Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 6, 2021, Pages. 9568 - 9582
Received 25 April 2021; Accepted 08 May 2021.

Comparison between Use of Perforated and Non-Perforated Collagen Membrane Using Guided Tissue Regeneration Technique for Management of Infrabony Defects – A Clinical and Radiographic Study

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Abstract

Aim: The study aimed to evaluate the effectiveness of perforated collagen membranes in comparison with non-perforated collagen membranes for guided tissue regeneration of infrabony defects.

Materials and Methods: A total of 30 intrabony defects that is 30 sites were randomly selected for the study. 10 infrabony defects each were treated using open flap debridement with the placement of nonperforated membrane, using open flap debridement with a placement perforated membrane and using open flap debridement in Groups A, B and C.

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Results: Intragroup comparison showed statistically significant difference from baseline to 9 months in nonperforated membrane and perforated membrane ($p<0.05$) for clinical and radiographical parameters. However, there was no statistically significant difference seen with open flap debridement for clinical and radiographical parameters. ($p>0.05$) Intergroup comparison did not show any statistically significant difference from baseline to 9 months in nonperforated membrane and perforated membrane ($p>0.05$) for clinical and radiographical parameters.

Conclusion: In conclusion, the present study did not demonstrate any enhanced clinical outcomes when using open flap debridement with the placement of nonperforated membrane, with a perforated membrane and using open flap debridement alone procedures.

Keywords: nonperforated membrane,perforated membrane, GTR, Regeneration

Introduction

Early tooth loss is due to progressive bone and attachment loss which is caused by aninfectious disease called Periodontitis. At the time of destructive periodontal disease,connective tissue attachment of the tooth is destroyed which leads to the pocket formationand is associated with alveolar bone resorption.[1] Complete regeneration of the functionalattachment apparatus has remained a difficult goal of periodontal therapy. Presently, byutilizing various regenerative procedures such as bone grafting, GTR techniques, andcombination therapy major progress has been made to achieve this end.[1,2]

Several treatment agreements have been introduced withassumptions that they might activate periodontal regeneration which includes various surgicalapproaches, adjunct root conditioning schemes, implantation of allogenic, alloplastic bonesubstitutes with or without application of barrier devices used alone or in combination.[3,4]It has beenshown that a barrier membrane (i.e. GTR) eliminates epithelial downgrowth as well as allowsperiodontal ligament and alveolar bone cells to repopulate the isolated space selectively whenplaced over the denuded root surfaces and the debrided periodontal defect. An environment offollowing a periodontal flap procedure and placement of a biocompatible barrier, allows cellsfrom the periodontal ligament to selectively repopulate a debrided root surface and form anew periodontal attachment, created by the process of guided tissue regeneration. Toovercome some of the disadvantages of non-resorbable barriers, previously studiedevaluation of GTR occupied different resorbable membranes. Furthermore, bioresorbablebarriers not only eliminate the need for a second surgery but also reduce the combineddisturbances to the

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newly formed osteoid which may result in bone resorption.[5]As limited studies in relation to this topic have been conducted, the objective of this studywas to analyze and evaluate the regenerative potential of perforated collagen membrane witha non-perforated collagen membrane using guided tissue regeneration for the management ofinfrabony defects.

Materials and Methods

30 patients between 25-60 years of age with chronic periodontitis were selected from the OutPatient Department (OPD) of Periodontics and Oral Implantology of Saraswati DhanvantariDental College And Hospital, Parbhani for this ethically approved prospective parallel-arm controlled clinical trial. The study and the procedure performed was explainedto the patients; a proforma designed for this study was filled, and written informed consentwas taken.

The patients were included if their probing pocket depth was ≥ 5mm following initial therapy, interproximal angular infrabony defects were of ≥3mm, demonstrated acceptable oral hygiene before access flap surgery and agreed to sign an informed consent and willing to return for the follow-upvisits. They were excluded if they had any systemic disease which would alter the clinical outcome, used of tobacco in any form, had no history of a previous periodontal surgery on a specified site for the last 6 months.

Pre-surgical procedure and Grouping

A total of 30 intrabony defects that is 30 sites were randomly selected for the study.10 infrabony defects each were treated using open flap debridement with the placement of nonperforated membrane, using open flap debridement with a placement perforated membrane and using open flap debridement in Groups A, B and C.

