

Colour Doppler Ultrasonographic Evaluation of Vascular Healing Dynamics After Endodontic Surgery Using Platelet-Rich Fibrin and Chorion Membranes: A Randomized Controlled Trial

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Research Article

Keywords: angiogenesis, chorion membrane, colour Doppler imaging, endodontic surgery, periapical healing, platelet-rich fibrin

Posted Date: June 30th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10035351/v1>

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Additional Declarations: No competing interests reported.

Abstract

Objectives

This study evaluated periapical healing and vascular response following endodontic surgery with platelet-rich fibrin and chorion membranes in combination with hydroxyapatite graft. Healing was assessed using ultrasonography and colour Doppler imaging.

Materials and Methods

This randomized controlled trial included 48 patients needing endodontic surgery for single-rooted front teeth with periapical lesions between 8 and 20 mm. Patients were divided into three groups: one received only hydroxyapatite graft, another received platelet-rich fibrin membrane with hydroxyapatite, and the third received chorion membrane with hydroxyapatite. All patients underwent the same surgical steps: cleaning, root-end removal, ultrasonic preparation, and filling with mineral trioxide aggregate. Ultrasonography and colour Doppler imaging were performed at baseline, 1 month, and 6 months. The researchers measured lesion surface area, volume, and peak systolic velocity.

Results

All groups demonstrated marked decreases in lesion surface area and volume over time. After 6 months, intergroup differences in surface area and volume reduction were not statistically significant. The chorion membrane group exhibited the greatest numerical reduction in lesion size and a substantially higher peak systolic velocity at 6 months.

Conclusions

Both platelet-rich fibrin and chorion membranes facilitated periapical healing when combined with hydroxyapatite graft. The chorion membrane group demonstrated a stronger vascular response on Doppler imaging; however, superiority for hard-tissue healing was not established.

Clinical Relevance

Colour Doppler ultrasonography offers a non-ionising modality for evaluating vascular healing following endodontic surgery.

Introduction

Apical periodontitis is an inflammatory disease of the periradicular tissues caused mainly by microbial infection within the root canal system. Persistent microbial stimulation activates the host immune response, resulting in cytokine release, osteoclast activation, periodontal ligament destruction, and progressive periapical bone resorption [1, 2].

Most periapical lesions heal after adequate nonsurgical root canal treatment. However, endodontic surgery may be required when persistent apical periodontitis remains after previous treatment, when retreatment is not feasible, or when anatomical and restorative factors prevent complete orthograde disinfection. Contemporary endodontic surgery aims to eliminate periapical pathology, resect the root end, prepare a retrograde cavity, and seal the apical root canal system with a biocompatible material [3, 4].

Healing after periapical surgery is influenced by lesion size, cortical plate integrity, surgical debridement, the quality of the apical seal, the host response, and the regenerative environment. Large defects and through-and-through lesions may heal less predictably because of epithelial migration and inadequate space maintenance. Guided tissue regeneration has been proposed to support healing by preventing epithelial downgrowth and allowing selective repopulation by osteogenic and periodontal ligament cells [5–7].

Hydroxyapatite is an osteoconductive bone graft material that provides a scaffold for bone formation but does not function as a biologically active barrier membrane or provide sustained release of regenerative mediators [8–11]. Platelet-rich fibrin is an autologous fibrin matrix containing platelets, leukocytes, and growth factors that may support angiogenesis, cellular migration, wound healing, and osteogenic differentiation [12–17]. Chorion membrane is a placental-derived biological membrane containing extracellular matrix components and growth factors and has been reported to possess anti-inflammatory, antimicrobial, immunomodulatory, and angiogenic properties [18–24].

Although biologic membranes have been evaluated in periapical surgery, interpretation of clinical outcomes is often limited by small sample size, short follow-up, and reliance on radiographic hard-tissue endpoints [5, 20, 21, 25, 26]. Conventional radiographic techniques are useful for evaluating mineralized tissue repair but provide limited information on early vascular events. Ultrasonography with colour Doppler imaging is a non-ionising modality that can evaluate lesion dimensions and vascular signals, providing additional information on healing dynamics [27–30].

This randomised controlled trial evaluated periapical healing after endodontic surgery using hydroxyapatite grafts alone, a platelet-rich fibrin membrane with hydroxyapatite, and a chorion membrane with hydroxyapatite. The primary objective was to assess lesion volume reduction, while the secondary objective was to evaluate lesion surface area reduction and vascular response using colour Doppler imaging. The null hypothesis stated that there would be no difference among the three groups in lesion volume reduction, lesion surface area reduction, or peak systolic velocity.

Materials and Methods

Study Design and Ethical Approval

This was a parallel-group, three-arm randomized controlled clinical trial with a 1:1:1 allocation ratio. The study was conducted in the Department of Conservative Dentistry and Endodontics in collaboration with

the Department of Radiodiagnosis, King George's Medical University, Lucknow, India.

The study protocol was approved by the Institutional Ethics Committee of King George's Medical University, Lucknow, India, under approval number ECR/262/Inst/UP/2013/RR-19. Written informed consent was obtained from all participants before enrolment. The trial was registered with the Clinical Trials Registry of India: CTRI/2024/02/062461. The manuscript was prepared in accordance with CONSORT principles for randomized controlled trials.

Participants

Patients aged 18–40 years who required endodontic surgery for single-rooted anterior teeth with a periapical radiolucency measuring 8–20 mm were screened for eligibility.

The inclusion criteria were persistent periapical pathology involving single-rooted anterior teeth, lesion size between 8 and 20 mm, and willingness to attend follow-up visits.

