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CLINICAL AND RADIOGRAPHIC EVALUATION OF THE EFFECTS OF PLATELET-RICH FIBRIN ON TREATMENT OUTCOMES AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLAR

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ABSTRACT

Introduction: Third molar surgical extraction can lead to several complications like pain and edema. Platelet-rich fibrin (PRF) promotes healing, tissue regeneration, and bone growth, offering a cost-effective, biocompatible solution for improved recovery in dental surgeries. **Aim:** To assess the effect of platelet-rich fibrin on postoperative clinical outcomes and radiographic findings after surgical extraction of impacted Mandibular third molar. **Materials and Methods:** The present study involved 20 individuals with bilaterally impacted mandibular third molar, aged from 20 to 40 years. The patients were divided into two groups utilizing the split-mouth technique: Group I (Control Group): Included 20 impacted mandibular third molar which were removed, and the extraction sockets were left empty, then the socket was sutured. Group II (Study Group): Included 20 impacted mandibular third molars that were extracted, and the dental sockets were filled with PRF followed by suturing of the sockets. **Results**: Clinical findings showed significantly lower edema and pain levels in the study group compared to the control group, with no significant difference in maximal mouth opening. Radiographically, bone density increased in both groups over time. Although no significant difference was found at one month between both groups, the study group showed significantly higher bone socket density levels than the control group at four months. **Conclusion:** Application of PRF following the surgical removal of impacted third molars reduces clinical post-surgical complications as discomfort and edema, in addition, it improves healing and increases bone density of the dental socket.

INTRODUCTION

Surgical removal of third molar is one of the most commonly performed operations in the field of maxillofacial surgery. The ease or difficulty of extracting a mandibular third molar depends on its location, depth, and angulation, A great deal of training, expertise, and experience are needed to carry out this procedure with the least amount of trauma [(1)].

The removal of alveolar bone results in tissue damage, which increases the complications that follow surgery. Heat is produced when alveolar bone is removed with a handpiece, which can hinder healing and regeneration and result in marginal osteonecrosis [(2)].

Postoperative sequalae such as oedema, pain, or trismus may affect a patient's social and professional activities and change the appearance

of their face after odontectomy of an impacted mandibular third molar [3].

PRF or platelet-rich fibrin, is the second-generation platelet concentrate. It's made without the need for neurochemical blood processing and is inexpensive and easy to use. PRF is used in several dental and surgical applications, including periapical surgery, extraction socket preservation, and implant surgery augmentation. In essence, the exposed extraction socket is covered with a fibrin layer of connective tissue that is sutured around the incisions. PRF is very effective in improving tissue repair because of its unique microstructure and potential applications [4].

After centrifuging blood for 10 mins at 3000 Revolution per minute, PRF, which is the layer in the middle of autologous blood is produced. It is situated between the lower, red-colored RBC fraction and the top, straw-colored, acellular plasma layer. In this platelet concentrate, the largest numbers of platelets, cytokines, PDGF, VEGF, TGF beta, EGF, etc., are found in around 65% of the leukocytes. It can encourage fibrin-based epithelial coating and osteogenesis in addition to revascularization. It has been revealed that 9.5% of people undergoing surgical extraction procedure suffer from dry socket when removal is not associated with PRF application according to certain worldwide surveys, although in recent years, 1% with PRF has been documented [5].

PRF can be used to encourage hemostasis, bone growth, and maturation by itself or in combination with bone grafts. Studies have demonstrated that (PRF) is a biocompatible material that enhances healing and has great promise for the regeneration of soft tissues and bone without inducing reactions of inflammation [6]. This autologous matrix has a strong potential to enhance cell adhesion and promote osteoblast proliferation and differentiation, according to several in-vitro studies[7].

During surgery, PRF may be used as guided bone regeneration (GBR) resorbable barrier. This would allow the blood clot beneath to mineralize by preventing unwanted cells from moving into bone defects and establishing a region where osteogenic and angiogenic cells can enter. Cross-linked fibers may offer defense against enzymatic deterioration and be more robust when the membrane heals, even though a conventional PRF membrane degrades quickly (1-2 weeks) [8].