Thorough scaling and root planing were performed withhand, rotary and ultrasonic instruments in all treated sites. Intra-oral antisepsis wasevaluated. Patients fulfilling the criteria for defects were appointed for surgery.Acrylic stents were fabricated for the selected sites. These acrylic stents were madeof uniform thickness with a groove placed in the line of interproximal defect,

adjacent to the study tooth. This groove was used as a fixed reference point forstandardized measurements at baseline, 3, and 6 months post-operatively. The preparation of perforated collagen membrane was done by making perforations justbefore surgery using a custom-

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made acrylic template, leaving a coronal occlusiverim of ~3mm. This was followed by manually perforating 0.5 to 1 mm diameterround holes at a distance of 2mm from occlusal edge throughout the membrane.

Group wise surgical procedure

1) Group A: Under local anesthesia, buccal and lingual crevicular incisions were givenusing a surgical blade, and mucoperiosteal flaps were reflected. Interproximal softtissue was preserved as much as possible. Thorough defect debridement and rootplaning were carried out with ultrasonic instruments and area-specific curettes, andthe site will be irrigated. Placement non-perforated resorbable membrane andprimary closure were obtained by 4-0 vicryl resorbable suture.

2) Group B: Same procedure as done for Group A was carried out for access flapsurgery in this group under local anesthesia. The defect was managed by placing aperforated the resorbable membrane covering the defect. Primary closure wasobtained by 4-0 vicryl resorbable suture.

3) Group C: Same procedure as done for Group A was carried out for access flapsurgery under local anesthesia. After debridement primary closure was obtained by4-0 vicryl resorbable suture.

Post-surgical protocols

The periodontal dressing was given in all 3 groups. Suitable antibiotics and analgesics wereprescribed along with Chlorhexidine digluconate rinses (0.2%) twice daily for 14 days.Periodontal dressing and sutures were removed at the end of 1 week for group C and 2weeks for group A and group B. Surgical wounds was gently cleansed with 0.2%Chlorhexidine digluconate. Patients were instructed regarding proper oral hygiene measures.

Patients were examined at 3, 6, and 9 months after surgery. Supragingival scaling wasperformed at these intervals if required. No subgingival instrumentation was attempted atany of these appointments.Soft tissue measurements were repeated with previously used custom acrylic stentsand the UNC-15 probe. For hard tissue re-evaluation, a second RVG (with the samestandardization as the baseline) using a radiographic grid was carried out, and infrabony

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defect measurement was repeated at the end of 3, 6, and 9 months.All clinical measurements like plaque index, gingival index, pocket probing depth and clinical attachment level were recorded with the help of the UNC-15 probe and an acrylicstent. A groove was made at the chosen interdental site in the acrylic stent to reproduce theposition and direct the probe entry into the site and. The radiographic measurements included osseous defect depth reduction(defect height and defect width) and percentage of bone fill.

Statistical Analysis

The data were analyzed with Statistical Package for Social Sciences (SPSS) for Windows 26.0 (SPSS, Inc. Chicago, Illinois). Confidence intervals were set at 95% and values of $p < 0.05$ were interpreted as statistically significant. Descriptive statistics were used to calculate numbers and percentages for demographic details. Repeated measures ANOVA was used to check the significance of the difference in mean plaque index, gingival index, probing pocket depth, clinical attachment level, linear bone growth, and percentage bone fill at baseline, 3 months, 6 months, and 9 months. Further Bonferroni's post hoc analysis was carried out to compare intragroup group differences. Unpaired t-test was applied to compare two groups for plaque index, gingival index, probing pocket depth, clinical attachment level, linear bone growth, and percentage bone fill at baseline, 3 months, 6 months, and 9 months.

Results

Table 1 shows age and gender details. Intragroup comparison showed statistically significant difference from baseline to 9 months in nonperforated membrane and perforated membrane ($p<0.05$) for clinical and radiographical parameters. However, there was no statistically significant difference seen with open flap debridement for clinical and radiographical parameters. ($p>0.05$) Intergroup comparison did not show any statistically significant difference from baseline to 9 months in nonperforated membrane and perforated membrane ($p>0.05$) for clinical and radiographical parameters.(Table 2,3,4) Graph 1, 2 and 3 shows mean values of plaque index, gingival index and percentage bone fill.

