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Therapeutic Strategies for Reducing Postoperative Discomfort in Mandibular Third Molar Surgery

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Abstract

Background: Surgical removal of mandibular third molars is one of the most frequent procedures in oral and maxillofacial surgery and is commonly associated with postoperative discomfort, including pain, swelling, trismus, and local infection. These sequelae may significantly impair patients' quality of life and daily oral functions.

Aim: The present study aims to evaluate and compare different therapeutic strategies for reducing postoperative discomfort following mandibular third molar surgery, with particular attention to biological adjuvants and local postoperative management.

Materials and Methods: A clinical experimental study was conducted on patients undergoing surgical extraction of mandibular third molars. Surgical procedures and postoperative protocols were standardised. Clinical outcomes, including pain, swelling, trismus, and postoperative complications, were recorded and statistically analysed.

Results: The adopted therapeutic strategies demonstrated a reduction in postoperative discomfort parameters, with statistically and clinically relevant differences among the evaluated approaches.

Conclusions: Appropriate postoperative management and the use of selected biomaterials may significantly improve patient comfort following mandibular third molar surgery, contributing to faster recovery and reduced morbidity.

Background

The surgical extraction of mandibular third molars is among the most frequently performed procedures in oral and maxillofacial surgery. Despite being considered routine, it is often associated with a wide spectrum of postoperative sequelae that may significantly affect patient comfort and quality of life. Pain, facial swelling, trismus, and local inflammatory or infectious complications remain the most commonly reported adverse outcomes, with variable intensity and duration depending on patient-related, anatomical, and surgical factors.

From a biological and clinical perspective, postoperative discomfort following third molar surgery is primarily the result of an acute inflammatory response triggered by surgical trauma. Tissue injury induces the release of inflammatory mediators, including prostaglandins, cytokines, and neuropeptides, which contribute to nociception, vasodilation, increased vascular permeability, and oedema formation. These mechanisms, while essential for physiological healing, may become excessive and lead to prolonged morbidity if not adequately controlled.

Several factors influence the degree of postoperative discomfort, including patient age, systemic health status, smoking habits, oral hygiene, and individual inflammatory response. In addition, local anatomical conditions—such as bone density, depth of impaction, angulation of the third molar, and proximity to the inferior alveolar nerve—play a crucial role in determining surgical difficulty and tissue trauma. The duration of surgery and the need for osteotomy and odontotomy have been consistently associated with increased postoperative pain and swelling.

Historically, the management of postoperative complications has been a central concern since the earliest descriptions of tooth extraction. Ancient medical texts already emphasised the importance of pain control and wound care. Aulus Cornelius Celsus, for instance, described both surgical principles and pharmacological remedies aimed at reducing postoperative pain and swelling. Over the centuries, advances in anaesthesia, surgical techniques, and pharmacotherapy have significantly improved patient outcomes;

however, postoperative morbidity following third molar surgery remains a relevant clinical issue.

In modern clinical practice, the reduction of postoperative discomfort is achieved through a combination of minimally invasive surgical techniques, appropriate flap design, atraumatic tissue handling, and optimised postoperative management. Pharmacological approaches, including non-steroidal anti-inflammatory drugs, corticosteroids, and antibiotics, are widely used but may be associated with adverse effects and contraindications in certain patient populations. For this reason, increasing attention has been directed towards biological adjuvants and local therapeutic strategies aimed at enhancing physiological healing while minimising inflammation.

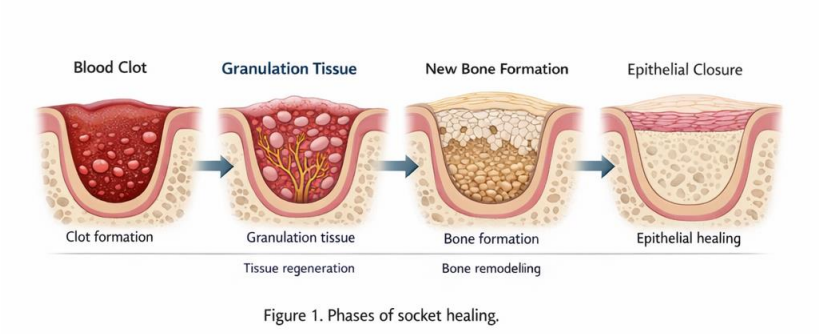


Figure 1. *Schematic overview of the main factors influencing postoperative discomfort following mandibular third molar surgery, including surgical trauma, inflammatory mediators, and patient-related variables.*

Principles of Post-Extraction Socket Healing

1.1 Biological Uniqueness of the Oral Environment

Post-extraction socket healing constitutes a highly specialised biological process that differs substantially from wound healing occurring in other anatomical regions of the body. The oral cavity represents a unique environment characterised by constant exposure to mechanical stress, fluctuations in temperature and pH, and the presence of a complex and highly diverse microbial ecosystem. These conditions impose specific biological demands on the healing tissues and significantly influence both the speed and quality of repair following tooth extraction.

Unlike cutaneous wounds, oral wounds are continuously bathed in saliva, a biologically active fluid containing enzymes, antimicrobial peptides, immunoglobulins, electrolytes, and growth factors. Saliva plays a dual role in post-extraction healing. On one hand, it provides protective and reparative functions, facilitating lubrication, epithelial migration, and antimicrobial defence. On the other hand, saliva represents a medium through which microorganisms may access the surgical site, potentially interfering with clot stability and increasing the risk of postoperative complications.

The alveolar socket represents a particularly complex healing model because it involves the simultaneous regeneration of soft tissues and alveolar bone. While mucosal healing primarily involves epithelial cells and connective tissue components, bone healing requires the coordinated activity of osteoblasts, osteoclasts, and osteoprogenitor cells. These two processes are biologically interconnected yet temporally distinct, making post-extraction healing a paradigmatic example of coupled tissue regeneration.

In mandibular third molar surgery, the biological challenge is further amplified by the frequent need for surgical flap elevation, osteotomy, and odontotomy. These procedures increase tissue trauma, disrupt local vascularisation, and enhance the inflammatory response. Consequently, the healing outcome is not determined solely by physiological mechanisms but is also heavily influenced by surgical technique and postoperative management strategies.

