

CLINICAL AND RADIOGRAPHIC EVALUATION OF PLATELET-RICH FIBRIN ON POSTOPERATIVE PAIN, EDEMA, TRISMUS, AND BONE HEALING AFTER IMPACTED MANDIBULAR THIRD MOLAR SURGERY IN HEAVY SMOKING PATIENTS

KAREEM MOKHTAR IBRAHIM*

Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Misr University for Science and Technology, Giza, Egypt. *Corresponding Author Email: kareem.mokhtar@yahoo.com

EMAN ABDELHALIM ELSHARRAWY

Professor of Oral and Maxillofacial Surgery, Faculty of Dentistry, Suez Canal University, Ismailia, Egypt.

AMR ALY EL-SWIFY

Professor of Oral and Maxillofacial Surgery, Faculty of Dentistry, Suez Canal University, Ismailia, Egypt.

Abstract

Introduction: Surgical extraction of impacted mandibular third molars frequently leads to postoperative pain, edema, and trismus. In heavy smoking patients, wound healing is further compromised. Platelet-rich fibrin (PRF) is a second-generation autologous platelet concentrate that promotes healing and reduces inflammation. **Aim:** To evaluate the efficacy of PRF in reducing pain, swelling, trismus, and its effect on bone healing after odontectomy of impacted lower third molars in heavy smoking patients. **Materials and Methods:** Twenty-eight healthy heavy smoking patients (≥ 20 cigarettes/day) with bilateral impacted mandibular third molars were included using a split-mouth design. Group I (control): routine extraction with saline irrigation. Group II (study): extraction followed by PRF placement into the socket. PRF was prepared by centrifuging 10 mL venous blood at 3000 rpm for 10 minutes. Postoperative pain (VAS and analgesic count), edema (linear and surface area measurements), trismus (interincisal distance), and bone density (panoramic radiographs with ImageJ software) were evaluated at 2, 7, 30 days, and up to 6 months. **Results:** The PRF group showed significantly lower pain scores (mean VAS 3.89 ± 0.44 vs. 5.21 ± 0.69 , $p < 0.001$) and fewer analgesics used (1.47 ± 0.21 vs. 2.16 ± 0.22 tablets/day, $p < 0.001$). Edema was significantly reduced in the PRF group at 2 and 7 days (average linear measurement 12.38 ± 0.75 vs. 13.14 ± 0.77 cm, $p = 0.003$; surface area 93.4 ± 5.32 vs. 119.4 ± 6.23 cm², $p = 0.0045$). Trismus was significantly improved (interincisal distance 41.64 ± 10.16 vs. 32.39 ± 12.75 mm at day 2, $p = 0.043$). No significant difference in bone density was found between groups at any time point. **Conclusion:** PRF effectively reduces postoperative pain, edema, and trismus in heavy smoking patients undergoing impacted third molar surgery, but does not improve bone remodeling.

Keywords: Platelet-Rich Fibrin, Impacted Mandibular Third Molar, Heavy Smoking, Postoperative Pain, Edema, Trismus, Bone Density.

INTRODUCTION

Odontectomy is defined as surgical extraction of a tooth that is partially or completely encompassed by bone. It is one of the most common surgical procedures in dentofacial area. The most common indication for the surgery is infection - pericoronitis - around a partially erupted third molar tooth that is impacted against adjacent soft tissue or bone. Other indications include unrestorable caries, internal or external resorption, fractured

tooth, dental follicle disease like cyst or tumor, and interference with other surgeries like reconstructive jaw surgery or tumor resection ⁽¹⁻⁴⁾.

The surgery is usually associated with detrimental side effects or unfavorable post-operative sequelae such as post-operative soft tissue inflammation, pain, swelling, trismus and temporary limitation of temporomandibular joint mobility during the first few days after surgery. These complications can affect the routine activities of patients, such as sleeping, eating, and chewing ^(5,6). The surgical trauma has been considered the etiological factor for the inflammatory process, which is associated with these postoperative sequelae. Although pain and swelling gradually decrease within the first week after surgery, decreasing of these complications is a very important aim for both the surgeon and the patient ⁽⁷⁾.

Healing after tooth extraction is of continuing interest to the oral and maxillofacial surgeons as it has a direct relation to these postoperative side effects. This process consists of four overlapping stages, which involve clotting, replacement of the blood clot with healthy granulation tissue, gradual replacement of the granulation tissue by connective tissue and new perosseous tissue, and finally bone trabeculae filling the alveolar socket ^(8,9). It is a complex process that requires many cellular and biological events such as cellular proliferation, differentiation, synthesis, and release of cytokines, growth factors, and other proteins. Healing process of tooth extraction sockets includes the formation and maturation of a blood clot, infiltration of fibroblasts to replace the coagulum, and establishment of a provisional matrix that is replaced by newly formed woven bone and ultimately by lamellar bone and bone marrow ^(10,11).

There are a lot of factors affecting the healing process. Some are locally like presence of infection, the site of extraction and others are systemic like using of certain medicines, age, general health and medical condition of the patient, and smoking ^(12,13). Cigarette smoking has been suspected to adversely affect intraoral wound healing for a long time ⁽¹⁴⁾. However, the precise mechanisms by which cigarette smoking interferes with wound healing are not completely understood. Carbon monoxide and nicotine in the smoke are thought to play primary roles in the adverse effects of cigarette smoking ⁽¹⁵⁾. Carbon monoxide combines with hemoglobin easier than oxygen, and the reduction in oxyhemoglobin can result in cellular hypoxia. The negative effects of nicotine are believed to be associated with vasoconstriction causing a reduction in the microcirculation to the tissues ⁽¹⁶⁾. Nicotine also reduces prostaglandin production and stimulates the carotid chemoreceptors, leading to catecholamine release ⁽¹¹⁾. It also inhibits immunohistochemically proliferation of fibroblasts and macrophages ⁽¹⁷⁾. A respondent is considered to be a heavy smoker if his consumption exceeded twenty or more cigarettes per day - more than one pack daily ⁽¹⁸⁾.

