Head & Face Medicine

RESEARCH

Open Access

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

Selene Barone[1†], Francesco Bennardo[1†], Marianna Salviati[1], Alessandro Antonelli[1*] and Amerigo Giudice[1,2]

Abstract

Background Third molar surgery is associated with various postoperative complications (PC). Different strategies, including the application of platelet-rich fibrin (PRF), have been implemented to reduce PC. Digital technologies have proven useful in objectively assessing postoperative facial swelling. This study aimed to evaluate the effect of PRF on reducing facial swelling after lower third molar surgery using a 3D face scanner.

Methods A randomized split-mouth clinical trial was set up and 32 patients (18 to 32 years), requiring extraction of both mandibular third molars, were recruited at the Oral Surgery Clinic of the Magna Graecia University of Catanzaro. The primary predictive variable was the application or not of PRF plugs and membranes in the post-extraction socket. Primary outcome variable was facial swelling recorded with a face scanner preoperatively (T0), after three (T1) and seven (T2) days. Qualitative and quantitative data analysis were conducted following an automated and standardized imaging analysis workflow using the 3D Slicer software. Secondary outcome variables were trismus, recorded by measuring the maximum buccal opening with a caliper, pain, recorded using a visual analogue scale (VAS), and duration of the surgery. Descriptive and bivariate analysis were performed by setting the significance level $\alpha = 0.05$.

Results All patients exhibited a significant increase in facial swelling at T1, followed by a subsequent reduction from day 3 to day 7, with a slight persistence of edema observed on the seventh day. No significant data emerged from the statistical analysis conducted. Linear differences in PRF group reported improved values of postoperative swelling only in the T1-T2 and T0-T2 phases of analysis. Volumetric differences favored PRF group compared with control group in all phases. VAS was lower in PRF group only at T2, compared with control group.

Conclusions Application of PRF in post-extraction sockets showed effectiveness in reducing facial swelling. Its advantages, including accessibility, cost-effectiveness, and absence of adverse reactions, make it an optimal treatment choice in reducing post-surgical sequelae.

[†]Selene Barone and Francesco Bennardo contributed equally to this work (first author shared position).

*Correspondence:
Alessandro Antonelli
alessandro.antonelli@unicz.it

Full list of author information is available at the end of the article

Keywords 3D analysis, Facial scanner, Platelet-rich fibrin, Swelling, Third molar surgery

Introduction

Third molar surgery is one of the most frequently performed procedures in oral surgery; nevertheless, because of the many different variables that influence both the surgical process and its postoperative consequences, it still represents a challenge for the surgeon [1–3]. The immediate postoperative period is marked by inflammatory symptoms such as pain, swelling, and trismus; while sequelae such as hypoesthesia or nerve paresthesia, hemorrhagic emergencies, hard tissue damage, and infection are less frequent complications [4].

Various therapeutic approaches have been studied and implemented to minimize side effects: pre- and/or postoperative use of nonsteroidal anti-inflammatory drugs, use of piezoelectric or laser devices, and the application of autologous platelet concentrates (APCs) [5]. However, the use of different approaches to minimize the side effects of third molar surgery is still under debate. Applying APCs after surgical procedures could be useful to accelerate tissue healing: alpha granules are the main platelet components that contribute to wound healing by releasing growth factors [6–12]. Platelet-rich fibrin (PRF) is a second-generation APC characterized by a single centrifugation protocol that leads to the formation of a fibrin network that incorporates platelets, leukocytes, and cytokines and ensures their release slowly and progressively for about seven days [13–16]. Several clinical studies have investigated the possible effects of PRF on postoperative sequelae after third molar surgery, showing its promising effects on reducing postoperative edema, trismus, and pain [17, 18]. Appropriate treatment of side effects is crucial for ensuring optimal healing and overall patient well-being; a thorough knowledge of postoperative sequelae and management strategies is necessary for the oral surgeon to achieve these goals. The qualitative and quantitative assessment of postoperative edema becomes an important starting point in scientific research to understand how to improve patient's quality of life [3, 19].

Various methods of analyzing and measuring swelling have been described, ranging from visual analysis scores and clinical observation to the use of linear and angular, analog and digital measuring instruments, facial arches, photographs, ultrasonography, photogrammetry, computed tomography, and facial scanners. Currently, scientific literature exhibits significant heterogeneity in the analysis of swelling; in recent years, new three-dimensional analysis methods have led to the search for an accurate and reproducible method for assessing soft tissue changes. Objective methods and advanced technologies, such as three-dimensional scanners, can provide precise and repeatable measurements and help evaluate PRF's effects on reducing postoperative facial swelling [20–22]. New technologies can help clinicians choose the most suitable treatment for each patient and monitor therapies that could improve healing and quality of life [23–27].

This randomized clinical trial aimed to evaluate the effects of PRF on reducing facial swelling after mandibular third molar (M3M) surgery using an innovative, reproducible, objective, and open-access swelling analysis method. The goal was to obtain accurate data regarding using PRF to improve patient's postoperative quality of life.

Materials and methods

The present article is reported according to the Consolidated Standards of Reporting Trials (CONSORT) statement and its extension for within-person randomized studies [28].

Study design

The authors designed a single-center split-mouth randomized clinical trial (www.clinicaltrials.gov — NCT06165692 retrospectively recorded — Date of registration: 2023-12-11). The authors designed and conducted this study according to the guidelines of the Helsinki Declaration on human experimentation and good clinical practice, and after obtaining ethical approval by the Ethical Review Board of Calabria Region (Prot. No. 02/2023; reference for Magna Graecia University of Catanzaro, Catanzaro, Italy). Informed consent was obtained from all subjects involved in the study.