Understanding the biological uniqueness of the oral environment is therefore essential for interpreting postoperative outcomes and for developing therapeutic approaches aimed at reducing morbidity and enhancing physiological healing following mandibular third molar extraction.

1.2 Oral Versus Extraoral Wound Healing

Significant differences exist between oral and extraoral wound healing in terms of inflammatory response, epithelial behaviour, and scarring tendency. Oral mucosal wounds generally exhibit faster healing and reduced scar formation compared with cutaneous wounds. This phenomenon has been attributed to differences in fibroblast phenotype, cytokine expression, and extracellular matrix remodelling.

Oral fibroblasts demonstrate a reduced pro-fibrotic response and a lower tendency towards excessive collagen deposition. In addition, oral wounds display a more controlled inflammatory response, characterised by rapid resolution and limited chronic inflammation. This favourable biological profile contributes to the typically rapid epithelial closure observed in oral surgical sites.

However, these advantages are counterbalanced by the challenges posed by the oral microbiota. The oral cavity harbours one of the most complex microbial communities in the human body, comprising hundreds of bacterial species organised in structured biofilms. Following tooth extraction, the exposed alveolar socket represents a vulnerable interface between the host tissues and the microbial environment.

The balance between microbial colonisation and host immune response plays a critical role in determining healing outcomes. Disruption of this balance may result in delayed healing, increased postoperative pain, or the development of complications such as alveolar osteitis. Consequently, post-extraction socket healing should be viewed as a dynamic equilibrium between regenerative processes and microbial control rather than as a purely sterile reparative phenomenon.

These considerations highlight why therapeutic strategies in oral surgery must aim not only to stimulate tissue regeneration but also to preserve clot integrity and regulate local inflammation in the presence of microbial challenge.

1.3 Role of Saliva and Oral Microbiota in Socket Healing

Saliva plays a fundamental yet often underestimated role in post-extraction healing. Its composition includes a wide range of biologically active molecules such as epidermal growth factor (EGF), transforming growth factor-alpha (TGF-α), histatins, defensins, and secretory immunoglobulin A (sIgA). These components contribute to epithelial cell proliferation, antimicrobial defence, and modulation of inflammation.

Histatins, in particular, have been shown to promote wound closure by stimulating epithelial migration, while defensins exert broad-spectrum antimicrobial activity. Salivary growth factors support re-epithelialisation of the extraction site and contribute to soft tissue healing. At the same time, saliva maintains tissue hydration, reducing mechanical stress on the healing wound.

Conversely, the oral microbiota may exert both beneficial and detrimental effects on healing. While commensal bacteria contribute to immune system maturation and competitive exclusion of pathogenic species, dysbiosis may promote inflammation and tissue breakdown. Surgical trauma, antibiotic therapy, and changes in oral hygiene practices can alter microbial composition, potentially affecting healing outcomes.

In the context of mandibular third molar extraction, bacterial contamination of the blood clot has been implicated in the pathogenesis of alveolar osteitis. The degradation of the fibrin matrix by bacterial fibrinolytic activity leads to premature clot loss, exposing the underlying bone and nerve endings. This process results in severe postoperative pain and delayed healing.

Therefore, maintenance of a stable blood clot in an environment that is inherently non-sterile represents a central biological challenge in post-extraction socket healing.

1.4 Haemostasis and Blood Clot Architecture

Haemostasis constitutes the first and most critical phase of post-extraction healing. Immediately after tooth removal, vascular injury triggers vasoconstriction and platelet aggregation, leading to the formation of a fibrin-rich blood clot within the alveolar socket. This clot serves not merely as a mechanical plug but as a biologically active scaffold that orchestrates subsequent healing events.

The fibrin network provides structural support for migrating cells and acts as a reservoir for platelets and growth factors. Platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF) are released in a controlled manner, promoting chemotaxis, angiogenesis, and cell proliferation.

The stability and architecture of the blood clot are decisive determinants of healing success. A dense, well-organised fibrin matrix supports cellular infiltration and protects the socket from mechanical disruption and microbial invasion. In contrast, an unstable or prematurely lysed clot compromises healing and increases the risk of postoperative complications.

Clinical factors such as excessive irrigation, negative pressure from suction, smoking, and inadequate postoperative instructions may disrupt clot integrity. From a biological perspective, increased fibrinolytic activity—either host- or bacteria-mediated—represents a key mechanism underlying clot degradation.

Preservation of the blood clot is therefore a primary therapeutic objective in mandibular third molar surgery and constitutes the biological rationale for the use of haemostatic agents and platelet-based biomaterials.

1.5 Alveolar Osteitis as a Model of Healing Failure

Alveolar osteitis, commonly referred to as dry socket, represents a paradigmatic example of disrupted post-extraction healing. It is characterised by premature loss of the blood clot, exposure of the alveolar bone, and severe postoperative pain, typically occurring between the second and fourth postoperative day.

From a biological standpoint, alveolar osteitis is not an infectious disease but rather a localised failure of haemostatic and inflammatory regulation. Increased fibrinolysis leads to clot dissolution, while exposed bone undergoes inflammatory changes that activate nociceptive pathways.

The incidence of alveolar osteitis is higher following mandibular third molar extraction, particularly in cases involving extensive bone removal, traumatic surgery, smoking, and oral contraceptive use. These risk factors further support the central role of clot stability and inflammation control in successful socket healing.

Understanding alveolar osteitis as a failure of physiological healing rather than as an infection has important therapeutic implications. Preventive strategies should therefore focus on preserving clot integrity, modulating inflammation, and enhancing biological healing rather than relying solely on antimicrobial interventions.