Platelet-rich fibrin (PRF) is a second-generation autologous platelet concentrate first described by Choukroun et al. ⁽⁶⁾. It is prepared by centrifuging venous blood without anticoagulant, producing a fibrin matrix that traps platelets, leukocytes, and growth factors (PDGF, TGF- β , VEGF, EGF) that promote cell proliferation and tissue regeneration ⁽⁷⁾. PRF releases growth factors that are responsible for cell mitosis, increasing collagen

production, recruiting cells to the injury site, initiating angiogenesis, and inducing cell differentiation. PRF-membrane is an autogenous leukocyte and platelet-rich fibrin biomaterial that is prepared from the patient's own blood and can be used as a membrane for usage in surgical field ⁽¹⁹⁾.

Recent evidence has shown that PRF significantly reduces postoperative pain and swelling after third molar surgery ^(8,9). However, most studies have excluded heavy smokers. Therefore, the present study was designed to evaluate PRF efficacy specifically in this population.

Thus, this study was conducted to evaluate the efficacy of using Platelet rich fibrin in healing, reduction of pain, swelling and trismus after surgical odontectomy of impacted lower third molar in heavy smoking patient.

PATIENTS AND METHODS

Ethical consideration

This clinical study was conducted after approval of the Research Ethics Committee, Faculty of Dentistry, Suez Canal University (SCU), Egypt. An informed written consent was obtained from all patients before beginning the study. All patients received full explanations of the surgical procedures, any complications, the entire study schedules, and the photographs that were used in the scientific study and signed the consent form.

Study design

This randomized controlled clinical study involved twenty-eight healthy heavy smoking patients, aged 25 to 45 years, who attended the outpatient clinic of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Suez Canal University (SCU), Egypt.

A total of 56 impacted mandibular wisdom teeth belonging to twenty-eight 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 28 impacted mandibular wisdom teeth which were removed, and the extraction sockets were left empty (irrigated with normal saline only), then the socket was sutured.
- **Group II (Study Group):** Included 28 impacted mandibular wisdom teeth that were extracted, and the dental sockets were filled with PRF followed by suturing of the sockets.

Inclusion criteria

- Patients of both genders
- Middle-aged adults (25-45) years
- Healthy according to the American Society of Anesthesiologists ASA I

- Heavy smokers (≥ 20 cigarettes/day according to WHO criteria)
- Patients with class III impacted lower third molars (Pell and Gregory classification)
- Position B and C impaction
- Mesioangular or horizontal impacted mandibular third molar

Exclusion criteria

- Pregnant or lactating females
- Patients having inadequate oral hygiene measures
- Unhealthy oral habits such as bruxism
- Patients with systemic conditions altering oral microbiota, immunologic system, or inflammatory response (e.g., Crohn syndrome, leukemia)
- Patients with conditions that compromise healing (e.g., diabetes mellitus)
- Patients on pharmacologic treatments altering oral microbiota or immunologic response (e.g., corticosteroids)
- Patients who had head and neck radiotherapy or chemotherapy
- Presence of benign or malignant neoplastic lesions in contiguity with the impacted tooth
- Presence of radiolucent lesions with a diameter less than 1 cm at the impacted tooth level
- Presence of acute inflammation or infection or lymphadenopathy on the side of impaction

Clinical examination

Personal and medical history sheets were performed for all patients of the study. The sheet included full personal data, chief complaint, history of the complaint, medical history, and dental history. Dental clinical examination was carried out for all the patients. Inspection of the mucous membrane surrounding the impacted tooth was done to identify any swelling, infection and caries arising in the tooth. Impression was carried out to make a lower night guard which was preoperatively fabricated to use as a tracing reference of bone density and radiographic assessment.

Radiographic examination

Digital panoramic and periapical radiographs were taken before surgery to assess tooth position, root morphology, relation to mandibular canal, and surgical difficulty. The anticipated degree of difficulty of all the impacted molar surgeries evaluated by the radiographic findings were almost at the same level for all patients ⁽¹⁾ (Fg.1).

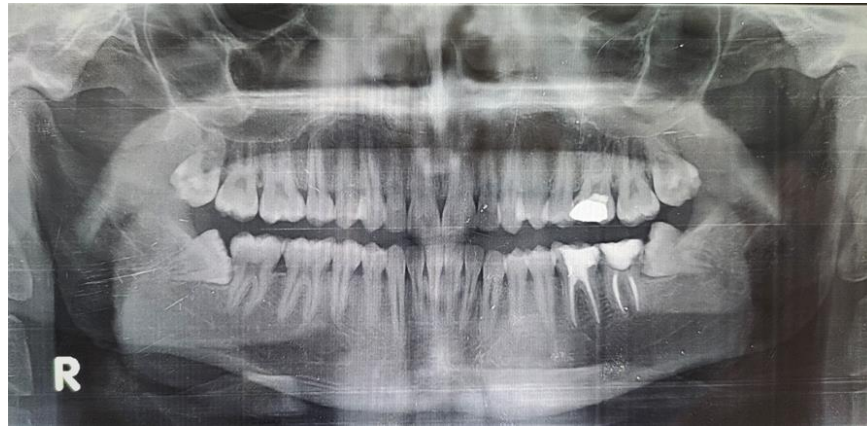


Figure (1): Preoperative radiograph shows impacted teeth of the patient

Preoperative measurements

Facial contour:

Preoperative assessment of the facial contour was measured using two different methods ⁽¹⁰⁾.

