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Evaluation of the Effect of Primary and Secondary Closure on the Use of Leukocyte and Platelet-Rich Fibrin in Impacted Lower Third Molar Surgery

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Abstract: The aim of this study was to compare the effect of using L-PRF in patients undergoing impacted lower third molar surgery with either primary or secondary closure techniques. Methods: This prospective, randomized, double-blind, split-mouth clinical trial was conducted on patients with bilateral impacted lower third molars of a similar position. Primary closure was performed in group 1 and secondary closure in group 2. The group 1 closure technique was applied to one side of the patients, and the group 2 closure technique was applied to the other side at different times. Of the 45 patients evaluated, 9 patients were excluded from the study because of alveolitis and failure to attend regular control visits out. Results: Of the 36 patients included in the study, 23 were female and 13 were male, with a mean age of 22.42 ± 3.36 years. The secondary closure group had lower VAS scores at hour 6 ($p < 0.05$). Pain decreased more in the primary closure group when comparing changes between the VAS scores at 6 hours and 7 days ($p < 0.05$). Conclusions: The results of this study, showing that both secondary and primary closure are effective, with similar outcomes in terms of pain, swelling, and trismus, should be supported by future clinical trials.

Keywords: leukocyte and platelet-rich fibrin; closure techniques; wound healing; regenerative medicine; primary closure; secondary closure; impacted third molar

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1. Introduction

Mandibular third molar surgery is one of the most common procedures in oral and maxillofacial surgery. Despite advances in atraumatic techniques for impacted third molar surgery, postoperative inflammatory reactions can lead to edema, pain, and trismus in the maxillofacial region. These postoperative symptoms have a significant impact on the patient's quality of life. Effective management of these inflammatory manifestations is critical to the long-term well-being of the patient. Various strategies and interventions have been proposed to manage the immediate inflammatory response associated with third molar removal surgery. These include analgesics, antibiotics, corticosteroids, surgical drains, various flap and wound closure designs, and adjunctive measures such as the use of laser therapy, cryotherapy, ozone gel, platelet-rich plasma, and platelet-rich fibrin [1–3].

The wound-healing process is a remarkably complex phenomenon that is still not fully understood. In oral surgery, the natural healing process, also known as first intention healing, is achieved via two main techniques: primary and secondary closure. Primary closure refers to the close approximation of the skin or mucosa for healing purposes; on the

other hand, secondary closure involves allowing the wound to heal via granulation and re-epithelialization [4–6].

It appears that primary closure has advantages over secondary closure in terms of postoperative infection, facial swelling, and trismus after lower impacted third molar surgery. This may be due to open flap debridement. However, some studies suggest that primary and secondary closure result in similar postoperative complications. For example, a systematic review by Bailey et al. showed a higher incidence of infection with primary wound closure compared with secondary intention to allow the wound to heal. However, the confidence intervals were wide and favored both methods of healing. It is not clear why this should be, but it is the case that pain and trismus have been shown to be reduced with primary closure compared with secondary intention healing. On the other hand, Morely et al. concluded that there was insufficient evidence to recommend either primary or secondary closure techniques. This is because the nature and quality of the data have been unjustified and imprecise over the years. This makes it difficult to determine the best techniques to use, especially as surgical training becomes more competency-based [4,5,7,8].

Leukocyte and platelet-rich fibrin (L-PRF) therapy is currently an area of significant interest in the field of regenerative medicine. This special type of platelet concentrate is now being used to accelerate the healing process in oral and maxillofacial surgical procedures involving both soft and hard tissues [9]. L-PRF is a simple and completely natural treatment option that does not require anticoagulants, bovine thrombin, or other additives. The procedure involves taking blood before surgery and centrifuging it for 12 min. This creates a pliable membrane and a collection of platelets- and growth-factor-rich clots held together by fibrin. The top layer, known as the red layer, has a high concentration of platelets that release growth factors as the fibrin matrix is formed. Of paramount importance is the layer known as the buffy coat, which consists of white cells, platelets, and significant amounts of fibrin. Fibrin plays a crucial role in the body's healing process and in the formation of connective tissue after trauma. The white cells in L-PRF are trapped and stimulated as part of the natural healing mechanism. The final layer is acellular and contains approximately twice the amount of platelets found in peripheral blood. It is worth noting that L-PRF uses the patient's own blood, removing any concerns about disease transmission. This should encourage clinicians to incorporate L-PRF into their practice [9–11]. L-PRF is currently being used in a number of procedures, including the treatment of drug-induced osteonecrosis of the jaw, extraction socket healing, and pre-prosthetic bone surgery [12–15].