The exclusion criteria were refusal to participate, systemic diseases that could influence healing, diabetes mellitus, hypertension, hepatitis, HIV infection, autoimmune disorders, malignancy, pregnancy, history of radiotherapy or chemotherapy, periodontally compromised teeth, and cases requiring surgical retreatment.

Sample Size

The sample size was calculated based on a previous randomized clinical trial evaluating periapical healing after endodontic surgery [26]. With a significance level of 5% and power of 80%, the minimum required sample size was 48 participants, with 16 participants in each group. The primary outcome considered for sample size estimation was the change in periapical lesion volume.

Randomization and Allocation Concealment

Participants were randomly allocated to one of three groups using a computer-generated random sequence prepared by an independent investigator not involved in recruitment, treatment, or outcome assessment. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes. The envelope was opened only after enrolment and immediately before the surgical procedure.

Blinding

Because of the nature of the intervention, the operating surgeon could not be blinded. Participants, the radiologist performing ultrasonographic and colour Doppler assessments, and the statistician analysing the data were blinded to group allocation.

Interventions

Participants were allocated into the following groups:

Group 1: Hydroxyapatite graft alone

Group 2: Platelet-rich fibrin membrane with hydroxyapatite graft

Group 3: Chorion membrane with hydroxyapatite graft

All surgical procedures were performed by a single experienced endodontist using a standardized protocol. Local anaesthesia was administered, and a full-thickness mucoperiosteal flap was raised. The periapical lesion was exposed, granulation tissue was curetted, and the osseous defect debrided. Root-end resection was performed, followed by ultrasonic retrograde cavity preparation. The root-end cavity was sealed with mineral trioxide aggregate.

In Group 1, sterile hydroxyapatite bone graft was placed into the osseous defect. In Group 2, platelet-rich fibrin was prepared by centrifuging 10 mL of venous blood at 3000 rpm for 10 minutes. The platelet-rich fibrin clot was compressed into a membrane and placed over the hydroxyapatite graft. In Group 3, dehydrated human chorion membrane was rehydrated in sterile saline for 1 minute and adapted over the hydroxyapatite-filled defect. The flap was repositioned and sutured. The clinical steps and placement of hydroxyapatite, platelet-rich fibrin and chorion membrane are shown in Fig. 1. The materials used in the three groups are shown in Fig. 2.

Ultrasonographic and Colour Doppler Assessment

Ultrasonographic imaging was performed using a high-frequency linear probe. Examinations were done at baseline, 1 month, and 6 months after surgery. Lesion dimensions were measured in three planes, and lesion surface area and volume were calculated. Colour Doppler imaging assessed vascularity. Peak systolic velocity was recorded as a quantitative indicator of vascular response during healing. Representative ultrasonographic and colour Doppler assessment at baseline, 1 month and 6 months is shown in Fig. 3.

Outcome Measures

The primary outcome was reduction in lesion volume at 6 months.

Secondary outcomes were reduction in lesion surface area and change in peak systolic velocity at 1 month and 6 months. Adverse events were recorded throughout the follow-up period.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics software, version 25.0. Continuous variables were expressed as mean and standard deviation. Baseline comparability among groups was assessed before outcome analysis. Repeated-measures analysis of variance was used to evaluate intragroup changes over time. One-way analysis of variance was used for intergroup comparisons. Post hoc comparisons were performed when appropriate. Categorical variables were analysed using the chi-square test. A p-value less than 0.05 was considered statistically significant.

The analysis was performed on participants who completed the follow-up assessment. Missing follow-up data were not imputed.

Results

Participant Flow and Baseline Characteristics

Forty-eight participants were enrolled and randomly assigned to three groups of 16 each. Forty-six completed the follow-up assessment and were included in the final analysis. Two participants were lost to follow-up. Baseline demographic and clinical characteristics were comparable among the groups, with no statistically significant differences. The participant flow is presented in the CONSORT diagram in Fig. 4.

Surface Area Reduction

Intragroup analysis demonstrated a significant reduction in lesion surface area over time in all three groups. The reduction was significant in the hydroxyapatite group ($F = 37.8, p < 0.001$), platelet-rich fibrin group ($F = 40.3, p < 0.001$), and chorion membrane group ($F = 25.3, p < 0.001$). At 6 months, the chorion membrane group had the highest mean percentage reduction in surface area ($84.28\% \pm 11.04$), followed by the platelet-rich fibrin group ($79.72\% \pm 11.02$) and the hydroxyapatite group ($75.61\% \pm 14.65$). The intergroup difference was not statistically significant ($F = 1.889, p = 0.164$), so superiority of the chorion membrane was not confirmed. The intergroup and intragroup changes in lesion surface area are shown in Fig. 5.

Volume Reduction All groups demonstrated significant reductions in lesion volume over time. The reduction was significant in the hydroxyapatite group ($F = 17.5, p = 0.001$), platelet-rich fibrin group ($F = 14.8, p = 0.002$), and chorion membrane group ($F = 9.5, p = 0.008$). fig6

At 6 months, the chorion membrane group showed the greatest mean percentage volume reduction ($93.90\% \pm 6.32$), followed by the platelet-rich fibrin group ($90.21\% \pm 8.66$) and the hydroxyapatite group ($84.59\% \pm 14.65$). The intergroup difference was not statistically significant ($F = 3.044, p = 0.058$), so superiority of the chorion membrane for volume reduction was not confirmed (Fig 7).

Vascularity Assessment at 1 month, the chorion membrane group showed the highest mean peak systolic velocity (11.72 ± 9.06), followed by the platelet-rich fibrin group (7.44 ± 4.59) and the hydroxyapatite group (5.79 ± 6.81). This intergroup difference was not statistically significant ($F =$

3.010, p = 0.059). The intergroup and intragroup changes in peak systolic velocity are shown in Fig. 8.”