The first method depended on linear measurement. In this method, the patient was seated in an upright position with his teeth in maximum occlusion. Five points were marked on the skin surface by a pen marker. The five points were: tragus of the ear, gonion, ala of the nose, corner of the mouth, and pogonion. Distances between tragus of the ear and ala of the nose, tragus of the ear and lip commissure, tragus of the ear and pogonion, gonion and ala of the nose, gonion and lip commissure, and gonion and pogonion were all measured and recorded in cm. The average of the sum of the six distances was considered as the baseline linear measurement (Fig.2). The second method depended on the surface area of the skin. In this method, the patient was also seated in an upright position with his teeth in occlusion. Four points were marked on the skin by a pen marker. The four points were tragus of the ear, outer canthus of the eye, gonion, and pogonion. The four points were matched together forming a quadrilateral shape with the previous points at the corners. The surface area of the shape was calculated in cm² and recorded as the surface area measurement (Fig.3).

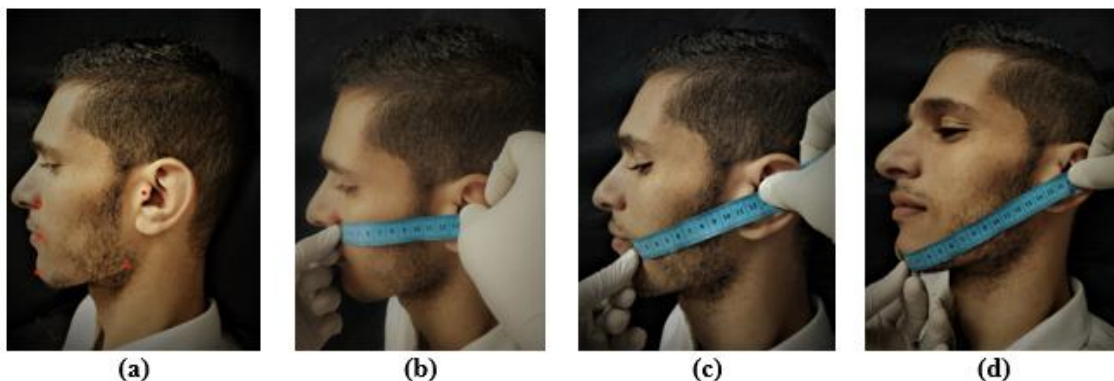




Figure (2): (a) Preoperative photo shows the position of the patient during measurements and the five marked points. (b) shows measurement of the distance between ear tragus and nose ala. (c) shows measurement of the distance between ear tragus and lip commissure. (d) shows measurement of the distance between ear tragus and pogonion. (e) shows measurement of the distance between gonion and nose ala. (f) shows measurement of the distance between gonion and lip commissure. (g) shows measurement of the distance between gonion and pogonion

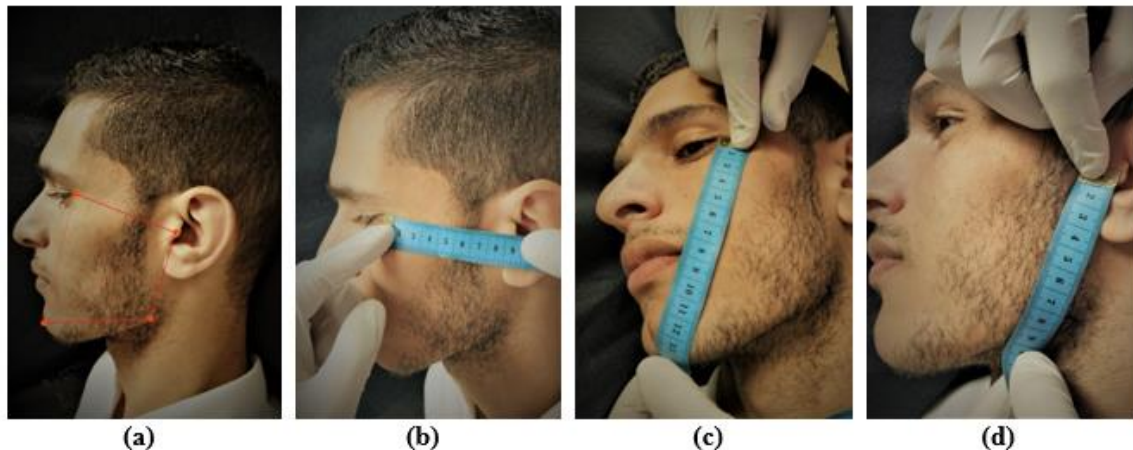


Figure (3): (a) Preoperative photograph shows the surface area of the quadrilateral shape formed after matching the four marked points. (b) shows measurement of ear tragus and eye canthus. (C) shows measurement of eye canthus and pogonion. (d) shows measurement of ear tragus and gonion

Mouth opening:

The amount of mouth opening was recorded by asking the patient to maximally open his mouth unforcefully and measuring the interincisal distance between the incisal edges of maxillary and mandibular central incisors in mm using a digital caliper before the surgery⁽¹¹⁾ (fig. 4).



Figure (4): Preoperative photograph shows measurement of mouth opening with digital caliper

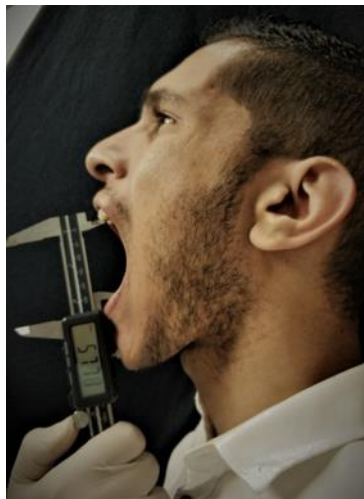


Figure (5): PRF preparation

PRF preparation

The method described by Choukroun et al. was followed ⁽⁶⁾. Approximately 10 mL of venous blood was drawn from each patient in the study group into a sterile glass tube without anticoagulant. The tube was immediately centrifuged at 3000 rpm for 10 minutes. After centrifugation, three layers appeared: bottom layer of red blood cells, middle layer of PRF clot (fibrin with trapped platelets and leukocytes), and top layer of acellular plasma. The PRF clot was carefully removed using sterile tweezers, separated from the red blood cell layer, and then gently squeezed between two sterile gauze pads to form a firm, flexible membrane suitable for placement into the extraction socket (fig.5).