Discussion

Regenerative therapy refers to modalities used to treat periodontal disease to reconstructperiodontium and supporting structures destroyed due to the disease process. Sites withlesions are at a higher risk of disease progression in subjects who had not receivedperiodontal treatment.[6]Bioresorbable membranes have been developed to avoid the

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need for surgical removal. Suchmembranes have been extensively studied, mainly in animals but also in humans inmaxillofacial, regenerative periodontal, and neuro-surgery.[7-13]There are two broad categories of bioresorbable membranes:the natural and the synthetic membranes. Natural membranes are made of collagen orchitosan, whereas synthetic products are made of aliphatic polyesters, primarily poly(L-lactide) (PLLA) and poly(L-lac-tide-co-glycolide) (PLGA) copolymers. Placement of a barrier membrane to cover debrided periodontal defects in GTRprocedures was proved to exclude epithelial down growth and allowed selective repopulationof the isolated space with the periodontal ligament and alveolar bone cells.[14,15] However, it hasbeen debated that barrier membranes deprive the wound area of the regenerative potential ofthe periosteum, including progenitor cells and biologic mediators.[16]

The present study aimed to evaluate the effectiveness of perforated collagen membranes incomparison with non-perforated collagen membranes for guided tissue regeneration ofinfrabony defects. The study was a randomized parallel-arm controlled clinical andradiographic study carried over a period of 12 months. The demographic data showed anequal distribution of defect type amongst individuals, also there was an equal distribution ofage and gender (10 females and 20 males) with the mean age being 38.7 + 10.5. Out of 30patients, 33.4% were females and 66.6% were males. This depicts a successful randomizationprocess. A total of 30 individuals participated in the study. 1 site in each individual wasselected with voluntary consent in the study.

Comparison between PPD scores of the non-perforated membrane and perforated membraneat baseline, 3 months, 6 months, and 9 months post-operatively did not show a statisticallysignificant difference. Comparison between PPD scores of the non-perforated membrane andopen flap debridement at baseline, 3 months, 6 months and 9 months post-operatively did notshow any statistically significant difference respectively. Comparison between PPD scores ofthe perforated membrane and open flap debridement at baseline, 3 months, 6 months and 9months post-operatively did not show a statistically significant difference.

Resorbable perforated barriers have proven to achieve better PD reduction, CAL gain, anddefect fill than open-flap debridement and certain cases as compare to nonperforatedmembrane too.This is agreement done in the past. The concept of porous guided tissuemembrane has been tested recently as a modality that could stimulate the bone

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formation ofcritical-sized bone defects. Kim et al in 2012 claimed that asymmetrically porous guidedbone regeneration membranes with dual bone morphogenetic protein-2 and ultrasoundstimulation may be promising for the clinical treatment of delayed and insufficient bonehealing.[17] For GTR in periodontal therapy, membrane perforations could allow for gingivalstem cells and periosteal cells to take part in supracrestal regeneration. The perforated sectionof the membranes would stabilize supracrestal fibrin clots through the mechanicalinterlocking of fibrin strands, with the membrane pores providing more membrane and clotstability. It has been suggested that regenerative failures may result when the tensile strengthof the fibrin clot is exceeded, resulting in a tear and a long junctional epithelium-typeattachment.[18] Mobility of the flap (wound margin) positioned directly adjacent to the potentialregenerative site may be a potential cause of this tear.[19] Placement of a perforated membranecould allow for more flap stability through membrane pores–gingival CT integration fromone side and membrane pore-clot integration from the opposing side. In addition, the authorshypothesized that early gingival CT–root surface adhesion achieved by membraneperforations would eventually provide additional protection against epithelial downgrowth.