Study sample

Patients were enrolled at the Oral Surgery Clinic of the Academic Hospital of Magna Graecia University of Catanzaro (A.O.U. Renato Dulbecco – Catanzaro, Italy) between January 2023 and December 2023. The inclusion criteria were as follows:

- patients aged between 18 and 32 years with a good state of health according to American Society of Anesthesiologists (ASA) physical status classification system (ASA 1) [29];
- patients requiring both M3Ms extraction with the same state of difficulty comparing the left and right side, according to the Juodzbalys and Daugela classification [30, 31];
- complete apexification of the tooth, stage H according to the Shumaker classification [32];

- available cone beam computed tomography (CBCT) with a good resolution and a large field of view (FOV), including the anatomical structures of the head and face from the sella turcica to the hyoid bone.

Patients excluded from the study protocol were those with allergies to used medications, a history of treatment with bisphosphonates, antiresorptive or anticancer drugs, coagulation disorders, uncontrolled diabetes, pregnancy, breastfeeding, the need for bone grafting at any extraction site, and facial malformations.

The required sample size was determined based on an effect size of 0.5, aiming for a power of 85% and a type I error of 0.05, using G* Power (G* Power version 3.1.9.7, G*Power Team, Heinrich Heine Universität Düsseldorf, Germany). To meet these criteria, 31 patients would have been necessary for the recruitment phase.

Procedure

Each patient underwent extraction of both M3Ms during two different sessions (5 weeks between two surgeries). The study's follow-up lasted one week after each extraction (total time 6 weeks). The randomization process involved generating a computer-generated random shortlist. Before extraction, patients received a single dose of prophylactic antibiotic 30 min before the intervention: 2 g of amoxicillin or 600 mg of clindamycin if allergic to penicillin. Patients rinsed with 0.2% chlorhexidine mouthwash for 1 min before the intervention. Local anesthesia was delivered as required, using mepivacaine hydrochloride 20 mg/ml 1:100,000 adrenalin (Optocain, Molteni Dental, Milano, Italy).

An oral surgeon (first operator) used identical opaque envelopes with various combinations to assign each treatment (test and control) to a specific site (left or right M3M) and prepared PRF on the day of surgery for test treatment (PRF group). The PRF was prepared in the clinic after collecting patients' autologous blood, according to the original protocol [33]: 36 mL of autologous blood were collected in four 9 mL-glass tubes without additives and rapidly centrifuged at 1300 rpm (~200 g RCF max; ~ 130 g RCF clot) for 8 min at room temperature. The tubes, specific for PRF preparation, were inserted in a balanced way in a dedicated centrifuge (Process for PRF, Nice, France). After centrifugation, the operator removed the PRF clots from the tubes and placed them into the PRF box (Process for PRF, Nice, France) to prepare the plugs and membranes necessary to fill the socket (Fig. 1).

Another expert oral surgeon (second operator) performed the M3M surgery without suturing. The first operator completed the intervention with PRF and sutures application (Vycril 4 – 0, Ethicon, J&J, Somerville, NJ, USA) in the PRF group and suturing alone for the control side (CTR group).

In case of pain, patients were instructed to take paracetamol 1 g or metamizole 500 mg if they were allergic to paracetamol. They were also instructed not to eat or drink for at least 90 min after surgery, brush, or use any mouthwash for the first postoperative day. Chlorhexidine mouthwash 0.2% had to be used for 1 min twice a day starting the second postoperative day until control.

Outcome assessment and data collection

The following data were collected by a blinded operator in the immediate pre-operative period (T0), three (T1), and seven days (T2) after surgery:

- a three-dimensional face scan was acquired using a specific protocol previously described to determine face swelling [34, 35];
- the patient's maximum buccal opening was measured with a caliper (distance between upper and lower central incisors at the incisal edge) to determine trismus;

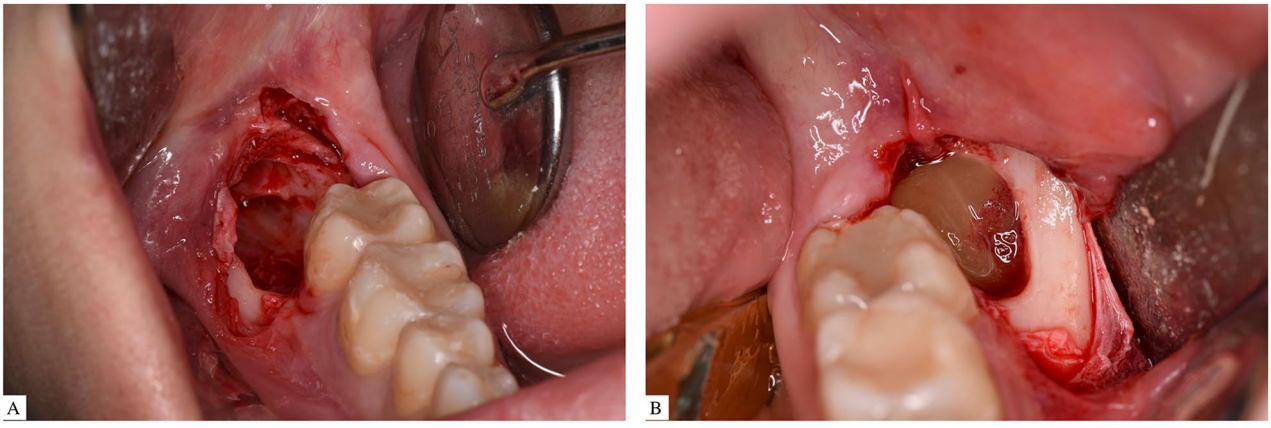

Fig. 1 Post-extractive socket (**A**) right side without PRF (**B**) left side with PRF positioning

- pain was assessed through a Visual Analog Scale (VAS) for each intervention: patients were asked to grade the severity of their symptoms in numbers from 0–no discomfort to 10–very severe pain);
- time to complete each individual procedure (measured in second);
- any additional complication (oroantral communication, root fracture, bleeding, dry socket or alveolitis, abscess, fistula, nerve injury).