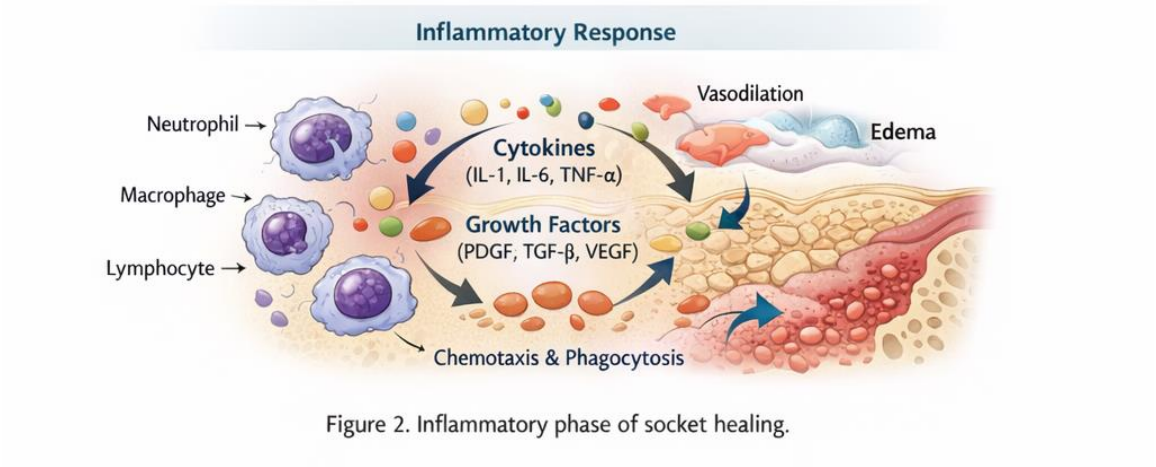


Figure 2. Inflammatory phase of socket healing.

Figure 2. *Formation of the blood clot and release of platelet-derived growth factors within the post-extraction socket.*

1.6 Inflammatory Phase: Cellular and Molecular Mechanisms

Following haemostasis and clot formation, the post-extraction socket enters the inflammatory phase, which represents a critical and unavoidable stage of the healing cascade. This phase is initiated within hours after tooth extraction and is characterised by a tightly regulated sequence of cellular and molecular events aimed at removing necrotic debris, controlling microbial contamination, and preparing the wound environment for tissue regeneration.

Neutrophils are the first inflammatory cells to infiltrate the extraction socket. Their primary function is to provide rapid antimicrobial defence through phagocytosis and the release of reactive oxygen species and proteolytic enzymes. While neutrophils are essential for early wound protection, excessive or prolonged neutrophil activity may result in collateral tissue damage and amplification of the inflammatory response. For this reason, timely resolution of neutrophil-driven inflammation is a key determinant of favourable healing.

Macrophages subsequently replace neutrophils as the dominant inflammatory cell population within the socket. Unlike neutrophils, macrophages exhibit a highly plastic phenotype and play a central regulatory role in coordinating the transition from inflammation to tissue repair. Through the release of cytokines, chemokines, and growth factors, macrophages act as biological “conductors” of the healing process.

The balance between pro-inflammatory (M1) and pro-regenerative (M2) macrophage phenotypes is particularly relevant in oral wound healing. Excessive persistence of the M1 phenotype has been associated with delayed healing and increased postoperative discomfort, whereas timely polarisation towards the M2 phenotype promotes angiogenesis, fibroblast activation, and extracellular matrix deposition. Therapeutic strategies capable of influencing macrophage behaviour may therefore exert a profound impact on postoperative outcomes.

1.7 Cytokine Cascade and Relationship with Pain and Swelling

The inflammatory phase is accompanied by the release of a complex network of cytokines and inflammatory mediators, including interleukin (IL)-1β, IL-6, tumour necrosis factor-alpha (TNF-α), prostaglandins, and bradykinin. These mediators are responsible for the classical signs of inflammation, namely pain, swelling, heat, and functional impairment.

Pain following mandibular third molar extraction is primarily mediated by prostaglandins and neuropeptides that sensitise peripheral nociceptors. Tissue injury induces the activation of cyclooxygenase pathways, leading to increased prostaglandin synthesis and heightened pain perception. This mechanism provides the biological rationale for the widespread use of non-steroidal anti-inflammatory drugs (NSAIDs) in postoperative pain control.

Swelling, on the other hand, results from increased vascular permeability and plasma extravasation driven by inflammatory mediators such as histamine, prostaglandins, and cytokines. The extent of postoperative oedema is closely related to the magnitude of surgical trauma and the intensity of the inflammatory response. In mandibular third molar surgery, extensive bone removal and prolonged operative time have been consistently associated with increased postoperative swelling.

Importantly, pain and swelling are not merely undesirable side effects but represent physiological consequences of inflammation. Complete suppression of the inflammatory response may impair healing, whereas excessive inflammation results in prolonged morbidity. Effective postoperative management therefore aims to modulate inflammation to an optimal level rather than abolish it entirely.

1.8 Angiogenesis and Hypoxia in Socket Healing

Angiogenesis represents a pivotal event linking the inflammatory and proliferative phases of socket healing. The formation of new blood vessels ensures adequate oxygenation, nutrient supply, and cellular trafficking to the healing tissues. In the post-extraction socket, angiogenesis is primarily stimulated by hypoxic conditions created immediately after extraction and clot formation.

Hypoxia-inducible factor-1 alpha (HIF-1α) is a key transcription factor activated under low oxygen tension. HIF-1α promotes the expression of vascular endothelial growth factor (VEGF), which acts as a potent stimulator of endothelial cell proliferation and migration. The resulting neovascular network penetrates the granulation tissue and supports subsequent phases of healing.

Inadequate angiogenesis has been associated with delayed healing, increased risk of infection, and impaired bone regeneration. Conversely, excessive or disorganised angiogenesis may contribute to persistent inflammation and tissue oedema. The regulation of angiogenic processes is therefore a critical determinant of healing quality and speed.

Biological adjuncts capable of enhancing physiological angiogenesis without inducing excessive inflammation represent a promising approach to improving postoperative outcomes. Platelet-based biomaterials, by providing a sustained release of angiogenic growth factors, may positively influence this delicate balance.