At 6 months, there was a significant intergroup difference in peak systolic velocity ($F = 4.858$, $p = 0.013$). The chorion membrane group showed higher peak systolic velocity (9.31 ± 6.02), suggesting a stronger vascular response during healing.

Intragroup repeated-measures analysis confirmed a significant increase in peak systolic velocity over time in all three groups: hydroxyapatite ($F = 10.0$, $p = 0.007$), platelet-rich fibrin ($F = 12.8$, $p = 0.003$), and chorion membrane ($F = 22.6$, $p < 0.001$).

Adverse Events

No intraoperative or postoperative adverse events were reported during the follow-up period.

Discussion

This randomized controlled trial evaluated periapical healing after endodontic surgery using hydroxyapatite graft alone, platelet-rich fibrin with hydroxyapatite, and chorion membrane with hydroxyapatite. Healing was assessed with ultrasonography and colour Doppler imaging. All groups showed significant reductions in lesion surface area and volume over time. The chorion membrane group had the largest numerical decrease in lesion size and a substantially higher peak systolic velocity at 6 months. However, intergroup differences in lesion area and volume reduction were not statistically significant.

The significant improvement observed in all groups is consistent with the expected healing response after adequate surgical debridement, root-end resection, and placement of a root-end filling material. Modern endodontic surgery aims to eliminate persistent periapical infection, achieve an apical seal, and create conditions favourable for periapical repair [3, 4]. Hydroxyapatite graft likely contributed by acting as an osteoconductive scaffold, supporting bone formation within the periapical defect [8–11].

Guided tissue regeneration has been advocated in endodontic surgery, particularly for large defects or lesions associated with cortical plate loss. Barrier membranes may prevent epithelial migration and support selective repopulation of the defect by cells involved in osseous and periodontal regeneration [5–7]. Previous clinical and systematic evidence suggests that guided tissue regeneration may improve healing in selected periapical surgical defects, although outcomes may vary depending on lesion size, defect morphology, graft material, membrane type, and follow-up duration [5–7, 20, 21].

Platelet-rich fibrin has been used as a bioactive membrane and scaffold in regenerative procedures due to its fibrin network, which releases growth factors over time [12–17]. These growth factors may facilitate angiogenesis, cell migration, and osteogenic differentiation. In this study, the platelet-rich fibrin group demonstrated significant reductions in lesion area and volume over time, supporting its role as an adjunct in periapical surgery. However, platelet-rich fibrin did not show statistically significant superiority

over hydroxyapatite alone for hard-tissue healing outcomes at 6 months. Chorion membrane contains extracellular matrix proteins and biologically active molecules that may support tissue repair, angiogenesis, and wound healing [18–24]. In this study, the chorion membrane group exhibited significantly higher peak systolic velocity at 6 months. This observation suggests a stronger vascular response, which may be biologically relevant since angiogenesis is essential for bone repair and regeneration [21, 22]. Nevertheless, this vascular advantage did not yield a statistically significant intergroup difference in lesion surface area or volume reduction during the 6-month follow-up period. Therefore, these results indicate a potential angiogenic benefit of the chorion membrane rather than confirmed superiority in hard-tissue healing.

A notable strength of this study is the use of ultrasonography with colour Doppler imaging. Conventional radiographic methods effectively evaluate mineralized tissue repair but may not detect early vascular changes during healing. Ultrasonography is valuable for assessing periapical lesions and monitoring healing, while colour Doppler imaging enables visualization of blood flow [27–30]. In this study, Doppler imaging provided additional biological information not available through standard radiography. These findings indicate that colour Doppler ultrasonography can facilitate early monitoring of healing after endodontic surgery. The higher peak systolic velocity observed in the chorion membrane group may reflect increased vascular activity, although this does not confirm superior bone regeneration. As all three interventions supported healing, membrane selection should consider availability, cost, ease of use, patient requirements, and long-term outcomes. This study has some limitations. The sample size was small, so it may not have detected small differences between groups in hard-tissue healing. The follow-up lasted only 6 months, which might not be enough to confirm full bone regeneration. Histological validation was not possible for ethical reasons, and cone-beam computed tomography was not used for 3D assessment. The results may not apply to posterior teeth, multi-rooted teeth, larger defects, or patients with medical conditions. Future multicentre randomized controlled trials should include larger sample sizes, longer follow-up periods, standardized defect classification, and both ultrasonographic and three-dimensional radiographic assessments. Further research should also address patient-centred outcomes, cost-effectiveness, and long-term stability of periapical healing.

Conclusions

In this randomized controlled trial, all three interventions—hydroxyapatite graft alone, platelet-rich fibrin with hydroxyapatite, and chorion membrane with hydroxyapatite—supported periapical healing following endodontic surgery. The chorion membrane group exhibited a substantially higher peak systolic velocity at 6 months, indicating a stronger vascular response. However, intergroup differences in lesion surface area and volume reduction were not statistically significant, and no method demonstrated superiority for hard-tissue healing. Ultrasonography with colour Doppler may serve as a valuable, non-ionising modality for monitoring vascular healing after endodontic surgery.

Colour Doppler ultrasonography is a non-ionising tool for assessing vascular healing after endodontic surgery. It enables clinicians to detect early biological healing before hard tissue changes are evident.

Declarations

Author Contributions

1. **Dr Promila Verma** contributed to the conception and design of the study, clinical supervision, interpretation of data, manuscript revision and final approval of the manuscript.
2. **Dr Mamidala Jyothi** contributed to patient recruitment, clinical procedures, data collection, literature review and manuscript drafting
3. **Dr Rhythm Bains** contributed to patient follow-up, data organization and manuscript preparation..
4. **Dr Anit Parihar** - contributed to ultrasonographic and colour Doppler assessment and interpretation radiological assessment, data interpretation,
5. **Dr Pragya Pandey**- contributed data interpretation, statistical analysis and critical revision of the manuscript.