Data processing

According to *Barone et al.* [34], the digital analysis was performed by a blinded operator using the open-source software 3D Slicer, which incorporates automated tools to apply a defined workflow: (1) data anonymization; (2) orientation; (3) surface registration; (4) qualitative comparisons; (5) linear measurements; (6) volumetric quantification. Each set of facial scans was imported as STL files, generating digital face models (visualization toolkit; vtk file format). The T0 facial scan underwent automated surface registration onto the 3D soft tissue model, segmented from the previously oriented CBCT (standardized according to the Frankfurt and midsagittal planes) [36, 37]. Subsequently, the T1 and T2 facial scans were registered on the oriented T0 using the same procedure [3]. The automated tool Model-to-Model-Distance allowed the superimposition of the facial models in pairs as follows: T0-T1, to evaluate facial swelling three days after surgery; T1-T2, to assess any changes in facial edema between three and seven days after surgery; and T0-T2, to evaluate swelling occurrence one week after surgery. The operator conducted a qualitative analysis by delineating the region of interest, identified by the zygomatic arch superiorly, submandibular fossa inferiorly, preauricular region posteriorly, and the facial midline anteriorly (Fig. 2). To highlight the specific localization of facial edema and to compare differential swelling at different time points, a colormap was obtained for each superimposed pair using the *ShapePopulationViewer* module. Automatic generation of a visualization of post-surgical changes, including the direction of movement (vectors), was performed. Automated quantification of soft tissue swelling involved two main steps: (1) calculation of the mean differential between linear measurements (in millimeters, mm) of surface area on the three paired models using the Mesh Statistic plugin and (2) quantification of volume differences (in cubic millimeters; mm^3) between pairs of models using the *Mesh Volume Comparison* module.

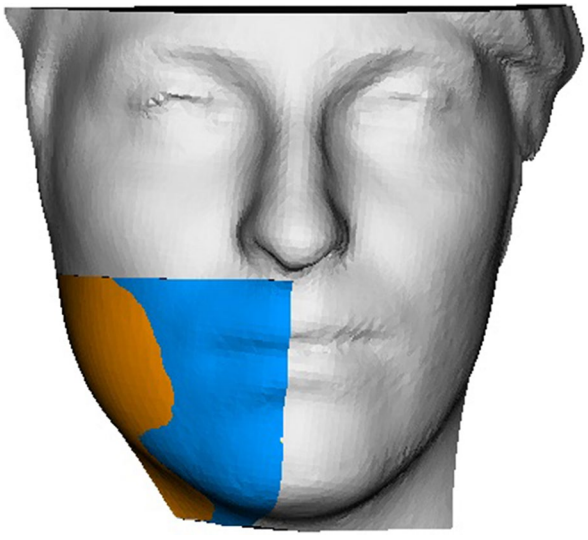

Fig. 2 Identification of the Region Of Interest (ROI) of the post-surgical edema for the volume measurement

Study variables

The primary predictor variable was the PRF application or no PRF application in the socket after M3Ms extraction.

The primary outcome variable was facial swelling.

The secondary variables were (1) trismus, (2) pain, (3) duration of the intervention, and (4) other reported complications.

Statistical analysis

An operator collected the data and reported them in a single database. The statistician analyzed the results with descriptive statistics: the mean and standard deviation were defined as continuous variables, while frequencies and percentages were defined as qualitative variables after calculation. The statistician performed a bivariate statistic analysis using Student's t-test and calculated the 95% confidence interval and the p-value by setting the significance level alpha = 0.05. Statistical analysis was performed using R (R Development Core Team; GPL). A linear regression model was used to correlate primary and secondary outcome variables.

Results

The authors recruited 32 patients, but one did not attend scheduled follow-up and was excluded from the study (Fig. 3). Consequently, 31 patients (22 female, 9 male) were included in the study. No additional complications were reported. The authors reported demographic data in Table 1. Qualitative analysis enabled the identification of the Region Of Interest (ROI) of the post-surgical edema (Figs. 4 and 5). Volumetric differences in the three phases of postoperative edema analysis favored the PRF group over the CTR group (Table 2). Linear measurements in the PRF group reported a better reduction of postoperative swelling only in the T1-T2 and T0-T2 periods. However, none of these data reached statistical significance in the analysis ($p > 0.05$; Table 2). Bivariate statistics showed