1.9 Fibroblast Activity and Extracellular Matrix Formation

As the inflammatory phase resolves, fibroblasts become the predominant cell type within the healing socket. Fibroblasts migrate into the fibrin scaffold and initiate the synthesis of extracellular matrix (ECM) components, including collagen, fibronectin, and proteoglycans. This newly formed matrix provides structural support for tissue regeneration and serves as a framework for epithelial migration.

Oral fibroblasts exhibit distinct biological characteristics compared with their cutaneous counterparts. They display enhanced migratory capacity, reduced fibrotic response, and increased production of matrix metalloproteinases, which facilitate controlled matrix remodelling. These properties contribute to the typically rapid and scarless healing observed in the oral cavity.

The quality and organisation of the extracellular matrix directly influence soft tissue healing outcomes. Excessive collagen deposition may result in fibrotic healing, whereas insufficient matrix formation compromises tissue stability. The balance between matrix synthesis and degradation is therefore essential for optimal wound repair.

Growth factors such as TGF-β play a dual role in regulating fibroblast activity. While they promote collagen synthesis and wound contraction, excessive TGF-β signalling may lead to pathological fibrosis. Therapeutic strategies must therefore aim to support fibroblast function while preventing dysregulated matrix deposition.

1.10 Transition from Soft Tissue Healing to Bone Regeneration

Soft tissue healing and bone regeneration are biologically interconnected processes that occur concurrently within the post-extraction socket. While epithelial closure and connective tissue maturation proceed at the socket entrance, deeper regions undergo osteogenic differentiation and bone formation.

Osteoprogenitor cells derived from the periodontal ligament and alveolar bone migrate into the socket and differentiate into osteoblasts under the influence of local growth factors and mechanical stimuli. The initial deposition of woven bone provides temporary structural support and is subsequently remodelled into lamellar bone through coordinated osteoblastic and osteoclastic activity.

The temporal overlap between soft tissue healing and bone regeneration highlights the importance of maintaining a favourable biological environment throughout the entire healing period. Disruption of soft tissue healing may expose underlying bone to microbial contamination, while impaired bone regeneration may compromise long-term structural stability.

Understanding this biological continuum provides the rationale for therapeutic interventions that simultaneously support soft tissue repair and bone healing, particularly in the context of mandibular third molar extraction where extensive bone involvement is common.

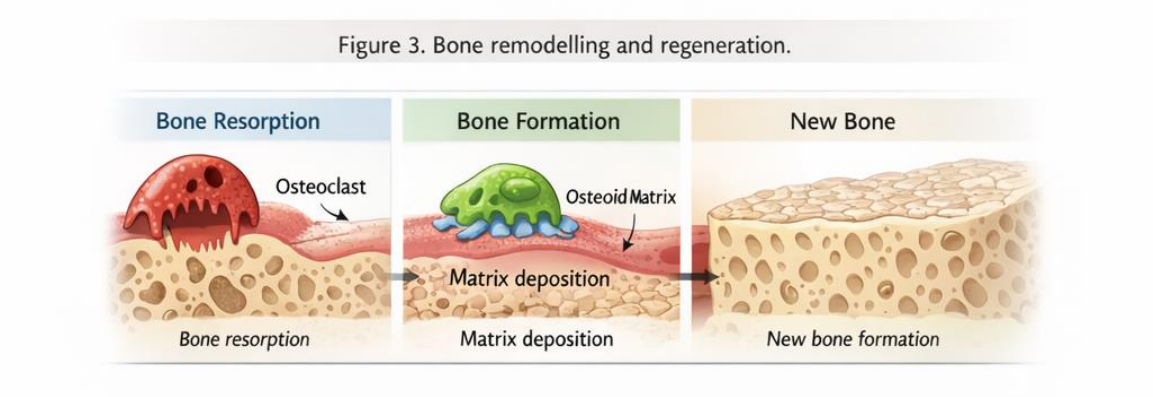


Figure 3. *Granulation tissue formation and angiogenesis during the proliferative phase of socket healing.*

1.11 Osteogenesis within the Post-Extraction Socket

Bone regeneration within the post-extraction socket represents a highly orchestrated biological process that begins shortly after tooth removal and continues over several months. Unlike fracture healing, socket healing occurs in the absence of rigid fixation and is strongly influenced by local mechanical conditions, vascular supply, and inflammatory mediators.

Osteogenesis initiates primarily from the apical and lateral walls of the alveolar socket, where osteoprogenitor cells residing in the periodontal ligament and endosteal surfaces differentiate into osteoblasts. These cells begin depositing osteoid, which subsequently mineralises to form woven bone. Woven bone is characterised by a random collagen fibre orientation and represents a temporary scaffold that provides early structural stability.

The formation of woven bone is closely linked to angiogenesis. Newly formed blood vessels provide oxygen, nutrients, and osteogenic signals essential for bone deposition. Inadequate vascularisation compromises osteoblast function and delays bone formation, whereas excessive inflammation may disrupt the delicate balance between bone formation and resorption.

1.12 Bone Remodelling: From Woven to Lamellar Bone

Following initial bone deposition, the socket enters a prolonged remodelling phase during which woven bone is gradually replaced by lamellar bone. Lamellar bone exhibits a highly organised collagen structure and superior mechanical properties compared with woven bone. This transformation is mediated through tightly coupled osteoblastic and osteoclastic activity.

Osteoclasts resorb immature bone in a controlled manner, creating space for new lamellar bone deposition by osteoblasts. This remodelling process allows the alveolar bone to adapt to functional loading and restore physiological architecture. In the mandible, where masticatory forces are significant, bone remodelling is particularly influenced by mechanical stimuli transmitted through surrounding tissues.

The remodelling phase may extend for several months and is influenced by systemic factors such as age, hormonal status, and metabolic health. Disruptions to this phase may result in incomplete bone regeneration, altered ridge morphology, or delayed functional recovery.

1.13 Systemic Factors Influencing Socket Healing

Systemic conditions play a critical role in modulating post-extraction socket healing. Patient age is a well-recognised factor, with younger individuals generally exhibiting faster healing and more robust regenerative capacity. Age-related changes in vascular function, cellular proliferation, and immune response may contribute to delayed healing in older patients.