All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethics Approval

The study was approved by the Institutional Ethics Committee of King George's Medical University, Lucknow, Uttar Pradesh, India.

Ethics approval number: **ECR/262/Inst/UP/2013/RR-19**

Consent to Participate

Written informed consent was obtained from all participants before enrolment in the study.

Consent for Publication

Written informed consent was obtained from the participants for publication of anonymized clinical and imaging data.

Clinical Trial Registration

Clinical Trials Registry of India: **CTRI/2024/02/062461**

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgements

The authors acknowledge the support of the Tata Memorial hospital, Mumbai for availability of Chorion Membrane, Department of Radiodiagnosis for ultrasonographic and colour Doppler evaluation.

Artificial Intelligence Disclosure

Artificial intelligence–assisted technology was used only for language refinement, formatting support and journal-style editing of the manuscript. It was not used for study design, patient recruitment, clinical intervention, data collection, image assessment, statistical analysis or interpretation of primary data. The authors take full responsibility for the accuracy, originality and integrity of the manuscript.

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Tables

Table 1: Intergroup& Intragroup Comparison of Surface Area

Surface Area	Hydroxyapatite		Platelet Rich fibrin		Chorion membrane		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F-value	p-value
Pre Operative	0.79	0.46	1.00	0.56	0.96	0.75	.536	.589
Post Operative 1 month	0.60	0.38	0.74	0.37	0.73	0.49	.532	.591
Post Operative 6 month	0.13	0.07	0.29	0.25	0.16	0.21	2.708	.078
Intragroup (RM ANOVA)	F=37.8, p<0.001		F=40.3, p<0.001		F=25.3, p<0.001			

Table 2: Intergroup & Intragroup Comparison of Volume

Volume	Hydroxyapatite		Platelet Rich fibrin		Chorion membrane		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F-value	p-value
Pre Operative	0.28	0.23	0.34	0.29	0.39	0.58	.301	.741
Post Operative 1 month	0.19	0.17	0.19	0.13	0.26	0.36	.499	.611
Post Operative 6 month	0.02	0.01	0.06	0.07	0.08	0.23	.677	.513
Intragroup (RM ANOVA)	F=17.5, p=0.001		F=14.8, p=0.002		F=9.5, p=0.008			

Table 3: Intergroup Comparison of % Surface Area and Volume Change

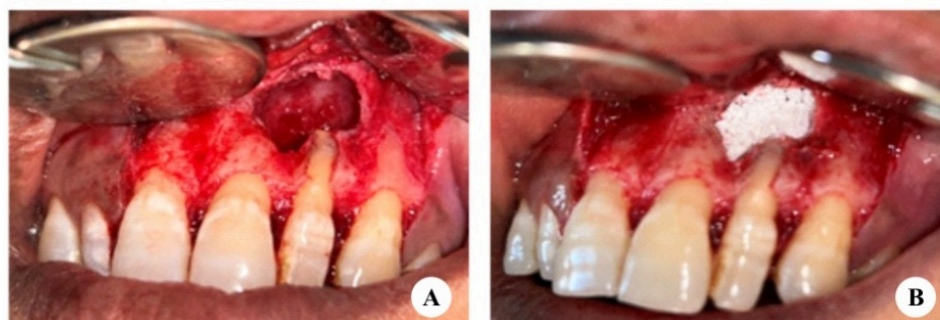
% change	Hydroxyapatite		Platelet Rich fibrin		Chorion membrane		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F-value	p-value
Surface area	75.61	14.65	79.72	11.02	84.28	11.04	1.889	.164
Volume	84.59	14.65	90.21	8.66	93.90	6.32	3.044	.058

Table 4: Intergroup & Intragroup Comparison of PSV

PSV	Hydroxyapatite		Platelet Rich fibrin		Chorion membrane		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F-value	p-value
Pre Operative	-0.21	5.28	-0.12	5.79	2.25	4.07	1.195	.312
Post Operative 1 month	5.79	6.81	7.44	4.59	11.72	9.06	3.010	.059
Post Operative 6 month	4.96	3.73	5.64	1.35	9.31	6.02	4.858	.013
Intragroup (RM ANOVA)	F=10.0, p=0.007		F=12.8, p=0.003		F=22.6, p<0.001			

Figures

Group I : Hydroxyapatite



Group 2 : Platelet Rich Fibrin



Group 3 : Chorion Membrane



Figure 1

Intra-operative photographs showing periapical defect preparation and placement of hydroxyapatite graft, platelet-rich fibrin membrane and chorion membrane in the respective groups.



Figure 2

Clinical materials used in the study: hydroxyapatite bone graft, platelet-rich fibrin preparation and activated chorion membrane.