The purpose of this study was to determine the impact of applying platelet-rich fibrin on postoperative clinical outcomes (discomfort (pain), buccal swelling, and inability to open the mouth) and radiographic findings after surgical removal of impacted mandibular third molar.

MATERIALS AND METHODS

This clinical study involved twenty patients, aged 20 to 40 years, who attended the oral and maxillofacial department's outpatient clinic at the Faculty of Dentistry, Suez Canal University (SCU), Egypt. This study was conducted after approval of the Research Ethicics Committee, Faculty of Dentistry, Suez Canal University (SCU), Egypt (Approval code: 640/2023). An informed written consent was obtained from all patients before beginning the study.

A total of 40 impacted mandibular wisdom teeth belonging to twenty patients were removed. They were divided into two groups utilizing the split mouth technique, where an impacted molar belonging to each patient's side was randomly allocated into one of the two study groups. **Group I (Control Group):** Included twenty impacted mandibular wisdom teeth, where the socket of extraction was left empty after impaction removal, and the socket was sutured**. Group II (Study Group):** Included twenty impacted mandibular wisdom teeth and PRF

was placed into the socket after tooth removal, and then the flap was sutured over the graft.

Inclusion criteria incorporated patients of both genders, middle-aged adults (20-40) years, healthy according to the American Society of Anesthesiologists ASA I, and patients with class I & II impacted lower third molars with position A&B and mesioangular impacted mandibular third molar only.

Exclusion Criteria included pregnant or lactating females, smoking patients, patients having inadequate oral hygiene measures, unhealthy oral habits such as bruxism, with periapical or peri coronal lesions and with aggressive gingivitis or periodontitis.

Pre-surgical phase:

Clinical examination:

The personal data of each patient was taken and recorded in full detail, including the patient's name, age, gender, occupation, residence, and phone number. The patient was explained to in full details the surgical procedures, and provided information regarding any problems associated with previous tooth extraction (Postoperative hemorrhage, discomfort, or buccal swelling). Photographs were then taken as part of patient documentation.

Radiographic Evaluation:

Preoperative digital panoramic radiographs were taken using the CS 8100 SC (Carestream Dental LLC) installed in the Oral and Maxillofacial Radiology Department, Faculty of Dentistry, Suez Canal University.

Surgical procedures:

All surgeries were performed under stringent aseptic circumstances.

All patients were anesthetized through inferior alveolar nerve block, lingual nerve block and buccal nerve block local anesthetic procedures using Articaine 4% (Alexandricaine, Alexandria Pharmaceutical Company, Alexandria, Egypt) with Epi-nephrine 1:100,000 as a vasoconstrictor.

The flap design was established according to the needs of each case using scalpel no15.

The mucoperiosteal flap was reflected, and bone was removed (osteotomy) around the impacted tooth using a surgical round bur and continuous saline irrigation.

During surgery, 0.9% saline (Intra pharm, Alexandria, Egypt) was used for irrigation to hydrate dehydrated tissues.

Removal of tooth resistance, tooth and fragments extraction was performed. The socket's granulation tissue or debris was eliminated using a bone curette following tooth removal.

In the control group, the socket was left empty (unfilled with any graft) following surgical extraction and closed with a simple interrupted suture. **(Fig. 1)**

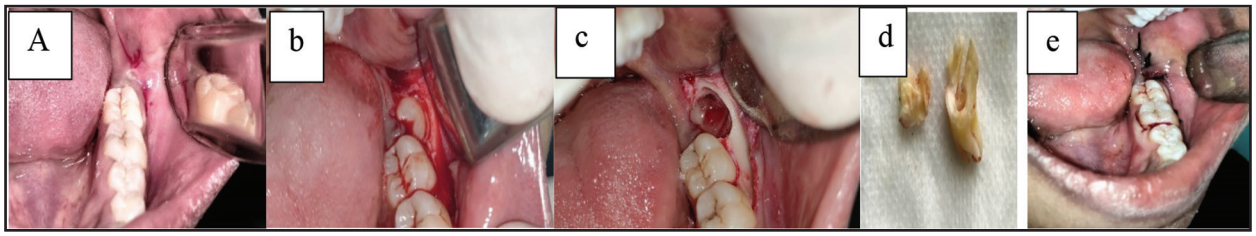

Fig. (1) Surgical procedures; (a) impacted mandibular third molar, (b) Reflection of mucoperiosteal flaps, (c) Removal of bone and tooth resistance (d) extracted impacted tooth (e) primary wound closure using interrupted sutures