Smoking represents one of the most significant modifiable risk factors affecting socket healing. Nicotine-induced vasoconstriction reduces blood flow to the surgical site, while carbon monoxide decreases oxygen delivery to tissues. In addition, smoking has been shown to increase fibrinolytic activity, thereby compromising clot stability and increasing the risk of alveolar osteitis.

Systemic diseases such as diabetes mellitus impair wound healing through multiple mechanisms, including microvascular dysfunction, altered immune response, and reduced growth factor activity. Similarly, medications such as corticosteroids, anticoagulants, and

bisphosphonates may interfere with different phases of healing and must be carefully considered during treatment planning.

1.14 Local Factors and Surgical Variables

In addition to systemic influences, several local factors directly affect post-extraction healing. The degree of surgical trauma, duration of the procedure, extent of bone removal, and quality of soft tissue management are among the most important determinants of postoperative outcomes.

Traumatic extraction techniques increase inflammatory burden and disrupt local vascular supply, thereby delaying healing. Conversely, atraumatic surgical approaches that preserve bone and soft tissue integrity promote faster resolution of inflammation and improved healing quality.

Primary wound closure and tension-free suturing contribute to clot stabilisation and protection of the healing socket. Inadequate flap adaptation or excessive tension may compromise blood supply and increase the risk of wound dehiscence and delayed healing.

1.15 Biological Rationale for Local Therapeutic Adjuncts

The complexity of post-extraction socket healing provides a strong biological rationale for the use of local therapeutic adjuncts aimed at supporting physiological repair mechanisms. Given the central role of the blood clot as a provisional scaffold, strategies that enhance clot stability and biological activity are particularly attractive.

Platelet concentrates, such as leukocyte- and platelet-rich fibrin (L-PRF), represent an evolution in this approach. Unlike earlier platelet-rich plasma formulations, L-PRF forms a dense fibrin matrix capable of releasing growth factors and cytokines in a sustained manner. This gradual release supports angiogenesis, modulates inflammation, and promotes fibroblast and osteoblast activity.

The inclusion of leukocytes within the L-PRF matrix further enhances its biological potential. Leukocytes contribute to antimicrobial defence and immune regulation through

cytokine production, thereby supporting a controlled inflammatory environment conducive to healing.

From a translational perspective, L-PRF can be viewed as a biologically active extension of the natural blood clot, reinforcing its structure and function rather than replacing it. This concept aligns closely with the principles of regenerative medicine and provides the theoretical foundation for its application in mandibular third molar surgery.

1.16 Summary and Clinical Implications

Post-extraction socket healing is a multifactorial process governed by the interaction of haemostasis, inflammation, angiogenesis, soft tissue repair, and bone regeneration. Each phase is influenced by systemic and local factors, as well as by surgical technique and postoperative management.

A thorough understanding of these biological principles is essential for interpreting clinical outcomes and for selecting therapeutic strategies aimed at reducing postoperative discomfort. Interventions that preserve clot integrity, regulate inflammation, enhance angiogenesis, and support tissue regeneration are most likely to result in favourable healing and improved patient comfort.

This biological framework provides the conceptual basis for the clinical investigation presented in this thesis and directly supports the evaluation of L-PRF and other local adjuncts in the management of postoperative morbidity following mandibular third molar extraction.

Surgical Extraction of the Mandibular Third Molar: Current Postoperative Management

2.1 Clinical Relevance of Mandibular Third Molar Surgery

The surgical extraction of mandibular third molars represents one of the most frequently performed procedures in oral and maxillofacial surgery worldwide. Despite its apparent routine nature, third molar surgery remains a major contributor to postoperative morbidity, accounting for a significant proportion of pain, swelling, trismus, and patient dissatisfaction encountered in daily clinical practice.

From a clinical perspective, mandibular third molar extraction occupies a unique position at the intersection between elective surgery and medically indicated intervention. While many extractions are performed prophylactically, others are required due to recurrent pericoronitis, caries of the second molar, cystic lesions, or orthodontic and prosthetic considerations. Regardless of indication, the procedure involves deliberate surgical trauma to bone and soft tissues, inevitably triggering an inflammatory response.

The high prevalence of third molar surgery, combined with its potential impact on patient quality of life, makes optimisation of postoperative management a topic of continuous scientific and clinical interest. Even modest reductions in postoperative discomfort may translate into substantial benefits at the population level, reducing analgesic consumption, improving functional recovery, and enhancing patient satisfaction.

2.2 Surgical Difficulty and Biological Burden

Mandibular third molar surgery encompasses a broad spectrum of surgical difficulty. Factors such as depth of impaction, angulation, root morphology, bone density, and proximity to the inferior alveolar nerve significantly influence operative complexity and postoperative outcomes. Classification systems, including those proposed by Pell and Gregory and by Winter, have been widely used to predict surgical difficulty and guide treatment planning.

Increased surgical difficulty is directly associated with a higher biological burden. Deeply impacted teeth often require extensive osteotomy and odontotomy, resulting in greater disruption of bone architecture and soft tissue integrity. Prolonged operative time further exacerbates tissue trauma, increasing local hypoxia, inflammatory mediator release, and postoperative oedema.

From a biological standpoint, surgical difficulty can be viewed as a surrogate marker for the magnitude of tissue injury. This concept underscores the importance of tailoring postoperative management strategies not only to the surgical procedure itself but also to the expected inflammatory response associated with individual cases.

2.3 Surgical Trauma as a Determinant of Postoperative Discomfort

Surgical trauma represents the primary driver of postoperative discomfort following mandibular third molar extraction. Tissue injury initiates a cascade of inflammatory events characterised by the release of cytokines, prostaglandins, and neuropeptides that contribute to pain, swelling, and functional limitation.

Bone removal is a particularly significant contributor to postoperative morbidity. Osteotomy disrupts local vascular supply and generates thermal and mechanical stress, both of which intensify the inflammatory response. Inadequate cooling, excessive pressure, or prolonged drilling may result in thermal bone injury, further delaying healing and increasing postoperative pain.