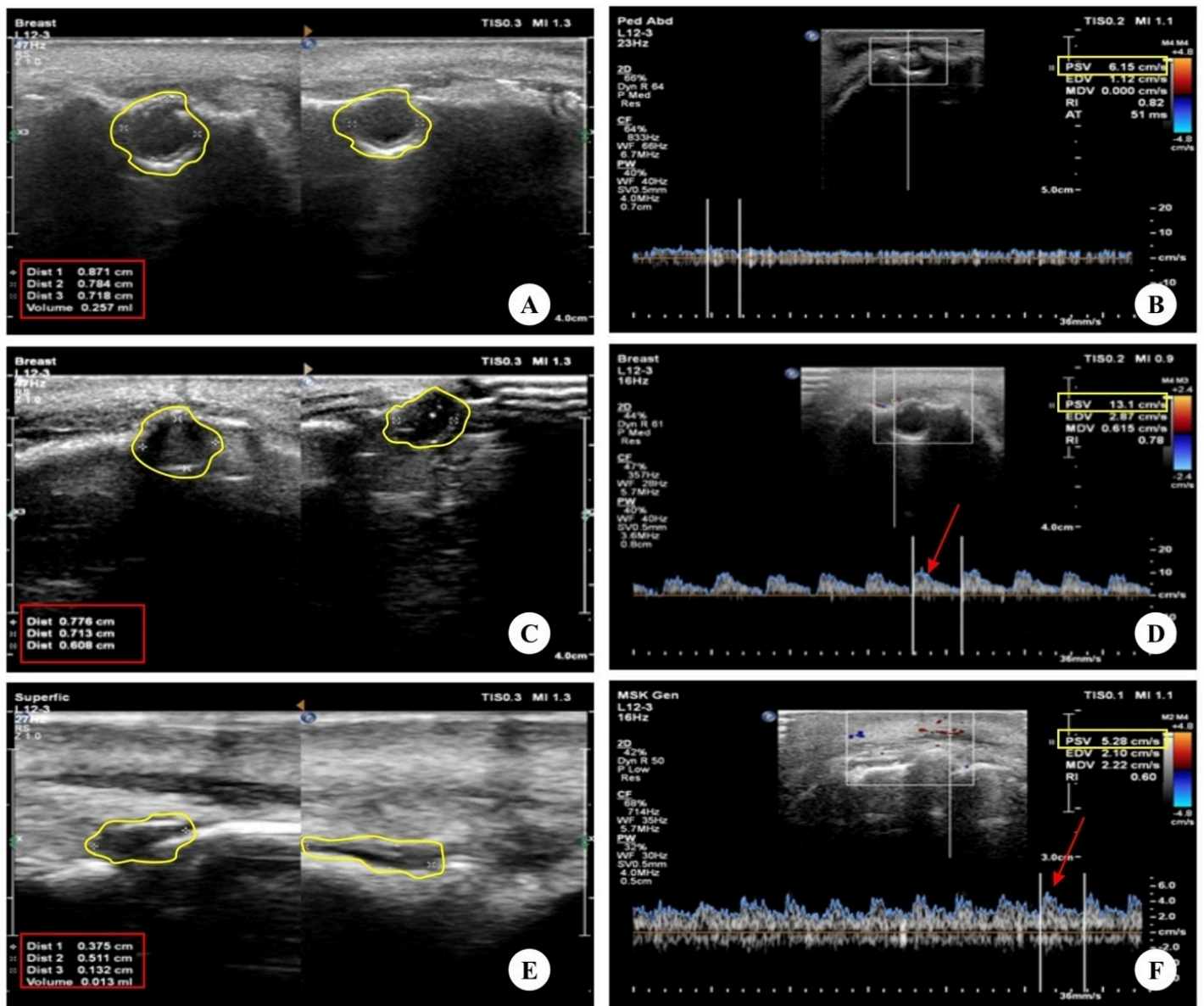


Figure 3

Representative ultrasonographic and colour Doppler images at baseline, 1 month and 6 months showing changes in periapical lesion dimensions and vascular response.