For the study group, the PRF preparation regimen was straightforward, with the standard armamentarium required for PRP. Two tubes with a capacity of 5 ml without anticoagulant were used to collect about 5 ml of whole venous blood. The vacutainer tubes were then centrifuged at (3000) revolutions per minute (RPM) for ten minutes in the centrifuge, resulting in layers: lower layer containing red blood cells, top layer colored cellular plasma, and middle layer composed of fibrin clot. Then, the fibrin clot (PRF) was removed using a tweezer. The method used here is that fibrinogen, which is first concentrated in the high part of the tube, combines with the circulating thrombin due to centrifugation, to form fibrin. Then, in the center of the tube, between the two layers, a fibrin clot was formed [9]. **(Figure 2)**

The prepared autologous PRF [9] was placed into the socket in the study group, then, the socket was sutured and closed.

Post-operative phase:

All patients were informed of the expected possibility of occurrence of facial swelling, pain, and trismus. They were also informed of post-operative instructions, where they were instructed to bite for one hour after surgery on a sterile gauze pack to their wounds. For 24 hours following surgery, they should avoid spitting or washing, avoid hot beverages, meals, and hard foods and avoid smoking.

Following the procedure, every patient was administered the following medications: Amoxicillin with Clavulanic acid (Hibiotic) 1 gm tablets every 12 hr. for 7 days, Metronidazole (Amrizole) in 500 mg tablets every 8 hrs. for 7 days, Acetaminophen (Panadol) tablets as required, and finally mouthwash (Gngicare) 200 ml mouthwash twice daily starting 8 hours after surgery for 7 days postoperatively.