The benefits of L-PRF in impacted third molar surgery are numerous and range from reducing the amount of pain and swelling the patient experiences after surgery to increasing the rate of soft tissue and bone healing. L-PRF provides a scaffold for hard and soft tissue to grow into and around, which is particularly important in impacted third molar surgery where there is a large bony defect to heal. The slow release of growth factors over the first week of healing is thought to significantly increase the speed of the healing process as growth factors are chemicals in the body that promote faster, more effective tissue repair. As a result, conventional surgical extraction in such cases often leads to potential complications, including severe pain, swelling, and trismus. Fortunately, with the development of platelet concentration techniques, surgeons now have the opportunity to use L-PRF in their daily practice [16–20].

The use of L-PRF in impacted third molar surgery has shown improved wound healing, reduced incidence of alveolar osteitis, and improved postoperative recovery [13]. However, wound closure after surgery is an ongoing debate. When reviewing the studies evaluating the closure technique for lower impacted wisdom tooth surgery without L-PRF, the older studies recommend primary closure, while the current studies recommend secondary closure in terms of complications [6,21–24]. There are no studies reporting which closure technique is more successful in preventing or reducing postoperative complications after impacted lower third molar surgery when L-PRF is used. We believe that demonstrating the potential benefits of L-PRF on postoperative complications and which type of closure is more effective will ensure that L-PRF is used with the correct technique for this purpose.

The aim of this study was to compare the effect of using L-PRF in patients undergoing impacted lower third molar surgery with either primary or secondary closure techniques. Our hypothesis is that there is no difference in L-PRF application between primary and secondary closure techniques in impacted lower third molar surgery.

2. Materials and Methods

This prospective, randomized, double-blind, split-mouth clinical study was conducted at Van Yüzüncü Yıl University, Faculty of Dentistry, Oral and Maxillofacial Surgery Clinic between October 2022 to May 2023. The study was conducted in accordance with the current version of the Declaration of Helsinki. The study was approved by Van Yüzüncü Yıl University Faculty of Medicine Clinical Research Ethics Committee (decision number: 07 dated 1 September 2022) and complies with the CONSORT guidelines. During the study period, 553 patients were admitted for extraction of impacted wisdom teeth. Of these, 98 patients had bilateral impacted wisdom teeth, and 45 of them met the inclusion criteria for the study. Among the volunteers, those who met the inclusion criteria were informed about the study, and signed informed consent was obtained. Medical and dental history was taken at the first clinic visit. The presence or absence of bilateral impacted third molars was assessed by clinical and radiographic examination. Demographic information, facial and mouth opening measurements, pain scores, and group numbers were recorded on the anamnesis forms.

Inclusion criteria were as follows: 18 to 40 years of age, no systemic disease, bilateral and similar (vertical or mesioangular) position, asymptomatic, and partial mucosa- and bone-retained lower impacted third molars.

Exclusion criteria were as follows: smokers, pregnant or breastfeeding women, those not attending follow-up visits, those allergic to the materials or drugs used in the study, those with alveolitis, and those taking additional or different drugs to the study drugs.

Randomization in the trial was achieved using the envelope method. From the envelopes given to the patients by the support staff, the patients chose which side to operate on first and which group to use first. Only the sessional staff knew the numbers on the envelopes. To ensure blinding of the study authors, the suturing phase, i.e., closure, including L-PRF placement, was performed by an independent experienced surgeon outside the study. Surgeries were performed on Mondays, Tuesdays, and Wednesdays to allow for postoperative day-2 controls. Second operations were performed at least 4 weeks later.

Primary outcomes of the study were facial measurements, mouth opening measurements, and visual analog scale (VAS) scores. Secondary outcomes included alveolitis, infection, and the effects of flap release for primary closure. Facial measurements for swelling assessment (the reference points for the facial measurements used in the swelling score were the angulus-lateral canthus, angulus-lateral nasal corner, and tragus-pogonion distances; a single value was obtained by averaging these 3 distances in the swelling score) and mouth opening measurements to assess trismus were performed preoperatively (on postoperative day 2 and on postoperative day 7) with the patients sitting upright in the unit. Pain was assessed according to VAS, and patients rated their postoperative pain at 6, 12, 18, and 24 h and on days 2, 3, 4, 5, 6, and 7.