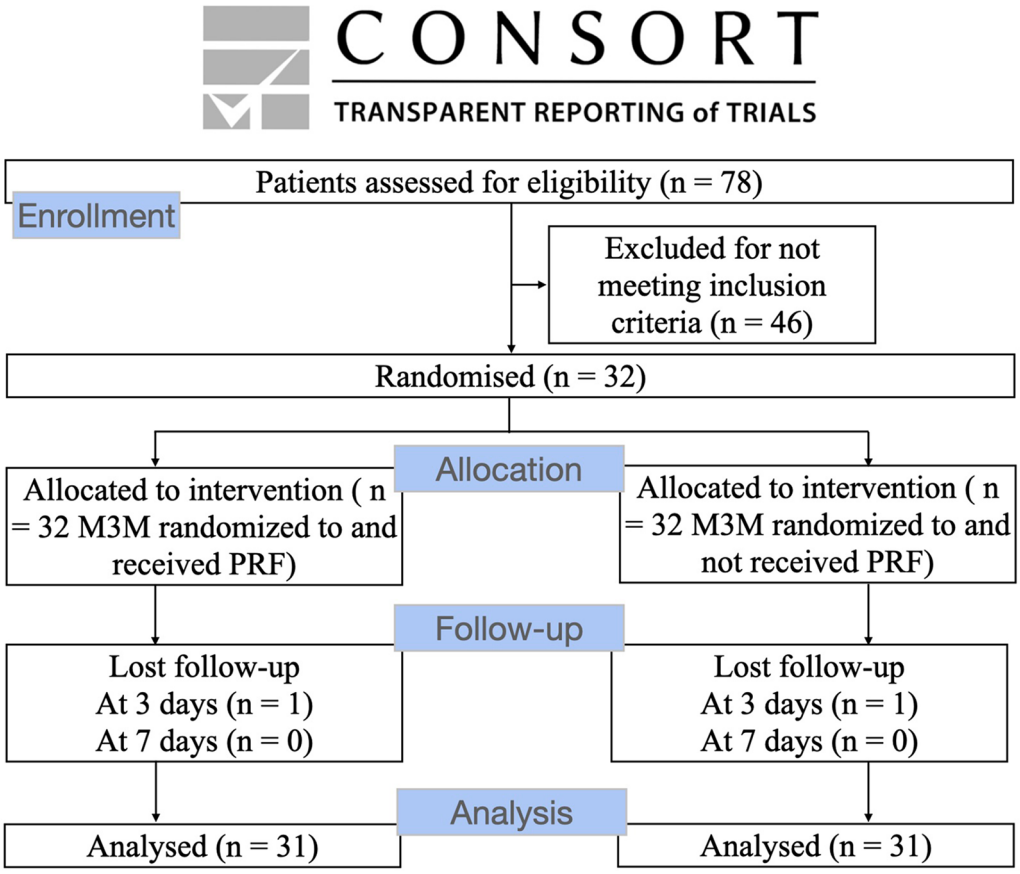

Fig. 3 CONSORT diagram: 31 patients were included and randomly assigned to two groups

Table 1 Descriptive statistics of the study sample

Demographic data	Study sample
Patient	31
Gender	
Female	22 (71%)
Male	9 (29%)
Age (years)	23,5 ± 3,3
Juodzbalys and Daugela classification	
Conventional	7 (22,58%)
Simple	9 (29,03%)
Moderate	10 (32,25%)
Difficult	5 (16,13%)

no significant differences in maximum buccal opening values between the two study groups ($p = 0.799$; Table 2). Pain values recorded on the third postoperative day were higher in the test group (4.57 ± 2.87) compared to the control group (4.21 ± 2.55), with no statistical significance emerging ($p = 0.731$). Similarly, there was no significant difference in pain values recorded at T2 ($p = 0.573$), with 1.50 ± 2.28 in the PRF group and 1.93 ± 1.64 in the CTR group.

Legend. T0: immediately before surgery; T1: three days after surgery; T2: seven days after surgery.

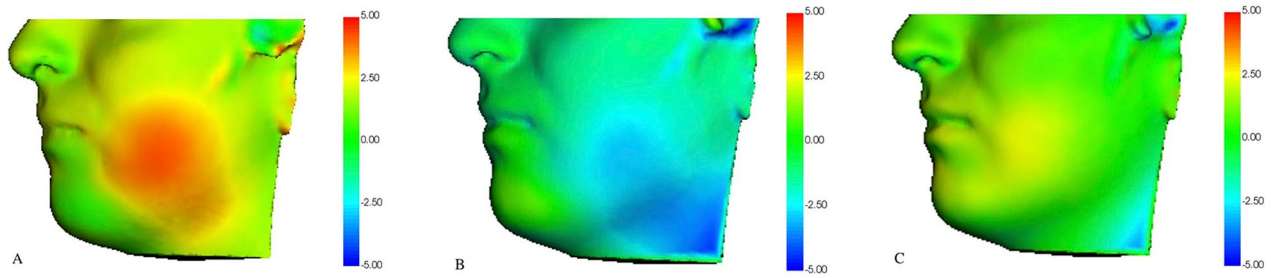

Fig. 4 Qualitative analysis of post-operative swelling in PRF group (A) T0-T1 (B) T1-T2 (C) T0-T2 (T0: immediately pre-surgery; T1: three days post-surgery; T2: seven days post-surgery)

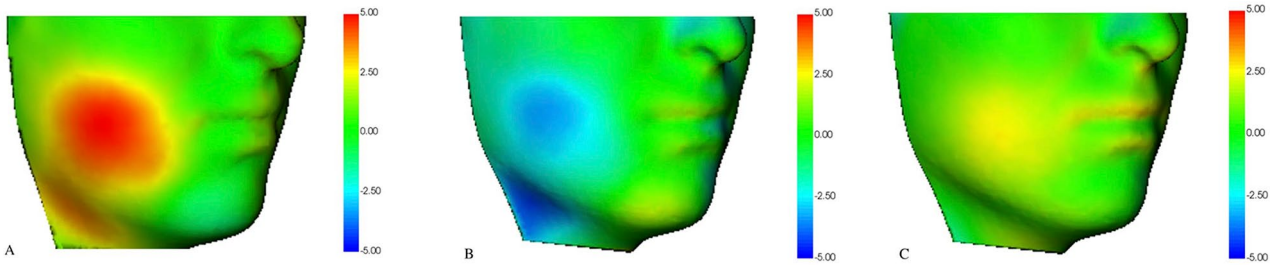

Fig. 5 Quantitative analysis of post-operative swelling in CTR group (A) T0-T1 (B) T1-T2 (C) T0-T2 (T0: immediately pre-surgery; T1: three days post-surgery; T2: seven days post-surgery)

Table 2 Bivariate analysis for comparison of PRF and CTR groups

Outcome variables	PRF Group	CTR Group	*P*-value
Maximum Buccal Opening T0	43.51 ± 6.91	42.79 ± 7.92	0.799
Maximum Buccal Opening T1	34.04 ± 10.08	32.01 ± 9.93	0.597
Maximum Buccal Opening T2	37.07 ± 8.25	35.86 ± 8.41	0.703
Pain T0	1.43 ± 2.87	1.07 ± 2.37	0.723
Pain T1	4.57 ± 2.87	4.21 ± 2.55	0.731
Pain T2	1.50 ± 2.28	1.93 ± 1.64	0.573
Swelling T0-T1 (Linear difference)	1.88 ± 1.00	1.28 ± 1.15	0.156
Swelling T1-T2 (Linear difference)	-0.89 ± 1.17	-0.73 ± 0.74	0.670
Swelling T0-T2 (Linear difference)	0.57 ± 0.63	0.64 ± 0.69	0.806
Swelling T0-T1 (Volumetric difference)	2039.24 ± 9430.07	3679.50 ± 5109.43	0.572
Swelling T1-T2 (Volumetric difference)	-3591.06 ± 8112.66	-1824.1 ± 4524.08	0.483
Swelling T0-T2 (Volumetric difference)	5625.23 ± 4907.16	5509.32 ± 7184.12	0.961