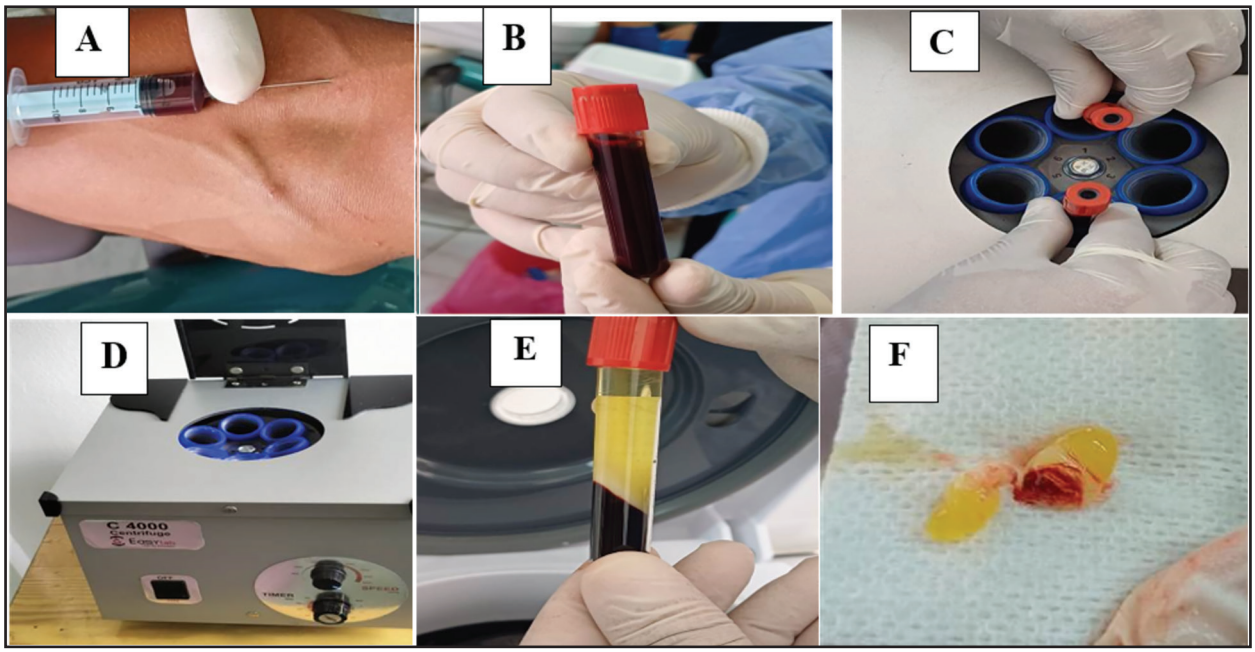

Fig. (2) Preparing the PRF (A) Blood Withdrawal from a cephalic vein (B) Blood in plain vacutainer tube (c) The tubes are then inserted in a centrifuge machine (D) The centrifuge device (E) Blood in the centrifuged tubes (F) Isolated Platelet-rich fibrin

Methods of post-operative Evaluation:

Clinical Assessment:

Postoperative pain: The intensity of pain was evaluated using a Visual Analog Scale (VAS), in which patients were asked to register their perceived discomfort on a 10-centimeter horizontal line, with 0 as no pain and 10 the most terrible pain. The pain level was assessed after 1st, 3rd, and 7th days of operation.

Postoperative edema: With the patient sitting upright, and his teeth in occlusion, a pen was used to mark four locations on the skin's surface. Facial swelling was calculated as the total length of two lines drawn at four pre-determined reference points on facial skin the length recorded in millimeters from the angle of the mandible to external canthus of the eye, and from the ear tragus to corner of the mouth. The amount of change in face contour was assessed again after 1-, 3-, and 7 -days following surgery by measuring the same distances [10]. **(Figure 3)**

Fig. (3) Measurement points for assessing post-operative edema

Postoperative Maximal mouth opening (MMO)

The degree of Maximal Mouth Opening was assessed postoperatively on days 1, 3, and 7, using a digital caliper (Total, Digital Caliper TmT321501, China) to measure the greatest inter-incisal distance between the upper and lower central incisors (in mm) [11].

Presence of postoperative complications

Inspection for the presence of alveolar osteitis or any other complications in each of the study and control groups was performed during patient follow-ups.

Surgical Time Factor

Time to perform surgical procedures starting from the beginning of administration of anesthesia to the end of wound suturing was measured in each of study group and the control group using a stopwatch (in minutes).

Postoperative Radiographic evaluation

Intra-oral paralleling periapical direct digital radiographic procedure:

Using KaVo Scan Exam™ One and Rinn extension cone paralleling (XCP) device with modified silicone bite, paralleling digital periapical radiographs were performed. A thin, flexible, and wireless phosphorescent imaging plate (PSP)served as a wireless receptor for the KaVo Scan eXamTM One intraoral digital imaging plate system.

The active surface area of the imaging plate size 2 is 31 × 41 mm, the picture size is 2.69 gigabytes, and the pixel size is 1034 x 1368 microns. The plastic targeting ring of the XCP film holder was positioned flush with the round end of a long (16-inch) cone that was fastened to the X-ray tube. The Fona XDC was used to expose the imaging plate.

Exposure parameters were fixed for all patients. Scan eXam™ was used for post-exposure

processing. To reduce intra and inter-observer variability, one examiner interpreted each patient's stored radiographs twice. The average value of both trials was used for density assessment.

Each patient was radiographically evaluated after 1 month and 4 months [12]. **(Figure 4&5)**

Digital Image analysis and measuring bone density: All images were saved in a computer's memory then, displayed on a 512 * 512-pixel array monitor with 256 gray scale for image analysis. Images at four-month follow-up were compared to the previous one-month follow-up images at the end of the study period.

With a scale ranging from 0 to 255, the Digora software provides evaluation using point brightness for measuring bone density. When using Digora Software's "Density Measurement Mode," these points are automatically measured in the region or line indicated. The average is calculated in conjunction with a curve representing the point density or brightness distribution.