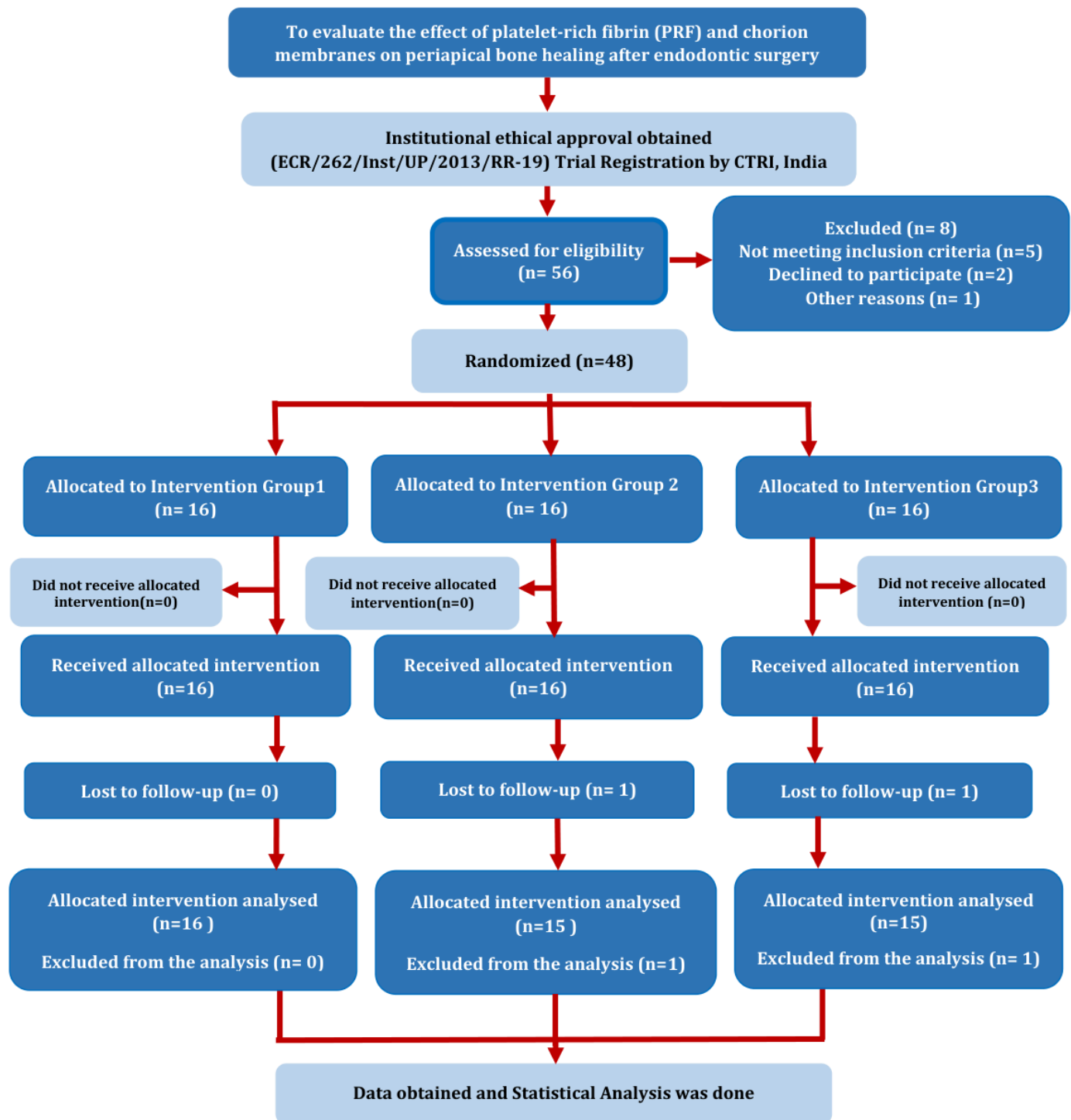


Figure 4

CONSORT flow diagram showing participant enrolment, allocation, follow-up and analysis.

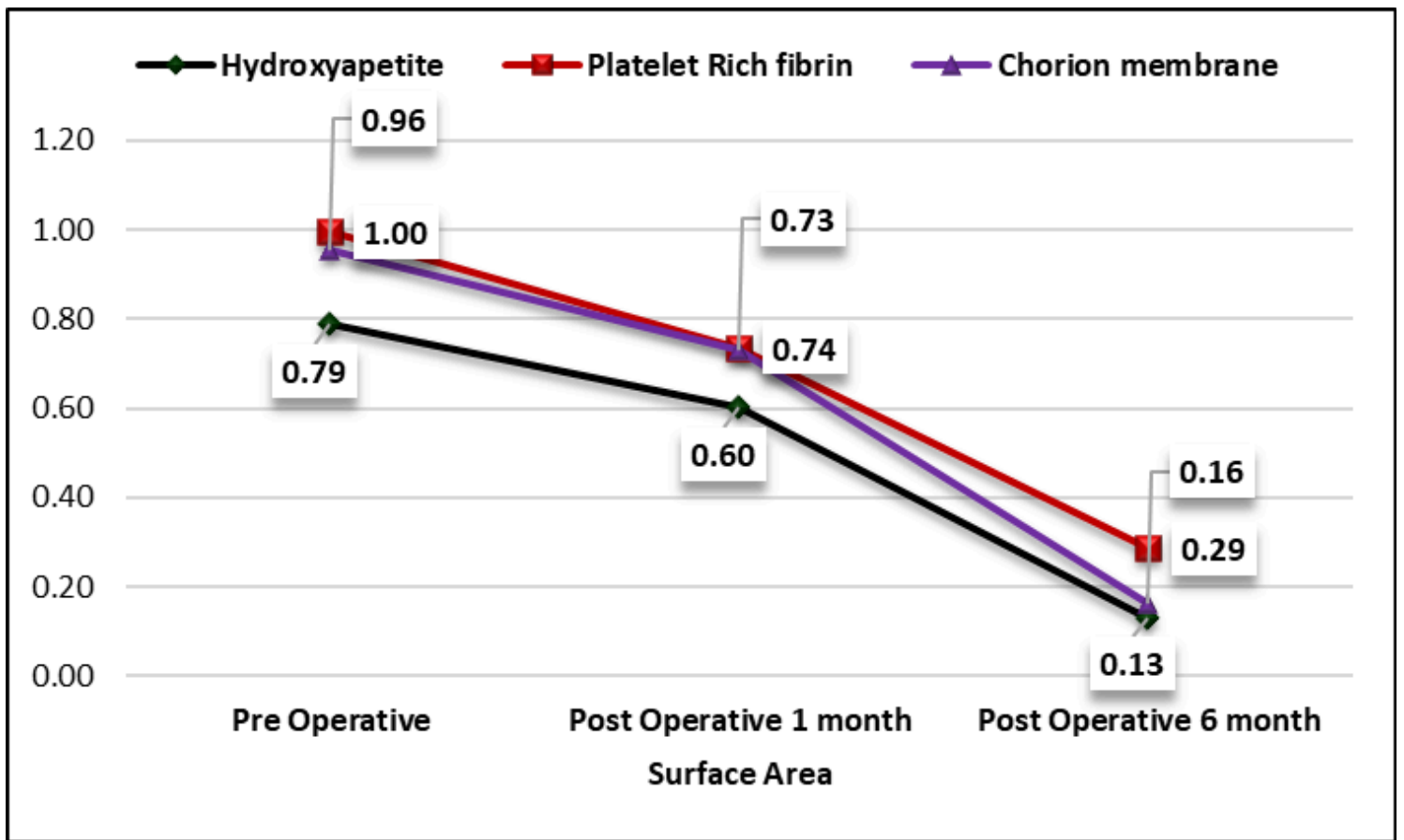


Figure 5

Intergroup and intragroup comparison of lesion surface area at baseline, 1 month and 6 months.