2.1. Study Groups

Patients underwent two different closure procedures. A total of 10 mL of blood was collected from the patients, and L-PRFs were centrifuged at 2700 rpm for 12 min in 1 tube without an activator and prepared by forming their final shapes into plugs in the L-PRF set for 5 min. The same surgical protocol was used in both groups, and 1 L-PRF plug was placed in the extraction sockets. At the suture stage, a 3/0 silk suture was used. Primary closure was performed in group 1 with periosteal release to achieve tension-free closure, and secondary closure was performed in group 2 of the approximately 5–7 × 5–7 mm space adjacent to the second molar (partial mucosal retention) that existed prior to surgery (Figure 1). Amoxicillin 1 g (2 × 1), naproxen sodium 550 mg (2 × 1),

and 0.15% benzidamine hydrochloride + 0.12% chlorhexidine digluconate (3 × 1) were used routinely in the postoperative period. Patients were advised to follow a soft diet and were instructed in oral care and the use of medications. Controls were performed on the 2nd and 7th postoperative days, and sutures were removed after the controls on the 7th postoperative day. One of the authors performed the surgery. Another author surgeon performed pre- and postoperative assessments.

(**a**) (**b**)

Figure 1. (**a**) Primary closure in group 1; (**b**) secondary closure in group 2.

Power analysis was performed using G*Power (v 3.1.7) to determine sample size. As a result of the calculation based on the reference study, the effect size was calculated as d = 0.512, and it was calculated that at least 32 people should be included in the study to have 80% power at the $\alpha = 0.05$ level [25]. A total of 45 patients were evaluated during the study period. Five of these patients were excluded from the study because of alveolitis, and four patients were excluded because they did not attend the controls regularly. Finally, data from 36 patients were analyzed.

2.2. Statistical Analysis

Our analyses were carried out using SPSS 26.0, with a confidence level of 95%. In our analyses, mean and standard deviation values were given for the measurements, and frequency and percentage values were given for the gender distribution. An examination of the measurements taken at different times with respect to side of surgery and gender was undertaken via an independent groups t-test. A repeated ANOVA test was used to analyze the change in measurements over time according to side of surgery and gender.

3. Results

Of the 36 patients included in the study, 23 were female and 13 were male, with a mean age of 22.42 ± 3.36 years (Table 1).

Table 1. Age and gender distribution.

Age	**Min–Max: (18–39)**	**Mean: 22.42 ± 3.36**	
		n	**%**
Gender	Female	23	63.9
	Male	13	36.1

VAS scores at hour 6 showed a significant difference between groups. VAS scores were higher in group 1 ($p < 0.05$). There was no significant difference between the groups in terms of the VAS (except for the 6th hour), rescue analgesic use, mouth opening, and facial measurements at other times ($p > 0.05$) (Table 2).

Table 2. Comparison of mouth opening, face measurement, VAS scores, and rescue analgesic number according to groups.

	Groups				p^2
	Primary Closure		Secondary Closure		
	Mean	Sd	Mean	Sd	
Preoperative mouth opening	45.56	6.51	44.23	6.37	0.547
2nd-postoperative-day mouth opening	26.47	8.26	25.56	6.93	0.612
7th-postoperative-day mouth opening	38.61	8.00	36.39	6.20	0.192
$p^1 = 0.528$					
Preoperative face measurements	109.67	7.73	110.21	7.47	0.179
2nd-postoperative-day face measurements	114.72	8.10	111.78	7.51	0.114
7th-postoperative-day face measurements	111.00	8.65	109.22	6.89	0.338
$p^1 = 0.157$					
6th-hour VAS	5.83	2.48	4.50	2.72	**0.033** *
12th-hour VAS	4.56	3.09	3.64	2.89	0.198
18th-hour VAS	4.50	2.91	3.53	2.61	0.141
24th-hour VAS	3.83	2.26	2.94	2.35	0.107
2nd-day VAS	3.14	2.11	3.50	2.78	0.537
3rd-day VAS	1.86	1.62	2.61	2.51	0.138
4th-day VAS	1.31	1.53	2.06	2.12	0.090
5th-day VAS	0.86	1.31	1.56	2.09	0.096
6th-day VAS	0.81	1.51	1.17	1.54	0.318
7th-day VAS	0.61	1.23	1.06	1.58	0.187
$p^1 =$ **0.000** *					
Rescue analgesic number	8.81	5.59	7.39	4.92	0.257

$p^1 < 0.05$, repeated ANOVA; $p^2 < 0.05$, independent groups *t* test. * statistically significant.

It was found that the change in mouth opening and facial measurements over time did not cause a significant difference between the groups ($p > 0.05$) (Table 2).