Guided tissue membrane applications are usually indicated to treat intrabony defects thatprotect the blood clot or the clot blended with graft material and provide the defect area withthe necessary elements required for regeneration. Supracrestal periodontally affectedcomponents are usually lacking regenerative power because of their anatomic limitations asnon-contained defects bordered by epithelial-covered gingival CT from one side and aperiodontally affected avascular root surface from the opposing side. Complete isolation ofthe supracrestal part of the defects with a non-perforated membrane coverage will eventuallylead to root surface epithelialization. The use of the perforated membrane will allow gingivalCT cells and periosteal cells to repopulate the supracrestal part of the root surface. In theabsence of epithelium via the occlusive collar, supracrestal healing will eventually occur byeither connective attachment to the root surface via gingival CT and fibroblast–root surfaceadhesion or enhanced true periodontal regeneration if the gingival stem cells are stimulatedby surgical trauma. Mesenchymal stem cells were found to display chemotactic propertiessimilar to immune cells in response to tissue insult and inflammation, thus exhibiting tropismfor the sites of injury via the production of anti-inflammatory cytokines and anti-apoptoticmolecules.[20-22] Postlethwaite et al., in 1978, showed that different types of collagen,including Type I, possessed chemotactic properties for human fibroblasts.[23]

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A study byGrinell et al. showed that human fibroblasts, cultured on hydrated collagen gels, did notdegrade the collagen, but instead extended numerous filopodia into the collagen matrix.[24]Nishikawa and co-workers found in cell cultures that aged collagen gel caused morefibroblast spreading and increased DNA synthesis.[25] These studies demonstrate that in vitroconditions, a collagen matrix is biocompatible to fibroblasts and can favorably influencecertain cellular activities observed in the culture systems.

Intergroup comparison of CAL score for all three group at baseline,3,6,9months showedstatistically significant reduction in overall scoreComparison between CAL scores of the non-perforated membrane and perforated membraneat baseline, 3 months, 6 months, and 9 months post-operatively did not show a statisticallysignificant difference. Comparison between CAL scores of the non-perforated membrane andopen flap debridement at baseline, 3 months, 6 months, and 9 months post-operatively didshow any statistically significant difference. Comparison between CAL scores of theperforated membrane and open flap debridement at baseline, 3 months, 6 months, and 9months post-operatively did not show a statistically significant difference.Machtei reported that, if proper preoperative and postoperative anti-infective care isprovided, membrane infection can be controlled and good regenerative results obtained.[26] Thepresent study reveals that perforated membrane treated sites showed no statisticallysignificant improvement in PD reduction compared with the nonperforated membrane controlgroup. Nonperforated membrane group, CAL improvement is in agreement with theconclusions of a systematic review by Parrish et al in 2009 that showed that intrabonydefects treated with perforated barriers without grafting materials resulted in a mean CALgain of 2.44 mm, with a range of 2.0 to 2.58 mm.[27] Perforated membrane single therapyattachment gain reported in the present study were superior to that of the reportednonperforated membrane CAL gain and comparable to that of the collagen barriers with graftmaterial of the same systematic review in which a mean CAL gain of 3.48 mm, with a rangeof 2.3 to 4.1 mm, was reported.[27] These findings support the hypothesis that it was thepresence of the perforated membrane that allowed gingival CT population to the root surface,contributing positively to improving CAL. Furthermore, Wikesjo in 1999 demonstrated thatgingival CT invasion to membrane perforations may contribute to wound stability, which is acrucial factor for obtaining periodontal regeneration.[28] This may also be the reason why alesser gain in CAL was observed in the control group relative to the perforated membrane.

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Comparison between linear bone growth score for non-perforated membrane and perforatedmembrane at 3 months, 6 months, and 12 months post-operatively did not show a statisticallysignificant difference. Comparison between linear bone growth score of the non-perforatedmembrane and open flap debridement at 3 months, 6 months, and 12 months post-operativelydid not show a statistically significant difference. Comparison between linear bone growthscore of the perforated membrane and open flap debridement at 3 months, 6 months, and 12months post-operatively did not show a statistically significant difference.Inter group comparison of bone fill score at baseline and 3,6 and 9 months for all 3 groups isstatistically non-significant.