Surgical procedure

All surgeries were performed by the same surgeon under strict aseptic conditions. Local anesthesia was achieved using articaine hydrochloride 4% with epinephrine 1:100,000 via inferior alveolar, lingual, and long buccal nerve blocks ⁽⁵⁾. A standard three-cornered mucoperiosteal flap was raised. Osteotomy around the impacted tooth was performed using a fissure surgical bur under continuous irrigation with normal saline. When needed,

the tooth was sectioned using a bur. After tooth delivery, the socket was debrided with a bone curette to remove any granulation tissue or debris. Sharp bony edges were smoothed with a bone file (fig.6).

Management for both groups:

Scrubbing and draping of patients were carried out in a standard fashion. Local anesthesia was injected around the planned surgical site. Full mucoperiosteal flap was made and elevated to expose the lesion.

The bone covering the defect was removed using a surgical bur for full exposure of the impacted tooth. After the tooth was visible, odontectomy was performed. Debridement of the socket was done using a bone curette for removal of granulation tissue or debris.

Management for study group:

The prepared PRF membrane was placed into the socket, then the flap was sutured.

Management for control group:

The socket was irrigated with normal saline and then sutured without PRF application. Flap closure was performed using 4-0 black silk interrupted sutures. Sutures were removed at the 7-day follow-up.

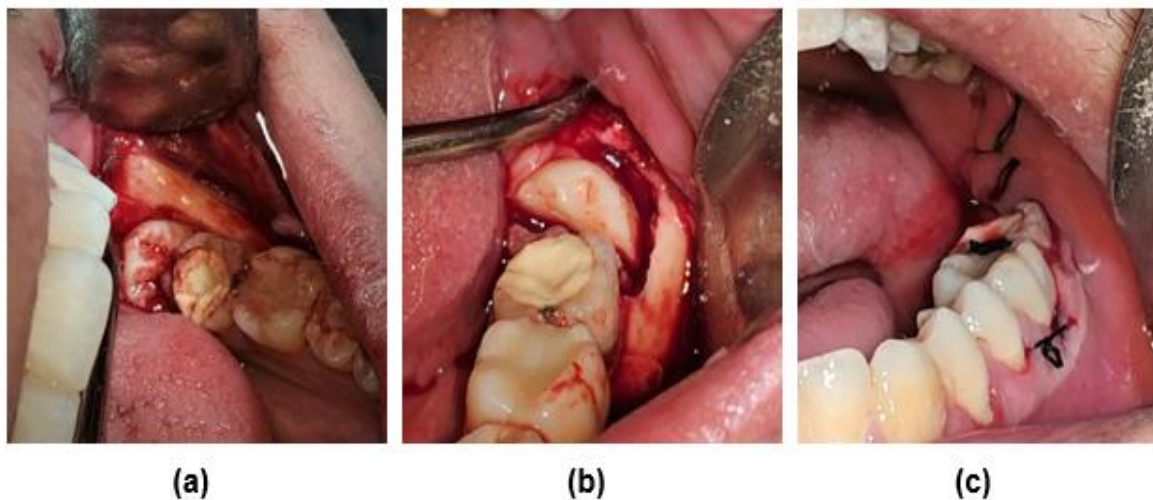


Figure (6): (a) Photograph after reflection of mucoperiosteal flap. (b) after osteotomy. (c) after suturing

Postoperative instructions

All patients were informed of the expected possibility of occurrence of facial swelling, pain, and trismus. They were instructed to bite on sterile gauze for one hour after surgery, avoid rinsing or spitting for 24 hours, avoid smoking for 24 hours, and avoid hot drinks, hard foods, and chewing on the operated side ⁽⁷⁾.

Postoperative medications

All patients in both groups were subjected to the following drugs after the surgery:

Amoxicillin with Clavulanic acid (Augmentin) available as 1 gm tablets every 12 hrs for 7 days. Metronidazole (Flagyl) available as 500 mg tablet every 12 hrs for 7 days. Ibuprofen (Brufen) available as 400 mg tablets as required.

Postoperative assessment

Subjective parameters:

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 as the most terrible pain ⁽⁹⁾. The pain level was assessed daily for six days after surgery. Additionally, the number of ibuprofen 400 mg tablets taken each day was recorded.

Objective parameters:

Edema: With the patient sitting upright and teeth in occlusion, facial swelling was measured using two methods ⁽¹⁰⁾. Linear method: five reference points (tragus, gonion, ala of nose, mouth corner, pogonion); six distances measured; average recorded. Surface area method: four points (tragus, outer canthus, gonion, pogonion) forming a quadrilateral; area calculated ($\frac{1}{2} ab \sin C$). Measurements were taken preoperatively and at 2, 7, and 30 days postoperatively.

Trismus: The degree of maximal mouth opening was assessed using a digital caliper to measure the greatest inter-incisal distance between the upper and lower central incisors (in mm) ⁽¹¹⁾. Measurements were taken preoperatively and at 2, 7, and 30 days postoperatively.

Postoperative complications: Inspection for alveolar osteitis or any other complications was performed during patient follow-ups. Soft tissue healing was assessed as rapid (within one week), normal (within two weeks), or slow (within three weeks) ⁽¹²⁾.