When the change in VAS scores was analyzed according to time, a difference was observed between the sixth hour and the seventh day. It was found that the decrease was greater in group 1 than in group 2 ($p < 0.05$). There was no difference between the groups in terms of change at other times ($p > 0.05$) (Table 2).

The preoperative, second, and seventh postoperative facial scores differed according to gender. It was found that the facial scores of males were higher than those of females ($p < 0.05$). Day-4 VAS scores differed by gender. Male VAS scores were higher than female VAS scores ($p < 0.05$). There was no statistically significant difference in VAS scores and rescue analgesic use between the genders at other times ($p > 0.05$) (Table 3).

Table 3. Comparison of mouth opening, face measurement, VAS scores, and rescue analgesic number according to gender.

	Gender				*p*
	Female		Male		
	Mean	Sd	Mean	Sd	
Preoperative mouth opening	44.48	6.70	47.46	5.94	0.191
2nd-postoperative-day mouth opening	24.96	6.69	29.15	10.24	0.146
7th-postoperative-day mouth opening	36.96	6.95	41.54	9.15	0.100
Preoperative face measurements	106.74	6.68	114.85	6.85	**0.001** *
2nd-postoperative-day face measurements	111.74	6.33	120.00	8.42	**0.002** *
7th-postoperative-day face measurements	108.48	8.04	115.46	8.13	**0.018** *
6th-hour VAS	5.83	2.64	5.85	2.27	0.982
12th-hour VAS	4.09	2.73	5.38	3.62	0.232
18th-hour VAS	4.22	2.81	5.00	3.14	0.447
24th-hour VAS	3.65	2.25	4.15	2.34	0.530
2nd-day VAS	3.13	1.71	3.15	2.76	0.975
3rd-day VAS	1.61	1.53	2.31	1.75	0.220
4th-day VAS	0.87	1.14	2.08	1.85	**0.020** *
5th-day VAS	0.61	0.94	1.31	1.75	0.201
6th-day VAS	0.48	0.85	1.38	2.18	0.172
7th-day VAS	0.35	0.78	1.08	1.71	0.166
Rescue analgesic number	8.17	5.20	9.92	6.28	0.375

* $p < 0.05$, independent groups *t* test.

4. Discussion

The extraction of the mandibular third molar ranks among the most common procedures in oral and maxillofacial surgery. Consequently, reducing postoperative complications holds substantial importance from medical, legal, and financial perspectives. Common postoperative complications include pain, trismus, and swelling [26]. The detection of these complications can be achieved via a number of different methods. Pain is a complex, subjective experience characterized by two distinct dimensions: sensory and affective. This dissociation is observed across various painful somatic conditions. However, the majority of experimental studies have focused primarily on the sensory aspect of pain, asking subjects to report only the intensity of pain using VAS [27]. Both objective and subjective methods exist for measuring trismus. Maximum mouth opening serves as a widely utilized objective measure for assessing trismus, representing the maximum distance between the edges of the upper and lower incisors [28]. Studies in the literature have documented the use of both subjective methods, such as the verbal rating scale and the visual analogue scale, and objective techniques, including 3D stereophotography, MRI, and metric measurements, to assess swelling after impacted third molar surgery. Among these methods, metric measurements are commonly used due to their simplicity, ease of use, cost effectiveness, and time efficiency [29,30]. For these reasons, these methods were used in the evaluation of complications in this study.

This is the first study to compare the primary and secondary closure techniques for L-PRF in impacted lower third molars. We compared primary and secondary closure techniques to determine which would have a greater effect on postoperative complications, or which would mask the potential benefits of L-PRF. There was no difference between the two closure techniques in terms of mouth opening, facial measurements, and use of rescue analgesics. At 6 h, more pain was observed on the primary closure side; on the other hand, the decrease in postoperative pain at the end of the first week was greater on the primary closure side. In the present study, there was only a difference in the facial measurements when compared by gender, and it was observed that the facial measurements of men were higher during the preoperative period and on the second and seventh postoperative days.

The main reason for this difference, apart from the gender difference causing swelling, is that men have a longer face. The fact that men's facial measurements were higher when compared to preoperative values supports this idea.