A point in the middle of the socket measurement (area density index) was utilized to calculate bone density. Using the "start and end" and "x &y coordinate" options included in the Digora software toolbox, the point measured in the center of the socket was standardized to ensure that data on every sequential image is repeatable. [13&14] **(Figure 6)**

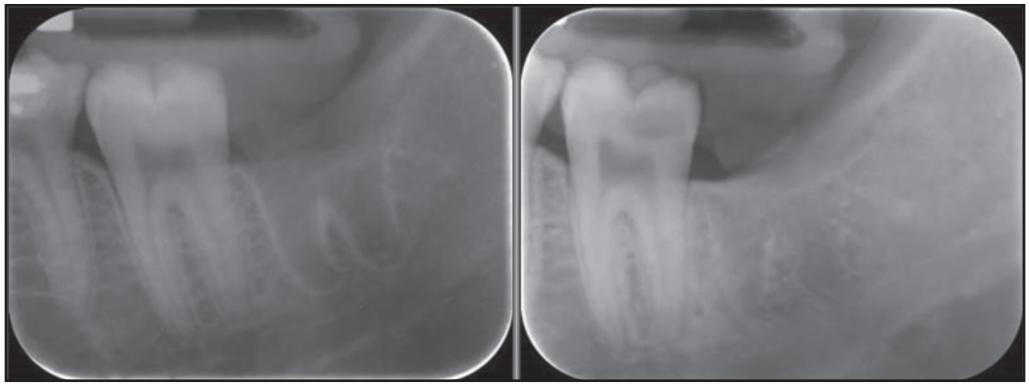

Fig. (4) Group I: one-month (left) and after four-month (right) radiographs for extraction socket without PRF

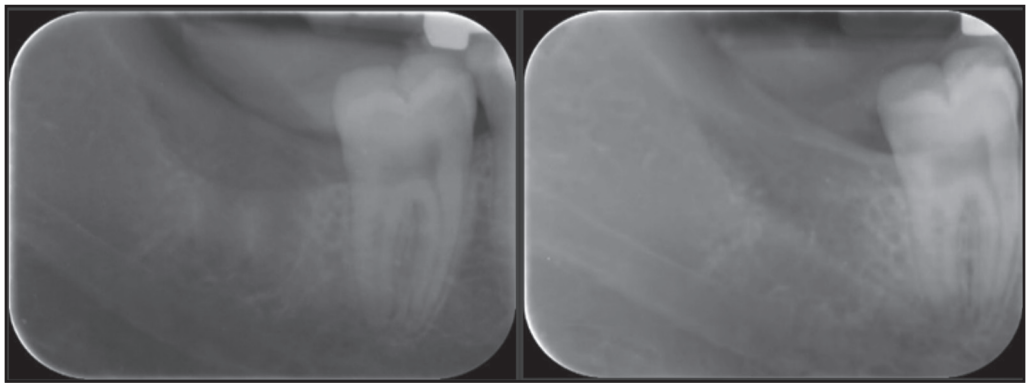

Fig. (5) Group II: one-month (left) and after four-month (right) radiographs for extraction socket with PRF