Radiographic evaluation: Panoramic radiographs were taken preoperatively and at 1 week, 1 month, 3 months, and 6 months postoperatively ⁽¹⁴⁾. Image analysis was performed using ImageJ® software. Relative bone density = (mean grey value of socket) / (mean grey value of surrounding bone) (15)(15). A prefabricated acrylic night guard was used as a radiographic reference.

Statistical analysis

Data was analyzed using SPSS. Results expressed as mean±SD. Wilcoxon signed-rank test for repeated measurements was used. A p-value <0.05 was considered significant.

RESULTS

Demographic data

The study was performed on twenty-eight healthy heavy smoking patients with bilateral impacted mandibular third molars. with mean age 35.4 ± 8.2 years.

Pain

The PRF group consistently showed lower pain scores than the control group. On the day of surgery, the mean VAS was 6.81 ± 0.71 in the PRF group vs. 7.10 ± 0.67 in controls ($p=0.168$, not significant). From day 2 onward, differences became significant. The most pronounced differences were on day 3 (4.75 ± 0.61 vs. 5.89 ± 0.76 , $p=0.001$) and day 4 (4.29 ± 0.43 vs. 5.58 ± 0.94 , $p<0.001$). By day 7, the PRF group reported no pain (0.00 ± 0.00) while controls still had moderate pain (2.64 ± 1.60 , $p<0.001$). The average VAS over six days was 3.89 ± 0.44 in the PRF group vs. 5.21 ± 0.69 in controls ($p<0.001$). Analgesic consumption followed the same pattern: average tablets per day was 1.47 ± 0.21 in the PRF group vs. 2.16 ± 0.22 in controls ($p<0.001$); (Table 1).

Edema

Preoperatively, there was no significant difference in linear measurements (control 12.00 ± 0.57 cm, PRF 10.19 ± 0.74 cm, $p=0.048$) or surface area (control 88.50 ± 6.31 cm², PRF 90.83 ± 8.02 cm², $p=0.231$). At day 2, the control group showed much more swelling: linear measurement 13.14 ± 0.77 cm vs. 12.38 ± 0.75 cm ($p=0.003$); surface area 119.4 ± 6.23 cm² vs. 93.4 ± 5.32 cm² ($p=0.0045$). At day 7, the PRF group was significantly less swollen: linear 11.84 ± 0.70 cm vs. 12.65 ± 0.66 cm ($p<0.0005$); surface area 88.2 ± 5.63 cm² vs. 114.7 ± 5.22 cm² ($p=0.0038$). At day 30, linear measurements were similar (10.96 ± 0.70 vs. 10.94 ± 0.64 cm, $p=0.89$), but surface area remained smaller in the PRF group (82.4 ± 6.35 vs. 100.4 ± 5.6 cm², $p=0.015$); (Table 1).

Trismus

Preoperative interincisal distance was similar (control 49.49 ± 10.10 mm, PRF 47.61 ± 5.53 mm, $p=0.545$). At day 2, the PRF group had significantly better mouth opening (41.64 ± 10.16 mm vs. 32.39 ± 12.75 mm, $p=0.043$). At day 7, the difference was no longer significant (47.24 ± 5.12 vs. 41.15 ± 13.01 mm, $p=0.115$). At day 30, both groups had nearly full recovery (48.39 ± 5.51 vs. 49.27 ± 9.91 mm, $p=0.772$); (Table 1).

Table 1: Comparison of postoperative outcomes between control and PRF groups (Mean $\pm$ SD)

Parameter	Time Point	Control Group (n=28 for pain, n=14 for others)	PRF Group (n=28 for pain, n=14 for others)	P-value	Sig.
Pain (VAS 0–10)	Day of surgery	7.10 ± 0.67	6.81 ± 0.71	0.168	NS
	2nd day	6.41 ± 0.78	5.64 ± 0.16	0.011	S
	3rd day	5.89 ± 0.76	4.75 ± 0.61	0.001	HS
	4th day	5.58 ± 0.94	4.29 ± 0.43	<0.001	HS
	5th day	4.82 ± 0.82	4.00 ± 0.83	0.052	NS

	6th day	4.04 ± 0.93	1.71 ± 1.82	0.001	HS
	7th day	2.64 ± 1.60	0.00 ± 0.00	<0.001	HS
	Average (1–6 d)	5.21 ± 0.69	3.89 ± 0.44	<0.001	HS
Analgesic tablets (n/day)	Day of surgery	3.36 ± 0.50	2.86 ± 0.66	0.040	S
	2nd day	3.21 ± 0.43	2.57 ± 0.76	0.009	HS
	3rd day	2.64 ± 0.50	1.71 ± 0.47	<0.001	HS
	4th day	2.14 ± 0.36	1.36 ± 0.50	<0.001	HS
	5th day	1.64 ± 0.50	1.29 ± 0.47	0.063	NS
	6th day	1.36 ± 0.50	0.50 ± 0.52	0.001	HS
	7th day	0.79 ± 0.43	0.00 ± 0.00	<0.001	HS
	Average (1–6 d)	2.16 ± 0.22	1.47 ± 0.21	<0.001	HS
Edema-linear (cm)	Preoperative	12.00 ± 0.57	10.19 ± 0.74	0.048	S
	2 days	13.14 ± 0.77	12.38 ± 0.75	0.003	HS
	7 days	12.65 ± 0.66	11.84 ± 0.70	<0.0005	HS
	30 days	10.94 ± 0.64	10.96 ± 0.70	0.89	NS
Edema-surface area (cm²)	Preoperative	88.50 ± 6.31	90.83 ± 8.02	0.231	NS
	2 days	119.4 ± 6.23	93.4 ± 5.32	0.0045	HS
	7 days	114.7 ± 5.22	88.2 ± 5.63	0.0038	HS
	30 days	100.4 ± 5.6	82.4 ± 6.35	0.015	S
Trismus (interincisal distance, mm)	Preoperative	49.49 ± 10.10	47.61 ± 5.53	0.545	NS
	2 days	32.39 ± 12.75	41.64 ± 10.16	0.043	S
	7 days	41.15 ± 13.01	47.24 ± 5.12	0.115	NS
	30 days	49.27 ± 9.91	48.39 ± 5.51	0.772	NS
Bone density – relative density	1 week	89.70 ± 17.97	87.25 ± 19.81	0.735	NS
	1 month	98.58 ± 14.12	96.71 ± 14.74	0.734	NS
	3 months	100.72 ± 11.36	108.28 ± 14.91	0.143	NS
	6 months	114.73 ± 12.69	114.48 ± 14.57	0.961	NS
Bone density (% change)	1 week	34.08 ± 4.57	36.44 ± 6.59	0.281	NS
	1 month	26.79 ± 3.26	28.57 ± 5.97	0.335	NS
	3 months	24.82 ± 5.85	19.99 ± 6.03	0.041	S
	6 months	14.57 ± 4.03	15.57 ± 4.62	0.547	NS