Daugela et al. compared L-PRF with a control group using a normal clot after lower impacted third molar surgery. In their study, in which primary closures were performed, they found that there was faster healing and less pain in the first postoperative week on the side where L-PRF was used. They also reported that there was less swelling on the first and third postoperative days in the L-PRF group [16]. In another study using primary closure, Dar et al. compared PRF with a normal empty extraction socket on postoperative days 1, 3, 7, and 14. They reported less pain and swelling in the L-PRF group at all postoperative assessments [31]. Tadic et al. compared the effect of L-PRF on periodontal pocket formation in the adjacent tooth and on new bone density and bone volume in the extraction socket of impacted lower third molars with an empty extraction socket left to heal normally. They reported that the parameters evaluated in both groups were similar after 8 weeks [32]. Caymaz and Uyanık compared the effect of L-PRF and A-PRF on complications after impacted lower third molar surgery. In their study, using the primary closure method, they found that A-PRF was more effective than L-PRF in alleviating pain [33]. da Silva et al. studied the effects of L-PRF on postoperative pain and wound healing in people undergoing extraction of lower third molars and showed that the pain was less and wound healing was faster on the side where L-PRF was used. The authors suggested that these results were related to the growth factors released by L-PRF [13]. In their study, Ritto et al. reported that there was no difference in pain and soft tissue healing on the side treated with L-PRF with primary closure after mandibular wisdom tooth surgery compared to the control group, contrary to the studies by Dauga et al., Dar et al., and Caymaz and Uyanık. Ritto et al. reported that L-PRF was effective in bone healing in the extraction socket, contrary to the results of Tadic et al. [34].

de Almeida Barros Mourao et al. used L-PRF with secondary closure in lower molar extraction sockets and found that the side with L-PRF had less pain and better wound healing than the side left to heal normally [35]. In their study, Afat et al. left the extraction sites to secondary healing after L-PRF following lower impacted third molar surgery. They showed that the groups treated with L-PRF had better wound healing scores than the control group at 1, 2, and 3 weeks [36]. When comparing the effects of primary and secondary closure methods in routine lower impacted wisdom tooth surgery without L-PRF, it is generally reported in the literature that the secondary closure method has fewer postoperative complications, especially pain and swelling [6,21,23,24]. In contrast to our study, studies using L-PRF have compared primary and secondary closure methods with the control group. The better wound healing and lesser pain and swelling in the primary and secondary closed extraction sockets with L-PRF compared to the control groups demonstrate the positive postoperative effects of L-PRF [16,31,33,35,36]. These data are the main reason why we preferred L-PRF in this study. In this first study evaluating the primary and secondary closure methods described in the literature for submerged wisdom tooth extraction sockets using L-PRF, it was observed that the effects of both methods on trismus and swelling were similar. In terms of pain, the side left to secondary healing was less painful during the first 24 h, and this difference was statistically significant at 6 h. From day 2, VAS scores were lower on the primary closure side, although not statistically significant. At the end of the first week, there was no difference in pain, swelling, and trismus. The fact that the primary closure side reduced pain more than the secondary closure side when the change in VAS scores was analyzed from hour 6 to day 7 (no difference in VAS scores on day 7) shows that the primary closure method also has an effect on pain. At hour 6, we believe that the reason for less pain on the side left to secondary healing is due to the lower degree of inflammatory response in the initial stage of this type of closure compared to primary closure. The null hypothesis is rejected due to the difference at hour 6.

Individuals with partially mucosa- and bone-retained impacted third molars were included in this study. In the primary closure group, some periosteal release was performed to ensure a tension-free closure. This procedure may have had a negative effect on postoperative complications in the primary closure group. The silk suture, which was preferred to avoid patient discomfort, may have influenced the results by increasing the inflammatory response in the region. Although bleeding was controlled in the groups, the differences in postoperative bleeding due to the different closure methods may have influenced the results. In addition, the anti-inflammatory analgesic and mouthwash used in the trial may have influenced the results. These were the limitations of the trial.

5. Conclusions

This was the first study to evaluate the effect of primary and secondary closure methods in extraction sockets with L-PRF after lower impacted third molar surgery. It was found that less pain was observed in the secondary closure group at the sixth hour. Pain decreased more in the primary closure group when comparing changes between VAS scores at 6 hours and 7 days. As in this study, in studies designed to use LPRF in postoperative complications of semi-mucosa-retained impacted third molars, the secondary closure method was found to be more effective in the early period (at 6 h). On the seventh postoperative day, both methods were found to be effective for pain edema trismus. The results of this study, showing that both secondary and primary closure are effective, with similar outcomes in terms of pain, edema, and trismus, should be supported by future prospective clinical trials.

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Informed Consent Statement: Informed consent was obtained from all subjects included in the study. Written informed consent was obtained from patients for the publication of this paper.

Data Availability Statement: The dataset used in this study is available on request. The data are not publicly available as they contains information that could compromise the privacy of research participants.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

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