Legend. T0: immediately before surgery; T1: three days after surgery; T2: seven days after surgery

The linear regression model (Table 3) showed the presence of a directly proportional correlation between the volumetric differences calculated throughout the postoperative period (T0-T2) with the following variables: volumetric differences of edema in the periods T0-T1 (b = 0.998; $p = 1.517$) and T1-T2 (b = 0.997; $p = 6.486$), and linear differences of postoperative edema at seven days (b = 0.998; $p = 1.517$). The increase in volumetric swelling data in the first three postoperative days appears to be proportionally related to a reduction of volumes occurring from day three to day seven postoperatively (b = 0.999; $p = 5.061$) and in a decrease in the seven-day follow-up in terms of linear differences (b=-30.617; $p = 2.150$). A trend of direct proportionality is present between the volumetric values of edema at T1-T2 and those at T0-T2 (b = 1.003; $p = 6.486$).

The linear differential values at T0-T2 exhibited negative correlations with the volumetric difference in the T0-T1 period (b=-0.005; $p = 0.036$) and the T1-T2 period (b=-0.005; $p = 0.037$). Conversely, there was a positive correlation with the difference in the T0-T1 period measured in only two dimensions (b = 0.272; $p = 0.002$). Surgical time was directly correlated to the volumetric differences calculated in T0-T1 (b = 1.575; $p = 1.727$) and T1-T2 (b = 1.564; $p = 1.832$) and to the linear differential values calculated in T0- T2 (b = 0.019; $p = 0.023$), a negative correlation was found with the volumetric differential values calculated in T0-T2 (b=-1.571; $p = 1.742$).

Discussion

The present study investigated the effects of PRF on improving patients' quality of life after M3Ms surgery, focusing on swelling, trismus, and pain. The authors collected each outcome variable at three specific pivotal time points: immediately before surgery and three and seven days after surgery. Building upon prior research demonstrating the efficacy of PRF in managing postoperative discomfort, swelling, and restricted jaw movement, this study stands out for its utilization of advanced 3D scanning techniques to evaluate swelling [6, 7, 18, 38, 39]. While previous investigations have provided valuable insights, some limitations have been highlighted [40]. Konuk et al. reported in their split-mouth study that PRF effectively reduces postoperative sequelae after lower third molar surgery, but concurrent surgeries could be recognized as a potential bias [39].

The authors adopted a rigorous split-mouth protocol to avoid previously reported limitations. Both M3Ms were extracted in the same patient at two surgical times, effectively mitigating interindividual variations. The authors improved the previously reported protocols [39, 40] to observe the significant potential benefits of PRF application in M3M surgery. Moreover, this study contributes by

Table 3 Linear regression model

Study variables	β Coefficient	*P*-value
Swelling T0-T1 (Volumetric difference)		
Age	-3.599	3.312
Swelling (Linear difference) T0-T2	-30.617	2.150
Surgical time	1.575	1.727
Swelling (Volumetric difference) T0-T2	1.001	1.517
Swelling (Volumetric difference) T1-T2	-0.999	5.061
Swelling T1-T2 (Volumetric difference)		
Age	-3.607	3.284
Swelling (Linear difference) T0-T2	-30.561	2.193
Surgical time	1.564	1.832
Swelling (Volumetric difference) T0-T2	1.003	6.486
Swelling (Volumetric difference) T0-T1	-1.001	5.060
Swelling T0-T2 (Volumetric difference)		
Age	3.589	3.335
Swelling (Linear difference) T0-T2	30.739	2.069
Surgical time	-1.571	1.742
Swelling (Volumetric difference) T1-T2	0.997	6.486
Swelling (Volumetric difference) T0-T1	0.998	1.517
Swelling T0-T1 (Linear difference)		
Swelling (Linear difference) T0-T2	1.199	0.0007
Swelling (Volumetric difference) T0-T2	-0.0001	0.0005
Swelling (Volumetric difference) T0-T1	0.0001	0.0000
Swelling T1-T2		
Buccal opening T0	0.058	0.005
Buccal opening T2	-0.051	0.007
Swelling (Linear difference) T0-T1	-0.397	0.002
Swelling (Volumetric difference) T1-T2	0.0000	0.003
Swelling T0-T2		
Swelling (Linear difference) T0-T1	0.272	0.002
Surgical time	0.019	0.023
Swelling (Volumetric difference) T0-T2	0.005	0.035
Swelling (Volumetric difference) T1-T2	-0.005	0.037
Swelling (Volumetric difference) T0-T1	-0.005	0.036

Legend. T0: immediately pre-surgery; T1: three days post-surgery; T2: seven days post-surgery

providing clarity on the units of measurement employed in the three-dimensional analysis, ensuring the precision and reliability of the findings.

The clinical efficacy of PRF application in M3M surgery is still under debate due to the conflicting results reported in the literature [17, 41–44]. A study conducted by Shruthi et al. showed encouraging data with a significant reduction in pain on the second, third, and seventh days after surgery in the PRF group compared with the control group. This result suggests that PRF could be an effective adjunct in reducing pain during complex M3Ms extractions. However, this randomized clinical trial did not consider the inter-individual differences regarding the perception of pain by different subjects and did not report detailed information regarding the medical therapy of enrolled patients [6]. Similar studies have reported a significant reduction in pain using PRF in third molar surgery, but they did not employ a split-mouth study design [18]. Singh et al. found higher pain levels on the second postoperative day in both study groups, with a decreasing trend on the fourth and seventh days. In this split-mouth investigation, the weakness of the results can be attributed to performing both interventions in the same session for each patient, implying that the control intervention could have influenced the pain values [45].