Comparison between bone fill score of the nonperforated membrane and open flapdebridement at baseline, 6 months and 12 months post-operatively did not show a statisticallysignificant difference. Comparison between bone fill score of the perforated membrane andopen flap debridement at baseline, 6 months and 12 months post-operatively did not show astatistically significant difference for perforated membrane and open flap debridementrespectively.The significant reduction in bone defects with no significant difference between the threestudy groups nonperforated membrane, perforated membrane, and open flap debridementrevealed that reported a similar level of intrabony defect base protection. However, thesignificantly higher crestal bone level that was reported in the perforated membrane groupwhen compared with that of the nonperforated membrane group at both observation periodscould reflect the enhanced osteogenic effect of periosteal active charity through membraneperforations in contrast to periosteal isolation by the nonperforated membrane. Yadav et al.reported crestal bone resorption of 0.5 mm at 6 months after the use of nonperforatedmembranes for treating intrabony defects.[29]

The results of the study were in agreement with those found in the other comparable studies.[30-32]With slightly lower bone growth and bone fill values, For example, in a study whereperforated and non-perforated barrier membrane,the percentage of defect fill in intraosseousdefects in the Guillemin study was 58% in the control group and 71% in the test group.[30]This can be explained by the fact that open probing new attachment was used to evaluatethe defect fill within furcation areas, a technique conducted by most investigators.[33] Thismethod measures both soft or hard tissues around the original defect after the flap is reflectedat reentry surgery. Therefore, when open probing new attachmentis used in evaluating thedefect fill, the results should be better, since the measurement was taken from

the new softtissue instead of from the hard tissue. In contrast, this study measured only newly formedhard tissue.

Limitations of this study include a small sample size and a relatively short study period. Alonger follow-up period (more than 12 months) and a larger sample size with an experimentaldesign including flap surgery alone (negative) control, bone graft only (positive control),membrane only, and membrane combined with bone graft groups could be beneficial. Due tothe nature of clinical trials and several other factors, these desired conditions were notfeasible. A real difference between treatment groups may have existed if the sample size hadbeen larger. Hence, further study with larger sample size is needed. An additionalincremental study is currently being conducted to answer some further questions.

Conclusion

Complete regeneration of the functional attachment apparatus has remained a difficult goal ofperiodontal therapy. Presently, by utilizing various regenerative procedures such as bonegrafting, GTR techniques, and combination therapy major progress has been made to achievethis end. The current status of new attachment therapy, which seems to be supported by sound prior research, suggests that clinicians who employ it accomplish a new dentogingival junction of a long epithelial attachment, backed up by healthy collagenous connective tissue, which is functional and maintainable for a long time. The key to success is the attention to hygienic measures.

Conflict of Interest: None
Funding: None

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Tables

Table 1: Demographic Details

		Number	Percentage (%)	Mean ±SD
Gender	**Female**	10	33.4	-
	Male	20	66.6	
Age (in years)	**16 - 25**	16	53.3	38.7 ± 10.5
	36 – 55	14	46.7	

SD: Standard Deviation

Table 2: Comparison of Probing Pocket Depth in all the Groups

Probing Pocket Depth	Nonperforated membrane	Perforated membrane	Open Flap Debridement
Baseline	8.5 ± 1.4	9.1 ± 0.9	9.7 ± 1.0
3 Months	4.8 ± 0.7	4.3 ± 0.6	4.5 ± 0.5

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6 Months	4.7 ± 0.6	4.8 ± 0.6	6.2 ± 0.7
9 Months	4.4 ± 0.5	4.9 ± 0.5	6.0 ± 0.6
F-value	33.37	82.65	66.76
p-value	0.001*	0.001*	0.5

Repeated measures ANOVA, p<0.05 significant

Table 3: Comparison of Clinical Attachment Level in all the Groups

Clinical Attachment Level	Nonperforated membrane	Perforated membrane	Open Flap Debridement
Baseline	8.9 ± 1.2	9.6 ± 0.8	9.9 ± 0.8
3 Months	4.8 ± 0.7	4.3 ± 0.6	4.7 ± 0.4
6 Months	4.7 ± 0.6	5.0 ± 0.6	6.3 ± 0.8
9 Months	4.4 ± 0.5	5.0 ± 0.6	6.2 ± 0.9
F-value	52.38	98.68	71.25
p-value	0.001*	0.001*	0.4