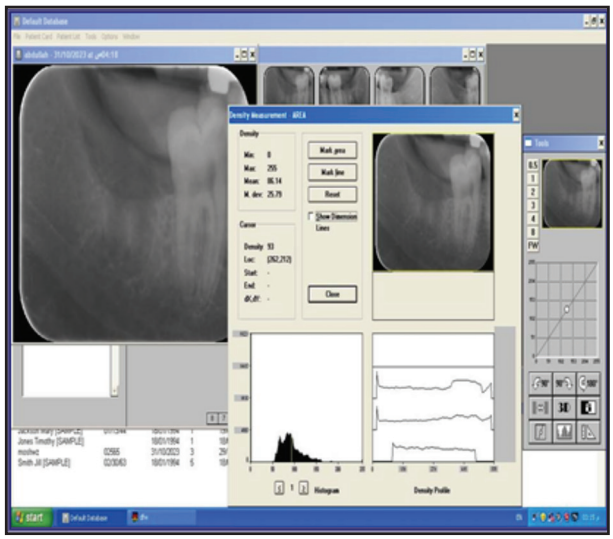

Fig. (6) Bone density measurement using Digora for windows software

Statistical analysis

Data was entered processed with IBM SPSS software version 20.0. The quantitative data were described using range (min and max), mean, standard deviation (SD), and median. The Shapiro-Wilk, D'Agstino, and Kolmogorov Smirnov tests were used to standardize the distributions of quantitative variables. Parametric tests were used if data distribution is normal. while nonparametric tests were performed when the data was abnormally spread out. The independent t-test was utilized to compare data that was regularly distributed. Two separate populations, whereas ANOVA, with repeated measurements to compare different times, the Post Hoc test (LSD) was employed. Two distinct populations were compared using the Mann-Whitney test for data that was irregularly dispersed. To compare the different periods, Both the Wilcoxon signed ranks test, and the Friedman test were applied. When the two-tailed P value was less than 0.05, it was deemed significant.

RESULTS

Twenty patients with bilateral impacted mandibular third molars, ages 20 to 40, who visited the clinic of the Oral & Maxillofacial Dept at the Faculty of Dentistry, Suez Canal University (SCU), Egypt, participated in this clinical trial utilizing the split-mouth technique. Group I (Control Group): included 20 impacted mandibular third molars that were removed then the extraction socket was left empty followed by suturing of the socket. Group II (Study Group): included 20 impacted mandibular third molar that were removed, after that, PRF was used to seal the extraction site followed by suturing of the socket.

Demographic data:

Age and Gender

According to the demographic data, the study population had a balanced gender distribution, with a slight predominance of males (55%). The average age of participants was 25.05 years.

Results of clinical assessment:

Pain measurements using (VAS) Score:

The study group experienced less pain than the control group; statistically significant difference was observed on the 1st and 3rd days (P = 0.002, 0.005), but by the 7th day, the relationship between both groups was no longer statistically significant (P = 0.192). (table 1)

Edema scale:

The study group experienced less edema than the unstudied group; the relationship was found to be significant on the 1st and 3rd days following surgery (P = 0.005, 0.004), but on the 7th day, it was statistically insignificant. (P = 0.497). (table 2)

Table (1) *Pain score measurements in both study groups.*

		Study group	Control group	p-value
1st day pain	Mean ± SD	5.45 ± 0.94	7.05 ± 1.15	0.002 (Sig.)
3rd day pain	Mean ± SD	2.05 ± 0.60	3.15 ± 0.88	0.005 (Sig.)
7th day pain	Mean ± SD	1.8 ± 0.47	2.05 ± 0.90	0.192 (NS)

*Z: Mann Whitney test, * for significant p value (<0.05)*

Table (2) *Comparison of edema values between both study groups*

		Study group	Control group	Test, p-value
1st day	Mean ± SD	10.39 ± 0.48	11.02 ± 0.52	0.005 (Sig.)
3rd day	Mean ± SD	10.05 ± 0.49	10.61 ± 0.48	0.004 (Sig.)
7th day	Mean ± SD	9.82 ± 0.58	10.33 ± 0.80	0.497 (NS)

*t: Student t test, * for significant p value (<0.05)*

Maximal Mouth opening (MMO):

The study group experienced less trismus than the unstudied group. However, during the first, third-, and seventh days following surgery, the difference between both groups was statistically insignificant. (table 3)

Table (3) *Trismus measurements in both study groups.*

		Study group	Control group	Test, p-value
1st day Trismus	Mean ± SD	35.99 ± 5.73	32.57 ± 6.06	0.074 (NS)
3rd day Trismus	Mean ± SD	44.15 ± 6.33	42.98 ± 6.77	0.579 (NS)
7th day Trismus	Mean ± SD	49.55 ± 6.64	49.74 ± 7.00	0.929 (NS)

*t: Student t test, * for significant p value (<0.05)*

The operation time between the two groups

The intervention time was significantly longer in the study group (mean ± SD: 45 ± 5.1 minutes) compared to the control group (mean ± SD: 30 ± 3.2 minutes) p <0.001.

Complications in each group.