The evaluation of maximum buccal opening showed no difference in the two study groups, contrary to the initial hypothesis and previous reports. Trebek et al. stated that trismus was significantly observable in the control group than in the PRF group at one, two, and seven days after surgery [46].

The same authors recommended jaw physiotherapy to patients, but muscle exercises performed during recovery can significantly influence muscle relaxation, resulting in a decrease in trismus. This factor prevents a valid comparison of the effect of PRF on the recovery rate of buccal trismus. No exercise was prescribed in the present clinical study. The maximum buccal opening was measured three times independently for each operated side and then compared.

Determining swelling after the M3Ms surgery is challenging due to the irregular facial surface. Papazov and Burschka defined the need for an automated and robust recording procedure that would increase the reliability of facial swelling analysis results [47].

For these goals, a three-dimensional non-contact scanning procedure could be used effectively because it can provide the requirements for clinical studies that require objective assessment of changes in facial dimensions [48, 49]. In contrast, analog measurements prove to be less accurate than digital ones. They are operator-dependent methods and, for this reason, not objective. To date, there is no standardized method of measuring facial swelling. This fact has always been a major limitation, especially in conducting systematic reviews of the literature and meta-analyses, because of the high heterogeneity rate of methods quantifying postoperative edema in clinical trials of lower third molar surgery [50].

With newer three-dimensional scanning technologies available, laser scanners, structured light scanners, and stereophotogrammetry scanners have become the first choice in research on volumetric measurements and related comparisons [21]. The principal limitations of reported methods are the need to identify the area of measurement of volume change and the errors caused by repositioning the patient at various stages of acquisition. In the first case, the lack of a clear anatomical landmark on the facial soft tissue was discriminative due to volume measurement errors between the samples [20]. The present study avoided these limitations by using a qualitative analysis step highlighting the boundaries of the region

affected by edema, so the automatic differential calculation is performed only on the identified ROI. Bias due to patient repositioning variation is the main source of error in the scanner method approach [20].

During the data processing phase, the segmentation of a 3D reference model from the pre-oriented CBCT scan, followed by automatic registration of overlapping scans, nullified the presence of any mesh positioning errors in space. Thus, using innovative digital measurements allows for reliable data for objective comparison. However, in some cases, while image acquisition can be considered a simple procedure that requires only a minimum of cooperation from the patient, image processing to assess swelling requires an experienced operator and can present a steep learning curve. A shortcoming of facial scanning methodology also lies in underestimating the actual volume of swelling that spreads in the lingual direction, which is not considered [22, 49]. For this purpose, three-dimensional reconstruction techniques using spiral computed tomography or magnetic resonance imaging could be an alternative, but these options are expensive and require technical expertise and exposure to ionizing radiation [20]. In contrast, scanners offer numerous advantages, such as low cost, speed, accuracy, noninvasiveness, no patient contact, and no radiation. Based on visible light, this method allows for images suitable for volumetric changes in the facial contour [22].

The main limitations of this study are the single-center design and the use of a 3D analysis method that requires a high level of technical expertise. Furthermore, the analysis of pain would also require objective analysis methods. Applying PRF in the post-extraction socket following surgical extraction of M3Ms effectively reduces edema, trismus, and postoperative discomfort. Although no statistically significant results emerged, the benefits of using PRF, including ease of access, low cost, and absence of adverse reactions as a strictly autologous material, make it an alternative therapeutic option in reducing post-surgical sequelae. Further clinical studies on PRF application in M3Ms surgery should have a multicenter design to increase the sample's number and heterogeneity, a simple three-dimensional digital analysis method to determine swelling in a standardized way, and future comparison among different studies.

Abbreviations

3D	Three-dimensional
CBCT	Cone beam computed tomography
CTR	Control
M3M	Mandibular third molar
M3Ms	Mandibular third molars
PRF	Platelet-rich fibrin
RCF	Relative centrifugation force
ROI	Region Of Interest

Acknowledgements
Thanks to Dipartimento di Scienze della Salute, Università degli Studi "Magna Graecia" di Catanzaro (Italy) for supporting the authors in the APC payment.

Author contributions
SB: Conceptualization, Data curation, Formal analysis, Methodology, Writing – review & editing. FB: Conceptualization, Data curation, Formal analysis, Methodology, Writing – review & editing.MS: Data curation, Formal analysis, Writing original draft, Software. AA: Data curation, Writing – review & editing, Methodology, Formal analysis. AG: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing. All authors have read and agreed to the published version of the manuscript.Selene Barone (S.B.) and Francesco Bennardo (F.B.) contributed equally to this manuscript (first author shared position).

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate
The ethical approval was obtained by the Ethical Review Board of Central Calabria (Prot. No. 02/2023). All patients enrolled for the study signed an informed consent.

Consent for publication
Patients provided informed consent regarding publishing their data and photographs.

Competing interests
The authors declare no competing interests.

Author details
[1]School of Dentistry, Department of Health Sciences, Magna Graecia University of Catanzaro, Viale Europa, Catanzaro 88100, Italy
[2]A.O.U. Renato Dulbecco, Academic Hospital of Magna Graecia University of Catanzaro, Catanzaro 88100, Italy

Received: 21 October 2024 / Accepted: 3 February 2025
Published online: 22 February 2025