Soft tissue manipulation also plays a critical role. Excessive periosteal stripping, traumatic flap elevation, and tension during closure compromise blood supply and increase the risk of wound dehiscence and delayed healing. These considerations highlight the importance of atraumatic surgical technique as the first and most effective strategy for reducing postoperative discomfort.

2.4 Flap Design and Soft Tissue Management

Flap design is a fundamental aspect of mandibular third molar surgery, directly influencing both intraoperative access and postoperative healing. An ideal flap provides adequate visibility and instrument access while preserving vascular supply and minimising tissue trauma.

Triangular and envelope flaps are among the most commonly employed designs. While triangular flaps offer improved access in deeply impacted cases, they may be associated with increased postoperative swelling due to greater soft tissue mobilization. Envelope flaps, by contrast, preserve blood supply more effectively but may limit access in complex cases.

Careful incision placement is essential to reduce the risk of lingual nerve injury and to promote favorable healing. Maintaining an adequate distance from critical anatomical structures and ensuring smooth, tension-free flap repositioning are key principles of soft tissue management.

Primary closure by first intention contributes to clot stabilization and protects the underlying socket from mechanical disruption and microbial contamination. Conversely, inadequate closure or excessive tension may compromise healing and increase postoperative morbidity.

2.5 Duration of Surgery as a Prognostic Factor

Operative time has emerged as a significant predictor of postoperative outcomes following mandibular third molar extraction. Numerous studies have demonstrated a positive correlation between longer surgical duration and increased postoperative pain, swelling, and trismus.

Prolonged surgery reflects both increased technical difficulty and cumulative tissue trauma. Extended operative time is associated with sustained inflammatory mediator release, prolonged tissue hypoxia, and greater disruption of local homeostasis. These factors collectively contribute to delayed resolution of inflammation and prolonged postoperative discomfort.

From a practical standpoint, reducing operative time through meticulous preoperative planning, appropriate instrumentation, and surgical experience represents an effective strategy for minimising postoperative morbidity.

2.6 Conceptual Framework for Postoperative Management

Postoperative management strategies must be understood within the broader context of surgical trauma and biological response. Rather than acting in isolation, pharmacological agents, local adjuncts, and patient-centred measures interact with the underlying healing processes initiated at the time of surgery.

Effective postoperative management aims to:

- control excessive inflammation without impairing healing,
- stabilise the blood clot and protect the surgical site,
- reduce pain and swelling to facilitate functional recovery,
- prevent local and systemic complications.

This integrated perspective forms the foundation for contemporary approaches to postoperative care following mandibular third molar extraction and provides the conceptual framework for the therapeutic strategies evaluated in the present thesis.

2.7 Pharmacological Management of Postoperative Inflammation

Pharmacological therapy represents one of the most widely adopted strategies for controlling postoperative discomfort following mandibular third molar extraction. The primary objective of pharmacological intervention is to attenuate the inflammatory response induced by surgical trauma while preserving the physiological mechanisms necessary for tissue repair.

Non-steroidal anti-inflammatory drugs (NSAIDs) are considered first-line agents for postoperative pain control. Their mechanism of action is based on the inhibition of cyclooxygenase (COX) enzymes, leading to reduced synthesis of prostaglandins, which are key mediators of pain and inflammation. Numerous clinical studies have demonstrated the effectiveness of NSAIDs in reducing postoperative pain intensity, particularly when administered pre-emptively or in the early postoperative period.

Despite their efficacy, NSAIDs are not devoid of adverse effects. Gastrointestinal irritation, renal impairment, and interference with platelet aggregation may limit their use in certain patient populations. Consequently, careful patient selection and dosage optimisation are essential components of evidence-based postoperative management.

2.8 Role of Corticosteroids in Reducing Oedema and Trismus

Corticosteroids are frequently employed as adjunctive agents to reduce postoperative swelling and trismus following third molar surgery. By inhibiting phospholipase A2 and suppressing multiple inflammatory pathways, corticosteroids exert a potent anti-inflammatory effect that extends beyond prostaglandin inhibition.

Clinical studies have consistently shown that perioperative administration of corticosteroids, such as dexamethasone, significantly reduces facial swelling and improves early postoperative function. The timing, dosage, and route of administration play a crucial role in determining clinical efficacy. Local infiltration, intramuscular injection, and oral administration have all been proposed, with varying degrees of effectiveness.

However, corticosteroids must be used judiciously. Potential side effects include immunosuppression, delayed wound healing, and alterations in glucose metabolism. While short-term use in healthy individuals is generally considered safe, clinicians must carefully evaluate the risk–benefit ratio in patients with systemic comorbidities.

2.9 Antibiotic Therapy: Evidence-Based Indications and Limitations

The use of antibiotics in mandibular third molar surgery remains a topic of ongoing debate. While antibiotics are unquestionably indicated in the presence of active infection or systemic risk factors, their routine prophylactic use in healthy patients undergoing uncomplicated extractions has been increasingly questioned.

Current evidence suggests that prophylactic antibiotics may not significantly reduce the incidence of postoperative infection or alveolar osteitis in low-risk patients. Moreover, indiscriminate antibiotic use contributes to the development of antimicrobial resistance and exposes patients to unnecessary adverse effects, including gastrointestinal disturbances and allergic reactions.

An evidence-based approach to antibiotic prescribing emphasises selective use based on individual risk assessment. Factors such as prolonged operative time, extensive bone removal, immunocompromised status, and poor oral hygiene may justify antibiotic prophylaxis. In contrast, routine administration in uncomplicated cases should be avoided in accordance with principles of antimicrobial stewardship.

2.10 Modulation Versus Suppression of the Inflammatory Response

A critical concept in postoperative management is the distinction between modulation and suppression of inflammation. Inflammation is an essential component of wound healing, facilitating debris removal, angiogenesis, and tissue regeneration. Excessive suppression of inflammation may impair these processes and delay healing.