Repeated measures ANOVA, p<0.05 significant

Table 4: Comparison of Linear Bone Growth in all the Groups

Linear Bone Growth	Nonperforated membrane	Perforated membrane	Open Flap Debridement
3 Months	4.8 ± 0.7	4.3 ± 0.6	4.7 ± 0.4
6 Months	4.7 ± 0.6	5.0 ± 0.6	6.3 ± 0.8
12 Months	4.4 ± 0.5	5.0 ± 0.6	6.2 ± 0.9
F-value	1.0	3.64	21.9
p-value	0.001*	0.05*	0.3

Repeated measures ANOVA, p<0.05 significant

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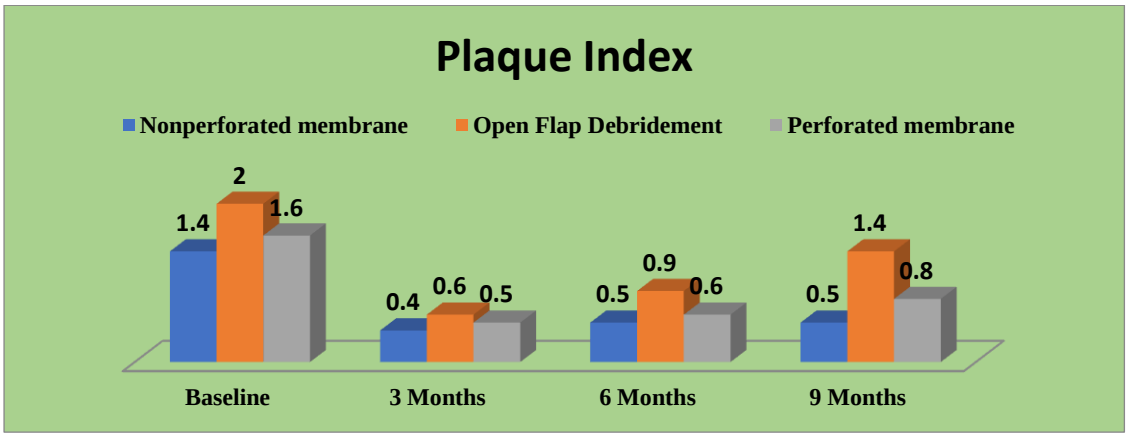
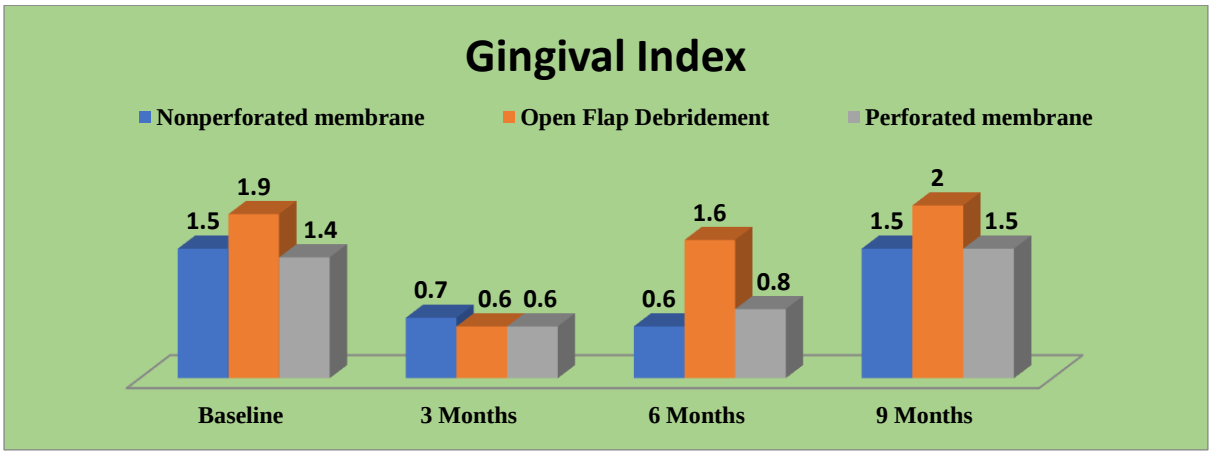
Graph 1: Comparison of Mean Values of Plaque Index in all the groups



Graph 2: Comparison of Mean Values of Gingival Index in all the groups



Graph 3: Comparison of Mean Values of Percentage Bone Fill in all the groups