resulted in initial positive clinical outcomes. A future, more robust study can be performed to confirm clinical outcomes. Lastly, there may be patients who refuse treatments based on religious grounds, and the piscine xenograft can be an alternative. Nevins et al (2011) also investigated a mucograft collagen matrix, instead of an FGG, as an alternative material for the xenograft. The study determined that this material was a viable alternative for the aforementioned graft, similar to previous studies that investigated the effectiveness of FGG alternatives. Results from these studies suggest that having two surgical sites is less preferred by patients than having one surgical site.

Multiple studies report on the successful clinical outcomes of using soft tissue alternatives to increase the width of KT and correct mucogingival deformities around teeth. However, the majority of the alternatives are derived from bovine and porcine species, and that might be a limitation for some patients with specific religious considerations. In addition, the possible risk of viral transmission should be considered. This piscine soft tissue material can be a viable alternative for those patients. Compared with other xenograft materials, the piscine alternative handled relatively well, was not friable during suturing, and it did not tear. The cost of each procedure with the different materials and techniques should also be considered, specially since this piscine xenograft material has been reported to reduce costs in the medical field. Omega3 Wound also promises that this piscine material is effective for wound closure compared to previous extracellular matrices, which is a further benefit. Piscine material is also used to reduce the risk of diseases derived from materials made from porcine matrices. Other advantages include a faster healing process and a better ecologic footprint for the piscine material compared to the material made from livestock. In addition, Dorweiler et al reported a faster healing process that led to an increase in patient satisfaction after using the Kerecis Omega3 Wound matrix.

While the clinical outcomes of this study are promising, some limitations should be considered. One limitation is the small sample size, since only nine surgical sites were part of the study. This soft tissue alternative is not recommended for any patients with known hypersensitivity to fish or any piscine products.

### Table 1 Effect of Both Treatment Methods on the Width of Keratinized Tissue Over Time

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Measurements are recorded in millimeters.
Future studies should include a diverse population, including subjects from various backgrounds and a larger sample size. In addition, future studies can compare different xenograft materials and determine how the outcomes differ after a minimum 12-month period.

Conclusions

This pilot clinical series showed the piscine xenograft to increase the width of KT and be safe and efficacious during healing. Omega3 Wound piscine xenograft might be an alternative graft material that could be used as a substitute for FGG for patients who need to increase their KT width and who have mucogingival deformities. Future studies may include a more robust study design with an increased number of subjects.

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References