Pharmacological strategies should therefore aim to attenuate excessive inflammatory responses while preserving the physiological cascade required for repair. This concept has important implications for the choice and timing of anti-inflammatory agents.

The recognition that inflammation plays a dual role—as both a source of postoperative discomfort and a prerequisite for healing—has driven interest in therapeutic approaches capable of fine-tuning the inflammatory response rather than abolishing it entirely. This paradigm shift supports the integration of biological adjuncts alongside conventional pharmacological therapy.

2.11 Limitations of Systemic Pharmacological Approaches

Although systemic pharmacological therapy is effective in controlling postoperative symptoms, it does not directly address the local biological environment of the extraction socket. Systemic drugs exert their effects throughout the body and may be associated with systemic side effects that limit their applicability in certain patients.

Furthermore, pharmacological agents primarily target symptom control rather than actively promoting tissue regeneration. As a result, their ability to enhance wound healing and accelerate recovery is inherently limited.

These limitations have prompted increasing interest in local therapeutic strategies capable of acting directly at the surgical site. Local adjuncts may complement systemic therapy by stabilising the blood clot, modulating inflammation, and providing biologically active signals that support healing.

2.12 Integration of Pharmacological and Local Strategies

Optimal postoperative management following mandibular third molar extraction requires an integrated approach that combines systemic pharmacological therapy with local interventions. Rather than viewing these strategies as mutually exclusive, they should be considered complementary components of a comprehensive postoperative care protocol.

Systemic agents provide effective control of pain and inflammation, while local adjuncts address the biological needs of the extraction socket. This integrated model reflects a shift towards more targeted, biologically informed postoperative management and sets the stage for the evaluation of local therapeutic strategies such as platelet-based biomaterials.

2.13 Local Postoperative Management Strategies

In recent years, increasing attention has been directed towards local postoperative management strategies aimed at reducing morbidity following mandibular third molar extraction. Unlike systemic pharmacological approaches, local interventions act directly within the extraction socket and surrounding tissues, targeting the biological processes that govern wound healing.

Local postoperative management strategies seek to stabilise the blood clot, protect the surgical site from mechanical and microbial insults, and modulate the local inflammatory response. These objectives are particularly relevant in the oral cavity, where continuous exposure to saliva and oral microbiota may compromise healing.

The effectiveness of local strategies depends on their ability to integrate harmoniously with physiological healing mechanisms rather than interfere with them. Consequently, the selection of appropriate local adjuncts should be guided by biological compatibility, ease of application, and evidence of clinical efficacy.

2.14 Haemostatic Agents and Clot Stabilisation

Haemostatic agents are among the most commonly used local adjuncts in oral surgery. Their primary function is to promote haemostasis and stabilise the blood clot within the extraction socket, thereby reducing the risk of postoperative bleeding and alveolar osteitis.

Absorbable gelatin sponges represent one of the most widely used haemostatic materials. Their porous structure facilitates blood absorption and clot formation, while their gradual resorption allows integration with the healing tissues. By providing a temporary scaffold, gelatin sponges support early wound healing and protect the socket during the critical initial postoperative period.

Collagen-based haemostatic agents function in a similar manner, promoting platelet aggregation and clot stabilisation. Both gelatin and collagen materials have demonstrated efficacy in controlling postoperative bleeding, particularly in patients receiving anticoagulant therapy. Importantly, these materials are generally well tolerated and do not interfere significantly with physiological healing processes.

However, haemostatic agents should not be viewed solely as mechanical devices. Their interaction with the blood clot and surrounding tissues may influence local inflammation and healing dynamics, highlighting the importance of material selection in postoperative management.

2.15 Antiseptic Agents and Microbial Control

Given the non-sterile nature of the oral environment, antiseptic agents are frequently employed to reduce microbial load following third molar surgery. Chlorhexidine remains the most commonly used antiseptic in oral surgery due to its broad-spectrum antimicrobial activity and prolonged substantivity.

Chlorhexidine may be administered in various formulations, including mouth rinses, gels, and impregnated materials. Its use has been associated with a reduced incidence of alveolar osteitis and postoperative infection in selected clinical scenarios. However, the biological effects of chlorhexidine extend beyond antimicrobial activity.

In vitro studies have demonstrated cytotoxic effects of chlorhexidine on fibroblasts and osteoblasts, raising concerns regarding its impact on wound healing. Prolonged or high-concentration exposure may impair cell proliferation and delay tissue regeneration. These findings suggest that antiseptic agents should be used judiciously and tailored to individual clinical risk rather than applied routinely.

The balance between microbial control and tissue biocompatibility represents a central consideration in the use of antiseptic agents for postoperative management.

2.16 Biological Adjuncts and Regenerative Approaches

Biological adjuncts have emerged as a promising category of local postoperative management strategies. Unlike traditional haemostatic or antiseptic agents, biological adjuncts actively participate in the healing process by delivering bioactive molecules that support tissue regeneration.

Autologous platelet concentrates represent the most extensively studied biological adjuncts in oral surgery. Among these, leukocyte- and platelet-rich fibrin (L-PRF) has gained particular attention due to its ease of preparation, autologous nature, and sustained release of growth factors.

L-PRF forms a dense fibrin matrix that mimics the natural blood clot while enhancing its biological activity. The gradual release of growth factors such as PDGF, TGF-β, and VEGF supports angiogenesis, fibroblast proliferation, and osteogenic differentiation. In addition, the presence of leukocytes contributes to immune regulation and antimicrobial defence.

From a regenerative perspective, L-PRF may be considered a biologically active scaffold that reinforces physiological healing rather than replacing it. This concept aligns with contemporary trends in regenerative medicine and supports its application in third molar surgery.

2.17 Comparative Effectiveness of Local Adjuncts

The comparative effectiveness of different local postoperative management strategies remains an area of active investigation. While haemostatic agents are effective in controlling bleeding, their capacity to influence inflammation and tissue regeneration is limited. Antiseptic agents provide microbial control but may adversely affect cellular viability if not used appropriately.