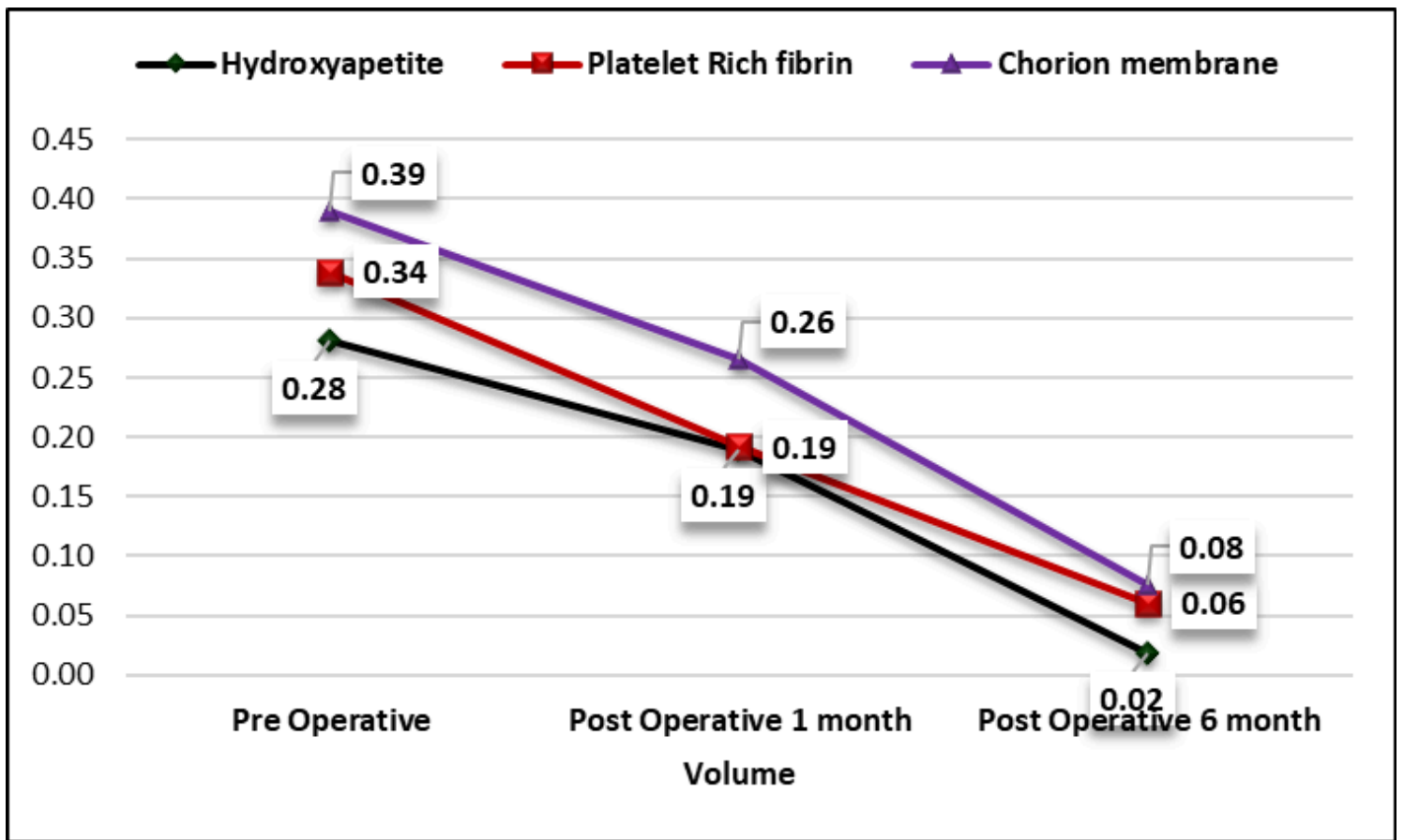


Figure 6

Intergroup and intragroup comparison of lesion volume at baseline, 1 month and 6 months.