Regarding postoperative complications, the control group showed one case of dry socket compared to the study group which had no cases of complications. However, the difference was statistically insignificant (table 4).

Results of radiographic assessment (relative bone density)

Regarding the bone density measurements in the study and control groups, although density values increased with time throughout the study period in both groups, data indicated no significant difference in bone density at 1 month between the study and control groups (p=0.055). However, at 4 months, the study group exhibited significantly higher bone density compared to the control group (p<0.001). (table 5)

Table (4) *Complications in both study groups*

		Study group	Control group	Test, p-value
Complications	Dry socket	0 (0.0%)	1 (5.0%)	X2:0.000, p=1.000
	No complication	20 (100%)	19 (95.0%)	

*X2: Chi-square test, t: student t test, * for significant p value (<0.05)*

Table (5) *Bone density measurement in study groups*

		Study	Control	Test, p-value
		n=20	n=20	
Bone density 1month	Mean ± SD	99.25 ± 10.03	93.15 ± 9.43	0.055
Bone density 4months	Mean ± SD	125.05 ± 9.30	109.05 ± 10.36	<0.001

*t: Student t test, * for significant p value (<0.05)*

DISCUSSION

The goal of this research is to assess the impact of utilizing platelet-rich fibrin on pain, swelling, trismus and bone density after surgical extraction of impacted mandibular third molar.

Our study employs split mouth design, which has the benefit of reducing inter-subject variability except from the estimated treatment effect. This is consistent with the findings of **Asutay *et al.*** [15] and **Caymaz *et al.*** [16], who included patients with bilateral mandibular impacted lower third molars in their research.

In line with **Wageeh *et al.*** [12]**, Shruthi *et al.*** [17]**,** and **Caymaz *et al.*** [16] who employed Platelet Rich Fibrin (PRF) to fill the socket following removal of an impacted mandibular third molar, we used PRF in this study to fill the socket following extraction of the mandibular third molar to reduce post operative complications following the surgery.

In this study, we measured the edema scale by dividing the sum of lengths of both lines between the determined points that served as references on the face, from the tragus of the ear to the corner of the mouth and from the outer corner of the eye to the angle of the lower jaw in line with the method

adopted by and **Lim & Ngeow** [18] **& Osunde *et al.*** [19] We used that method because it simple, non-invasive, and applicable can be performed with flexible rulers or tape.

In our study we used digital caliper for measuring the maximal mouth opening because it is easy to read, and has built-in measurements conversion system that are more accurate and sensitive, this is in line with **Agarwal *et al.*** [11] who used the vernier digital caliper for measuring the maximal interincisal opening.

Although, **Wageeh *et al.*** [12] and **Shruthi *et al*** [17] measured the maximal mouth opening by using different tools like a normal caliper or ruler, which might be not as accurate as the digital due to the hard application of the ruler on the exact points and accuracy of the measurements of the digital caliper.

In our study, we used a digital periapical radiograph for post-operative radiographic assessment since it is simple, standardized, widely used and is an important diagnostic aid. It has low magnification, produces a geometrically accurate image, has a low cost, and low radiation dose. This is consistent with **Naser *et al.*** [21], **Carneiro *et al.*** [22] and **Takeshita *et al*** [23].

On the contrary, **Malhotra *et al.*** [24] and **Veerabhadrappa *et al.*** [25] recorded the changes in the socket using another radiographic technique, namely panorama, which has higher magnification than periapical x-rays, and these radiographs were analyzed to determine bone density in their study.

The present study was consistent with **Abdelwahab &Awaad** [13], **El-Hawary & Shawky** [26], **Obradovic & Stojčev** [27], and Tavano et al. [28] who used the Digora software and demonstrated the software's effectiveness in measuring the relative bone density which allowed precise analysis of radiographic data.

Conversely, **Malhotra *et al.*** [24] and **Njokanma *et al.*** [29] employed different softwares for assessing bone density such as HL Image software and ImageJ Software.