NS = not significant ($p>0.05$); S = significant ($p<0.05$); HS = highly significant ($p<0.01$). For pain and analgesic tablets, $n=28$ per group; for all others, $n=14$ per group (split-mouth design).

Bone density

Relative bone density showed no significant difference between groups at any time point: 1 week (87.25 ± 19.81 vs. 89.70 ± 17.97 , $p=0.735$), 1 month (96.71 ± 14.74 vs. 98.58 ± 14.12 , $p=0.734$), 3 months (108.28 ± 14.91 vs. 100.72 ± 11.36 , $p=0.143$), and 6 months (114.48 ± 14.57 vs. 114.73 ± 12.69 , $p=0.961$). Percentage change from baseline was also non-significant except at 3 months ($19.99\pm6.03\%$ vs. $24.82\pm5.85\%$, $p=0.041$), but this difference was not sustained at 6 months (Table 1).

Postoperative complications

No postoperative complications such as infection, wound dehiscence, or alveolar osteitis were observed in either group at each time interval.

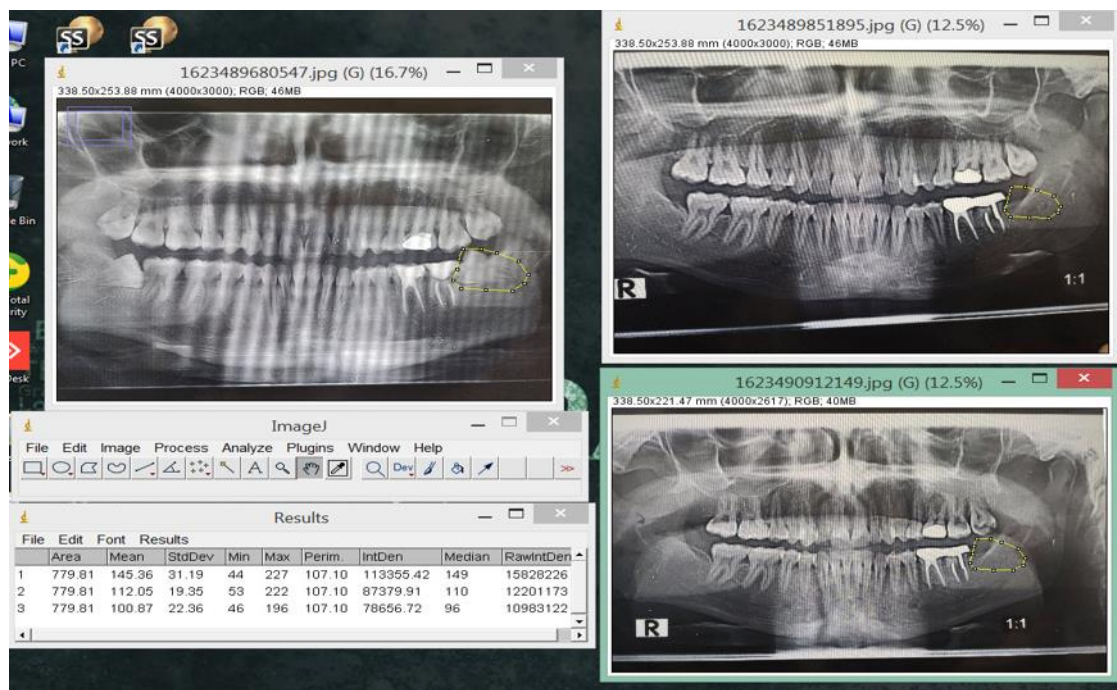


Figure (7): Relative bone density calculation using ImageJ® software

DISCUSSION

The objective of this study was to assess the efficacy of PRF in the promotion of healing of smoking patients after odontectomy of impacted lower third molar surgery in heavy smoking patients. Twenty-eight heavy smoker patients suffering from bilateral impacted mandibular third molars were treated in the current study with surgical odontectomy followed by PRF application on one side before suturing, and the other side was left as a control using only saline. Our results demonstrated that PRF significantly reduced pain, edema, and trismus during the first postoperative week, but did not improve bone density up to six months.

In accordance with our findings, a 2023 network meta-analysis by Costa et al. ⁽¹⁷⁾ including 31 randomized clinical trials and evaluating up to 1240 surgeries found that among all blood concentrates, advanced platelet-rich fibrin (A-PRF) performed best, decreasing postoperative pain on days 1, 2, 3, and 7 and reducing trismus up to the inflammatory peak compared to blood clots. The authors concluded that based on the analyzed evidence, using concentrates seemed efficient in reducing pain and trismus after mandibular third molar surgeries.