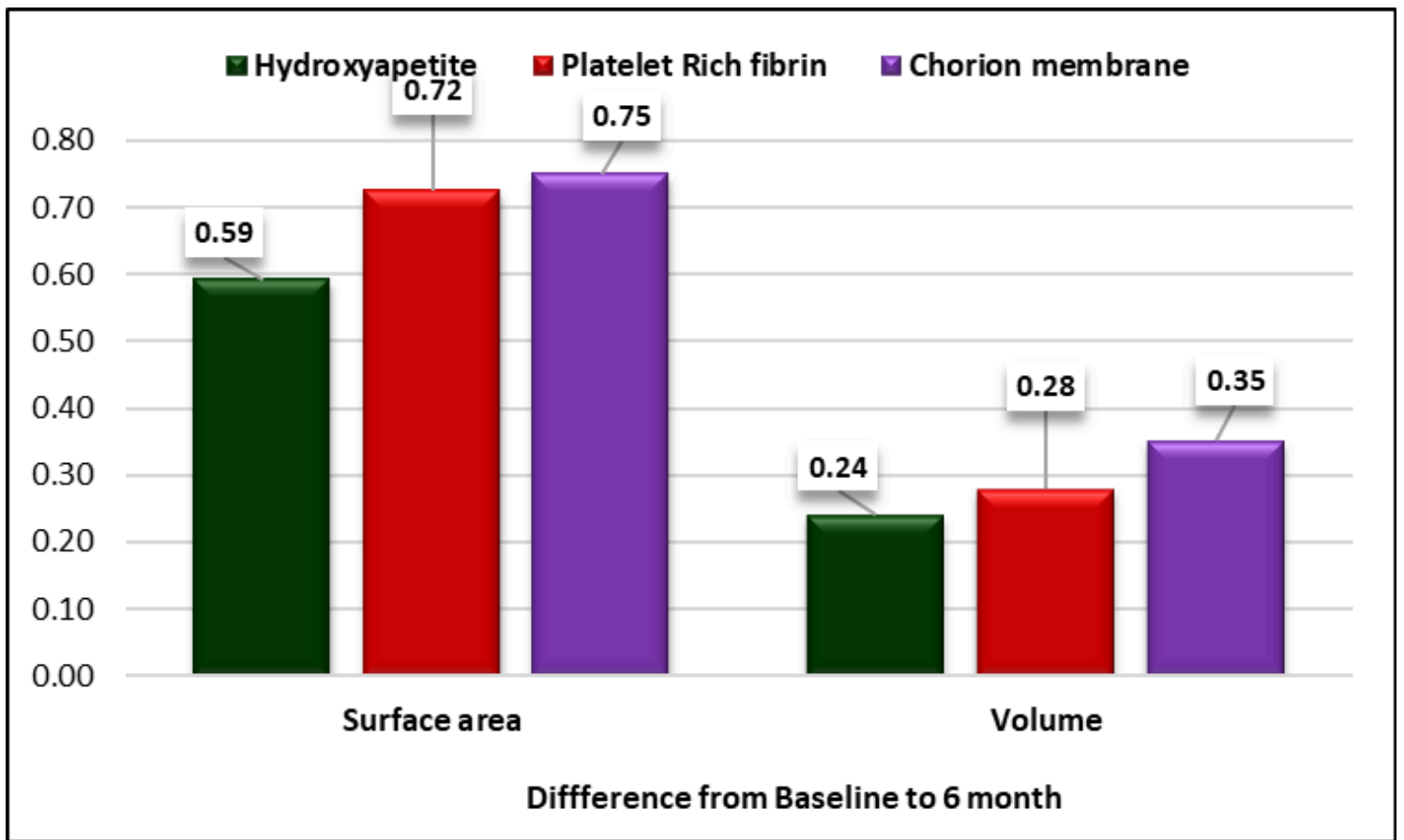


Figure 7

Intergroup comparison of percentage change in lesion surface area and volume from baseline to 6 months.

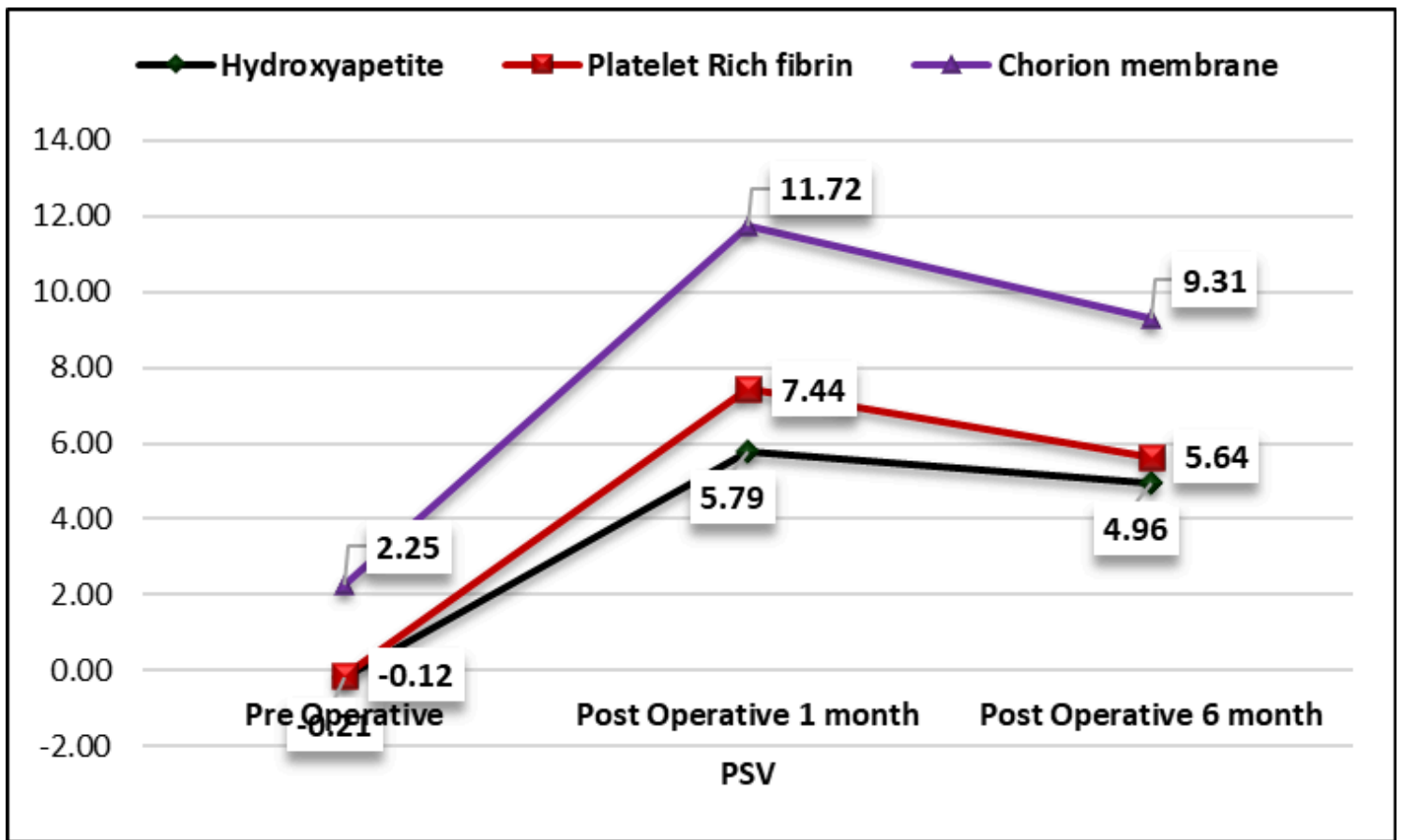


Figure 8

Intergroup and intragroup comparison of peak systolic velocity at baseline, 1 month and 6 months.