Regarding results of the present study, our findings concur with those of **Shruthi *et al.*** [17] and **Malhotra *et al.*** [24], who showed that using PRF after oral surgery greatly lowers postoperative discomfort and speeds up the healing process because PRF contains platelets, which are essential for blood clot formation. White blood cells are part of your body's immune response **Janeway *et al*** [30]. and promote healing by bringing the surgery site's blood flow back. The oxygen and other nutrients tissues require to recover are then better delivered as a result **Kumar *et al*** [31]. Additionally, it aids in the removal of poisons and other infections from the area.

In contrast, some studies have reported different outcomes. For instance, a study by **Wageeh *et al.*** [12] and **Jankovic *et al.*** [32] found no discernible difference regarding pain relief between PRF-treated and control groups after oral surgery. This discrepancy could be attributed to variations in study design, sample size, or PRF preparation techniques. Additionally, the difference in results may also reflect variability in individual patient responses to PRF treatment.

Our results matched with **Wageeh *et al.*** [12] and **Bilginaylar *et al.*** [33] who found that PRF treatment leads to a marked reduction in swelling compared to conventional treatments. These findings support that PRF might enhance postoperative recovery by decreasing the inflammation and edema.

In contrast, **Kuroda *et al.*** [34] found that PRF does not significantly outperform conventional methods in managing edema and observed that while PRF had certain benefits, its impact on edema reduction was not consistently superior to traditional methods.

This is maybe because of variations in study design, PRF application methods, or patient-specific factors.

In agreement with a study by **Gupta *et al.*** [35] who did not find a significant difference in trismus recovery between patients treated with PRF and those receiving conventional treatments. This divergence may be due to differences in study design, such as variations in PRF application techniques or the use of additional therapies that might influence trismus outcomes.

However, a study by **Malhotra *et al.*** [24] and **Shruthi *et al.*** [17] found that applying PRF in the socket after extracting an impacted mandibular third molar resulted in significantly better trismus outcomes and increased interincisal mouth opening when compared to leaving the socket empty. This discrepancy could be caused by different study designs, such as different PRF application methods or the use of additional therapies that could affect trismus outcomes.

Regarding the operation time, **Lambade *et al*** [36] found the operation time range for the study group from 10-40 minutes with mean of 25.8 ± 8.56, while **Bede *et al*** [37] found the operation time in moderate difficulty impaction cases to be (25-30) minutes for the control group which was in agreement with our results.

Based on studies conducted by **Chakravarthi *et al.*** [38] and **Ye L *et al.*** [39], applying PRF to the socket following extraction reduces the risk of alveolar osteitis, a consequence of extracting any tooth. However, the third molar area is where the majority of dry socket instances occur.

Comparison of bone density measurements between the study group (which received platelet-rich fibrin, or PRF) and the control group in the first and fourth months indicates that there was no significant difference in the bone density at 1 month between the study and control groups However, at 4 months, the study group exhibited significantly higher bone density compared to the control group.

Our outcomes are in line with those of **Wageeh *et al.*** [12], who investigated PRF's impact on the development of bone and showed that, in comparison to traditional techniques, PRF improves bone healing and density. These results are consistent with the notable rise in bone density in the PRF group, suggesting that PRF promotes more efficient bone regeneration throughout the follow-up period.

Contrarily, **Saluja *et al.*** [40] found that while PRF showed some benefits, the impact on bone density was not as substantial as seen in the current study. This disparity could be attributed to variations in PRF preparation, the specific clinical context, or differences in measurement techniques and study durations.

We recommended that further clinical studies should be performed using PRF in addition to other materials like (PRP, hyaluronic acid, dexamethasone, anticox2, honey, apitoxin, aloe vera gel, vit D gel, and ozone gel) to evaluate postoperative clinical outcomes after odontectomy of impacted mandibular wisdom, additionally, use of other radiographic 3-D imaging modalities such as CBCT for evaluation of bone density as well as use of other soft-wares for measuring bone density as Idrisi, HLImage++, MATLAB is recommended.

CONCLUSIONS

Following the surgery of an impacted mandibular third molar, PRF administration decreases post-operative discomfort, edema, and while also increasing bone density over four months period.

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Conflict of Interest: Nil

Financial Disclosure: Nil

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