References

1. Vranckx M, Fieuws S, Jacobs R, Politis C. Surgical experience and patient morbidity after third molar removal. J Stomatol Oral Maxillofac Surg. 2022;123:297–302.
2. Barone S, Antonelli A, Averta F, Diodati F, Muraca D, Bennardo F, et al. Does Mandibular Gonial Angle Influence the Eruption Pattern of the Lower Third Molar? A three-dimensional study. J Clin Med. 2021;10:4057.
3. Antonelli A, Barone S, Bennardo F, Giudice A. Three-dimensional facial swelling evaluation of pre-operative single-dose of prednisone in third molar surgery: a split-mouth randomized controlled trial. BMC Oral Health. 2023;23:614.
4. Chuang S-K, Perrott DH, Susarla SM, Dodson TB. Risk factors for inflammatory complications following third molar surgery in adults. J Oral Maxillofac Surg. 2008;66:2213–8.
5. Ozgul O, Senses F, Er N, Tekin U, Tuz HH, Alkan A, et al. Efficacy of platelet rich fibrin in the reduction of the pain and swelling after impacted third molar surgery: randomized multicenter split-mouth clinical trial. Head Face Med. 2015;11:37.
6. Shruthi TM, Shetty AD, Akash KS, Ahmed F, Shetty N, Singarapu R. Evaluation of effects of platelet-rich fibrin on treatment outcomes after impacted mandibular third molar surgery. Natl J Maxillofac Surg. 2022;13:S46–51.
7. Afat İM, Akdoğan ET, Gönül O. Effects of leukocyte- and platelet-rich fibrin alone and combined with Hyaluronic Acid on Pain, Edema, and Trismus after