Consistent with our pain results, a 2025 prospective, randomized, controlled, patient-blinded clinical trial by Öhrnell Malekzadeh et al. ⁽¹⁸⁾ investigated whether PRF applied to the extraction socket reduces postoperative symptoms and complications in 90 patients scheduled for mandibular third molar removal. The study found that PRF treatment significantly reduced postoperative pain during the first six days, suggesting that PRF can

contribute to improved patient comfort and recovery by decreasing early postoperative pain.

In line with our results regarding reduced analgesic consumption, a 2024 randomized controlled split-mouth study by Pabst et al. ⁽¹⁹⁾ included 25 patients and found that in the test group treated with solid PRF clots, the number of painkillers taken and the number of days painkillers were needed were significantly lower ($p < 0.05$). The authors concluded that PRF affects the long-term outcomes of third molar removal by reducing swelling and reducing as well as shortening painkiller consumption.

On the same line of our results, a 2025 randomized controlled clinical trial by Aliberti et al. ⁽²⁰⁾ evaluated submucosal infiltration of injectable platelet-rich fibrin (i-PRF) after extraction of impacted lower third molars in 56 patients. The study found a significant reduction in pain scores in the i-PRF group on days 1 and 3 ($p < 0.001$), and surgical wound healing showed statistically significant improvement in the i-PRF group at all time points (days 3, 7, 14, and 21; $p < 0.05$). The authors concluded that submucosal infiltration of i-PRF effectively reduces postoperative swelling and pain while also promoting faster wound healing.

Regarding edema, in agreement with our findings, a 2024 systematic review by Pattnayak et al. ⁽²¹⁾ evaluating the impact of PRF and PRP on pain, swelling, trismus, soft tissue healing, and bone regeneration following mandibular third molar extraction concluded that both materials positively influence healing after mandibular third molar extraction, with PRF offering an advantage due to its ease of preparation and complete autologous nature.

A 2025 split-mouth randomized clinical trial by Barone et al. ⁽²²⁾ using 3D facial swelling analysis on 32 patients found that volumetric differences favored the PRF group compared with the control group in all phases, and linear differences showed improved values of postoperative swelling. The authors concluded that application of PRF in post-extraction sockets showed effectiveness in reducing facial swelling, and its advantages including accessibility, cost-effectiveness, and absence of adverse reactions make it an optimal treatment choice in reducing post-surgical sequelae.

Specifically for smokers, a 2022 randomized controlled clinical trial by Alrayyes et al. ⁽²³⁾ evaluated the ability of platelet-rich fibrin to enhance socket wound healing in smokers with 18 smoker participants and forty non-restorable upper molars. The study found that different forms of PRF exhibited enhanced wound closure and healing patterns, as well as reduced post-operative complications among smokers. The authors concluded that A-PRF and A/S-PRF showed significant results in terms of mesio-distally ($p = 0.012$) and healing pattern parameters ($p < 0.0001$) among smokers.

Concerning trismus, in line with our results, the 2023 network meta-analysis by Costa et al. ⁽¹⁷⁾ confirmed that among the analyzed blood concentrates, A-PRF decreased postoperative pain throughout the evaluated time and reduced trismus during the acute inflammatory peak compared to blood clots.

The clinical relevance of this study emphasized that A-PRF after mandibular third molar extractions performed better among the analyzed blood concentrates and seemed efficient in improving postoperative quality by decreasing inflammatory signs and symptoms.

Regarding bone healing, consistent with our findings, a 2022 split-mouth randomized clinical trial by Pereira et al. ⁽²⁴⁾ evaluated the effects of advanced platelet-rich fibrin (A-PRF+) on the healing of upper third molar post-extraction sockets using CBCT scans to assess healing stage, bone density, and fractal analysis 1 week and 90 days post-extraction.

The study found that at 7 days, the alveoli treated with A-PRF+ presented a suggestive sign of higher bone density than the control alveoli, which was not confirmed 90 days after the surgical procedure. The authors concluded that the use of A-PRF+ does not demonstrate a clinical advantage in the repair of post-extraction sockets of upper third molars.

On the same line, a 2023 systematic review and meta-analysis by Queneau et al. ⁽²⁵⁾ on the impact of PRF on bone preservation after dental extraction, which included 15 articles published between 2000 and 2022, found that PRF plays a positive role in vertical bone preservation ($p = 0.024$), horizontal bone preservation ($p < 0.001$), and bone filling ($p < 0.001$) after three to six months of tooth extraction.

However, the authors concluded that the level of evidence on the clinical application of PRF on hard tissue healing after tooth extraction is not sufficient, and there is a need to standardize methods for measuring bone preservation over a long follow-up period.

In agreement with our findings regarding the limited effect of PRF on bone density, a 2023 systematic review and trial sequential analysis by Caponio et al. ⁽²⁶⁾ evaluated the effect of platelet concentrates on new bone formation in alveolar ridge preservation. The review concluded that although some studies reported positive effects, the overall evidence was not robust enough to definitively support the routine use of PRF for bone regeneration, and further high-quality randomized controlled trials with standardized protocols are needed.

CONCLUSION

Within the limitations of this study, PRF has an effective role in minimizing the postoperative complications after extraction of impacted third molars in heavy smokers, such as trismus, pain, and edema, but has no effect on bone healing. PRF is a simple, low-cost, autologous adjunct that improves early recovery in heavy smokers undergoing impacted third molar surgery.

References

- 1) Coulthard P, Bailey E, Esposito M, Furness S, Renton TF, Worthington HV. Surgical techniques for the removal of mandibular wisdom teeth. Cochrane Database Syst Rev. 2014;7:CD004345.