Surgical extraction of impacted Mandibular Third molars. J Oral Maxillofac Surg. 2018;76:926–32.
8. Njokanma AR, Fatusi OA, Ogundipe OK, Arije OO, Akomolafe AG, Kuye OF. Does platelet-rich fibrin increase bone regeneration in mandibular third molar extraction sockets? J Korean Assoc Oral Maxillofac Surg. 2022;48:371–81.
9. Quirynen M, Sculean A, Blanco J, Wang H, Donos N. Introduction and overview on Autogenous Platelet Concentrates. Periodontol. 2000. 2024.
10. Rechichi M, Ferrise M, Romano F, Gallelli L, Toschi V, Dominijanni A et al. Autologous platelet-rich plasma in the treatment of refractory corneal ulcers: A case report. Am J Ophthalmol Case Rep [Internet]. 2020;20:100838. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2451993618300641
11. Silva FFVe, Chauca-Bajaña L, Caponio VCA, Cueva KAS, Velasquez-Ron B, Padín-Iruegas ME, et al. Regeneration of periodontal intrabony defects using platelet-rich fibrin (PRF): a systematic review and network meta-analysis. Odontology. 2024;112:1047–68.
12. Caponio VCA, Baca-González L, González-Serrano J, Torres J, López-Pintor RM. 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;27:4131–46.
13. Blanco J, García A, Hermida-Nogueira L, Castro AB. How to explain the beneficial effects of leukocyte- and platelet-rich fibrin. Periodontol. 2000. 2024.
14. Dohle E, Parkhoo K, Bennardo F, Schmeinck L, Sader R, Ghanaati S. Immunomodulation of Cancer cells using autologous blood concentrates as a patient-specific cell culture system: a comparative study on Osteosarcoma and Fibrosarcoma Cell lines. Bioengineering. 2024;11:303.
15. Bennardo F, Barone S, Antonelli A, Giudice A. Autologous platelet concentrates as adjuvant in the surgical management of medication-related osteonecrosis of the jaw. Periodontol. 2000. 2024.
16. Bennardo F, Gallelli L, Palleria C, Colosimo M, Fortunato L, De Sarro G et al. Can platelet-rich fibrin act as a natural carrier for antibiotics delivery? A proof-of-concept study for oral surgical procedures. BMC Oral Health [Internet]. 2023;23:134. Available from: https://bmcoralhealth.biomedcentral.com/articles/https://doi.org/10.1186/s12903-023-02814-5
17. Siawasch SAM, Yu J, Castro AB, Temmerman A, Teughels W, Quirynen M. Autologous platelet concentrates after third molar extraction: A systematic review. Periodontol. 2000. 2024.
18. Torul D, Omezli MM, Kahveci K. Evaluation of the effects of concentrated growth factors or advanced platelet rich-fibrin on postoperative pain, edema, and trismus following lower third molar removal: a randomized controlled clinical trial. J Stomatol Oral Maxillofac Surg. 2020;121:646–51.
19. Fortunato L, Amato M, Simeone M, Bennardo F, Barone S, Giudice A. Numb chin syndrome: a reflection of malignancy or a harbinger of MRONJ? A multicenter experience. J Stomatol Oral Maxillofac Surg. 2018;119.
20. Yamamoto S, Miyachi H, Fujii H, Ochiai S, Watanabe S, Shimozato K. Intuitive facial imaging method for evaluation of postoperative swelling: a combination of 3-Dimensional Computed Tomography and Laser Surface scanning in orthognathic surgery. J Oral Maxillofac Surg. 2016;74:e25061–250610.
21. Harrison JA, Nixon MA, Fright WR, Snape L. Use of hand-held laser scanning in the assessment of facial swelling: a preliminary study. Br J Oral Maxillofac Surg. 2004;42:8–17.
22. van der Meer WJ, Dijkstra PU, Visser A, Vissink A, Ren Y. Reliability and validity of measurements of facial swelling with a stereophotogrammetry optical three-dimensional scanner. Br J Oral Maxillofac Surg. 2014;52:922–7.
23. Rieder M, Remschmidt B, Gsaxner C, Gaessler J, Payer M, Zemann W, et al. Augmented reality-guided extraction of fully impacted Lower Third molars based on Maxillofacial CBCT scans. Bioengineering. 2024;11:625.
24. Pellegrino G, Lizio G, Ferri A, Marchetti C. Flapless and bone-preserving extraction of partially impacted mandibular third molars with dynamic navigation technology. A report of three cases. Int J Comput Dent. 2021;24:253–62.
25. Femiano F, Femiano R, Femiano L, Nucci L, Minervini G, Antonelli A, et al. A New Combined Protocol to treat the dentin hypersensitivity Associated with non-carious cervical lesions: a Randomized Controlled Trial. Appl Sci. 2020;11:187.
26. Giudice A, Bennardo F, Antonelli A, Barone S, Fortunato L. COVID-19 is a New Challenge for Dental Practitioners: Advice on Patients' Management from Prevention of Cross Infections to Telemedicine. Open Dent J [Internet]. 2020;14:298–304. Available from: https://opendentistryjournal.com/VOLUME/14/PAGE/298/
27. Giudice A, Antonelli A, Bennardo F. To test or not to test? An opportunity to restart dentistry sustainably in the 'COVID-19 era'. Int Endod J. 2020;53:1020–1.
28. Pandis N, Chung B, Scherer RW, Elbourne D, Altman DG. CONSORT 2010 statement: extension checklist for reporting within person randomised trials. BMJ. 2017;j2835.
29. Horvath B, Kloesel B, Todd MM, Cole DJ, Prielipp RC. The evolution, current value, and future of the American Society of anesthesiologists physical status classification system. Anesthesiology. 2021;135:904–19.
30. Spiotto MT, Juodzbalys G, Daugela P. Mandibular third molar impaction: review of literature and a proposal of a classification. J Oral Maxillofac Res. 2013;4.
31. Barone S, Bennardo F, Salviati M, Cosentino V, Finamore R, Greco V, et al. Concordance analysis of lower third molar surgery classifications: a comparative study. Dent J (Basel). 2024;12:167.
32. Shumaker DB. A comparison of chronologic age and physiologic age as predictors of tooth eruption. Am J Orthod. 1974;66:50–7.
33. El Bagdadi K, Kubesch A, Yu X, Al-Maawi S, Orlowska A, Dias A, et al. Reduction of relative centrifugal forces increases growth factor release within solid platelet-rich-fibrin (PRF)-based matrices: a proof of concept of LSCC (low speed centrifugation concept). Eur J Trauma Emerg Surg. 2019;45:467–79.
34. Barone S, Antonelli A, Salviati M, Greco V, Bennardo F, Becker K, et al. Accuracy Assessment of EM3D App-based 3D facial scanning compared to Cone Beam Computed Tomography. Dent J (Basel). 2024;12:342.
35. Barone S, Zaffino P, Salviati M, Destito M, Antonelli A, Bennardo F, et al. Automated pipeline for linear and volumetric assessment of facial swelling after third molar surgery. BMC Oral Health. 2024;24:1404.
36. Anchling L, Hutin N, Huang Y, Barone S, Roberts S, Miranda F et al. Automated Orientation and Registration of Cone-Beam Computed Tomography Scans. 2023. pp. 43–58.
37. Ruellas AC, de O, Tonello C, Gomes LR, Yatabe MS, Macron L, Lopinto J, et al. Common 3-dimensional coordinate system for assessment of directional changes. Am J Orthod Dentofac Orthop. 2016;149:645–56.
38. Kapse S, Surana S, Satish M, Hussain SE, Vyas S, Thakur D. Autologous platelet-rich fibrin: can it secure a better healing? Oral Surg Oral Med Oral Pathol Oral Radiol. 2019;127:8–18.
39. Konuk B, Şentürk M. Three-dimensional evaluation of the effect of platelet-rich fibrin on Edema in Lower impacted third molar surgery performed with Piezosurgery. Niger J Clin Pract. 2022;25:1107–14.
40. Asutay F, Ozcan-Kucuk A, Alan H, Koparal M. Three-dimensional evaluation of the effect of low-level laser therapy on facial swelling after lower third molar surgery: a randomized, placebo-controlled study. Niger J Clin Pract. 2018;21:1107.
41. Costa MDM, de Paranhos A, de Almeida LR, Oliveira VL, Vieira LM, de Dechichi W. 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;27:7045–78.
42. Zhu J, Zhang S, Yuan X, He T, Liu H, Wang J, et al. Effect of platelet-rich fibrin on the control of alveolar osteitis, pain, trismus, soft tissue healing, and swelling following mandibular third molar surgery: an updated systematic review and meta-analysis. Int J Oral Maxillofac Surg. 2021;50:398–406.
43. Ramos EU, Bizelli VF, Pereira Baggio AM, Ferriolli SC, Silva Prado GA, Farnezi Bassi AP. Do the New protocols of platelet-rich fibrin centrifugation allow Better Control of Postoperative Complications and Healing after surgery of impacted Lower Third Molar? A systematic review and Meta-analysis. J Oral Maxillofac Surg. 2022;80:1238–53.
44. Bao M, Du G, Zhang Y, Ma P, Cao Y, Li C. Application of platelet-rich fibrin derivatives for mandibular third molar extraction related post-operative sequelae: a systematic review and network Meta-analysis. J Oral Maxillofac Surg. 2021;79:2421–32.
45. Singh A, Kohli M, Gupta N. Platelet Rich Fibrin: a Novel Approach for Osseous Regeneration. J Maxillofac Oral Surg. 2012;11:430–4.
46. 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;18:8249.
47. Papazov C, Burschka D. Stochastic global optimization for robust point set registration. Comput Vis Image Underst. 2011;115:1598–609.
48. Bjørnsson GA, Haanæs HR, Skoglund LA. Naproxen 500 mg bid versus Acetaminophen 1000 mg qid: Effect on Swelling and other Acute postoperative events after bilateral third molar surgery. J Clin Pharmacol. 2003;43:849–58.
49. Civak T, Ustun T, Yilmaz HN, Gursoy B. Postoperative evaluation of Er:YAG laser, piezosurgery, and rotary systems used for osteotomy in mandibular third-molar extractions. J Cranio-Maxillofacial Surg. 2021;49:64–9.

50. Duarte de Oliveira FJ, Brasil GMLC, Araújo Soares GP, Fernandes Paiva DF, de Assis de Souza Júnior F. Use of low-level laser therapy to reduce postoperative pain, edema, and trismus following third molar surgery: a systematic review and meta-analysis. J Cranio-Maxillofacial Surg. 2021;49:1088–96.

Publisher's note