- 2) Lago-Mendez L, Diniz-Freitas M, Senra-Rivera C, Gude-Sampedro F, Rey JMG, García-García A. Relationships between surgical difficulty and postoperative pain in lower third molar extractions. *J Oral Maxillofac Surg.* 2007;65(5):979-983.
- 3) Diegelmann RF, Evans MC. Wound healing: an overview of acute, fibrotic and delayed healing. *Front Biosci.* 2004;9:283-289.
- 4) World Health Organization. WHO Report on the Global Tobacco Epidemic 2008. Geneva: WHO; 2008.
- 5) Ozkan A, Bayar GR, Altug HA, Sencimen M, Dogan N, Gunaydin Y. The effect of cigarette smoking on the healing of extraction sockets: an immunohistochemical study. *J Craniofac Surg.* 2014;25(4):e397-e402.
- 6) Choukroun J, Adda F, Schoeffler C, Vervelle A. Une opportunité en paro-implantologie: le PRF. *Implantodontie.* 2001;42:55-62.
- 7) Dohan Ehrenfest DM, Diss A, Odin G, Doglioli P, Hippolyte MP, Charrier JB. In vitro effects of Choukroun's PRF (platelet-rich fibrin) on human gingival fibroblasts, dermal prekeratinocytes, preadipocytes, and maxillofacial osteoblasts in primary cultures. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;108(3):341-352.
- 8) Herrera-Briones FJ, Prados Sanchez E, Reyes Botella C, Vallecillo Capilla M. Update on the use of corticosteroids in third molar surgery: systematic review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2013;116(5):342-351.
- 9) Kumar N, Prasad K, Ramanujam L, Dexith RKJ, Chauhan A. Evaluation of treatment outcome after impacted mandibular third molar surgery with the use of autologous platelet-rich fibrin: a randomized controlled clinical study. *J Oral Maxillofac Surg.* 2015;73(6):1042-1049.
- 10) Uyanik LO, Bilginaylar K, Etikan I. Effects of platelet-rich fibrin and piezosurgery on impacted mandibular third molar surgery outcomes. *Head Face Med.* 2015;11:25.
- 11) Bilginaylar K, Uyanik LO. Evaluation of the effects of platelet-rich fibrin and piezosurgery on outcomes after removal of impacted mandibular third molars. *Br J Oral Maxillofac Surg.* 2016;54(6):629-633.
- 12) Gülşen U, Şentürk MF. Effect of platelet rich fibrin on edema and pain following third molar surgery: a split mouth control study. *BMC Oral Health.* 2017;17(1):1-6.
- 13) Al-Hamed FS, Tawfik MAM, Abdelfadil E, Al-Saleh MA. Efficacy of platelet-rich fibrin after mandibular third molar extraction: a systematic review and meta-analysis. *J Oral Maxillofac Surg.* 2017;75(6):1124-1135.
- 14) Trybek G, Rydlińska J, Aniko-Włodarczyk M, Jaroń A. Effect of platelet-rich fibrin application on non-infectious complications after surgical extraction of impacted mandibular third molars. *Int J Environ Res Public Health.* 2021;18(16):8249.
- 15) Gürbüz B, Pikdöken L, Tunalı M, Urhan M, Küçükodacı Z, Ercan F. Scintigraphic evaluation of osteoblastic activity in extraction sockets treated with platelet-rich fibrin. *J Oral Maxillofac Surg.* 2010;68(5):980-989.
- 16) Schneider CA, Rasband WS, Eliceiri KW. NIH Image to ImageJ: 25 years of image analysis. *Nat Methods.* 2012;9(7):671-675.
- 17) Costa MDMA, et al. Do blood concentrates influence inflammatory signs and symptoms after mandibular third molar surgery? A systematic review and network meta-analysis of randomized clinical trials. *Clin Oral Investig.* 2023;27(12):7045-7078.
- 18) Öhrnell Malekzadeh B, et al. Effects of platelet-rich fibrin on outcomes following mandibular third molar removal: a randomized controlled clinical trial. *Int J Oral Maxillofac Surg.* 2025;54(11):1131-1137.

- 19) Pabst A, et al. Effectiveness of platelet-rich fibrin in third molar extractions: a randomized controlled split-mouth study. Clin Oral Investig. 2024;28(11):615.
- 20) Aliberti A, Mariniello M, Bergaminelli M, et al. Using injectable Platelet-rich fibrin to improve recovery after impacted lower third molar extraction: a randomized controlled clinical trial. Clin Oral Investig. 2025;29(10):467.
- 21) Pattnayak A, Ramanna PK, Mahabala KY, et al. Impact of Platelet-rich Plasma and Platelet-rich Fibrin in Mandibular Third Molar Extraction: A Systematic Review. J Contemp Dent Pract. 2024;25(9):904-910.
- 22) Barone S, Bennardo F, Salviati M, Antonelli A, Giudice A. Evaluation of the usefulness of platelet-rich fibrin (PRF) in mandibular third molar surgery with 3D facial swelling analysis: A split-mouth randomized clinical trial. Head Face Med. 2025;21(1):8.
- 23) Alrayyes Y, et al. Soft-Tissue Healing Assessment after Extraction and Socket Preservation Using Platelet-Rich Fibrin (PRF) in Smokers: A Single-Blinded, Randomized, Controlled Clinical Trial. Diagnostics (Basel). 2022;12(10):2403.
- 24) Pereira DA, et al. Advanced platelet-rich-fibrin (A-PRF +) has no additional effect on the healing of post-extraction sockets of upper third molars. A split mouth randomized clinical trial. Oral Maxillofac Surg. 2023;27(3):411-419.
- 25) Queneau V, et al. The impact of platelet rich fibrin on bone preservation after dental extraction: A systematic review and meta-analysis. SFPIO, Société Française de Parodontologie et d'implantologie Orale. 2023. HAL Id: hal-04329537.
- 26) Caponio VCA, et al. Effect of the use of platelet concentrates on new bone formation in alveolar ridge preservation: a systematic review, meta-analysis, and trial sequential analysis. Clin Oral Investig. 2023;27(8):4131-4146.