Biological adjuncts offer a more comprehensive approach by addressing multiple aspects of the healing process simultaneously. Clinical studies have reported reductions in postoperative swelling, improved soft tissue healing, and enhanced patient comfort following the application of platelet-based biomaterials.

However, the heterogeneity of study designs, outcome measures, and surgical protocols complicates direct comparison among different local strategies. Standardisation of clinical methodologies is therefore essential to establish evidence-based guidelines for postoperative management.

2.18 Patient Compliance and Behavioural Factors

The success of local postoperative management strategies is strongly influenced by patient compliance. Regardless of the materials or techniques employed, inappropriate postoperative behaviour may compromise healing outcomes.

Instructions regarding oral hygiene, dietary modifications, smoking cessation, and physical activity play a critical role in preserving clot stability and preventing complications. Patient education should be considered an integral component of postoperative management rather than an ancillary measure.

Behavioural factors such as smoking have a particularly detrimental impact on healing and may negate the benefits of advanced local adjuncts. Consequently, patient selection and counselling remain essential considerations in clinical decision-making.

2.19 Integration of Local Strategies into Clinical Practice

The integration of local postoperative management strategies into routine clinical practice requires a balanced consideration of efficacy, cost, ease of use, and patient-related factors. While advanced biological adjuncts may offer superior healing outcomes, their routine use should be justified by clear clinical benefits.

An evidence-based, patient-centred approach that tailors postoperative management to individual risk profiles represents the most rational strategy. In this context, local adjuncts should be viewed as components of a comprehensive treatment protocol rather than isolated interventions.

2.20 Cryotherapy and Physical Postoperative Measures

In addition to pharmacological and local biological strategies, physical measures play a complementary role in reducing postoperative discomfort following mandibular third molar surgery. Among these, cryotherapy remains one of the most widely adopted non-pharmacological interventions during the immediate postoperative period.

Cryotherapy exerts its effects primarily through vasoconstriction, which reduces blood flow to the surgical site and limits inflammatory exudation. By decreasing capillary permeability, cryotherapy contributes to reduced postoperative oedema and may indirectly attenuate pain by lowering tissue pressure and nociceptor stimulation. The application of intermittent cold packs during the first postoperative hours has been associated with improved patient comfort and reduced facial swelling.

However, the effectiveness of cryotherapy depends on appropriate timing, duration, and patient compliance. Excessive or prolonged application may result in tissue injury or diminished returns. Therefore, cryotherapy should be considered an adjunctive measure rather than a standalone intervention, integrated into a broader postoperative management protocol.

2.21 Postoperative Instructions and Behavioural Compliance

Patient behaviour during the postoperative period represents a decisive determinant of healing outcomes. Even the most advanced surgical techniques and therapeutic adjuncts may fail to produce optimal results in the absence of adequate patient compliance.

Postoperative instructions typically include guidance on oral hygiene, dietary modifications, physical activity limitation, and medication adherence. Avoidance of vigorous rinsing, suction, and mechanical trauma to the surgical site is essential for preserving blood clot integrity. Similarly, adherence to a soft and cool diet during the initial postoperative phase reduces mechanical stress on the healing tissues.

Smoking cessation deserves particular emphasis. Smoking has been consistently associated with increased postoperative pain, swelling, delayed healing, and higher incidence of alveolar osteitis. Patient education regarding the biological mechanisms through which smoking impairs healing may enhance compliance and improve clinical outcomes.

2.22 Patient-Reported Outcomes and Quality of Life

Traditional clinical outcome measures such as swelling, pain, and healing indices provide valuable information regarding postoperative morbidity. However, increasing attention has been directed towards patient-reported outcome measures (PROMs) as indicators of treatment success.

Mandibular third molar surgery may significantly affect patients' quality of life during the postoperative period, impacting speech, mastication, social interaction, and sleep. Even transient discomfort may result in substantial functional limitation and psychological distress.

The incorporation of PROMs into clinical research allows for a more comprehensive assessment of postoperative outcomes, capturing subjective experiences that may not be fully reflected by clinical measurements alone. Reductions in pain intensity, swelling, and healing time translate into tangible improvements in daily functioning and patient satisfaction.

From this perspective, postoperative management strategies should be evaluated not only in terms of biological efficacy but also in their ability to enhance overall quality of life.

2.23 Critical Appraisal of Postoperative Management Strategies

Despite significant advances in surgical techniques and postoperative care, postoperative discomfort following mandibular third molar extraction remains a clinically relevant issue. The multiplicity of available management strategies reflects the complexity of the biological processes involved and the absence of a single universally effective solution.

Systemic pharmacological approaches provide effective symptom control but are limited by potential adverse effects and lack of direct regenerative action. Local haemostatic and antiseptic agents address specific aspects of healing but may fail to influence the broader biological environment. Biological adjuncts, particularly platelet-based biomaterials, offer a more comprehensive approach by actively participating in tissue regeneration and inflammatory modulation.

However, the clinical effectiveness of these strategies is influenced by numerous variables, including surgical technique, patient-related factors, and methodological heterogeneity among studies. As a result, evidence-based decision-making requires careful interpretation of the available literature and consideration of individual clinical contexts.

2.24 Towards an Integrated and Personalised Approach

The contemporary trend in oral surgery increasingly favours integrated and personalised postoperative management strategies. Rather than adopting uniform protocols for all patients, clinicians are encouraged to tailor interventions based on individual risk profiles, surgical complexity, and biological considerations.

An integrated approach combines atraumatic surgical technique, selective pharmacological therapy, local biological adjuncts, physical measures, and patient education. This multifaceted strategy acknowledges the multifactorial nature of postoperative discomfort and aims to optimise healing through synergistic interventions.

Personalisation of postoperative care may enhance clinical outcomes while reducing unnecessary interventions and associated risks. In this context, biological adjuncts such as L-PRF may be selectively employed in cases where enhanced healing is particularly desirable or where increased surgical trauma is anticipated.

2.25 Clinical and Translational Implications

The principles outlined in this chapter provide the clinical and biological framework for the experimental investigation presented in this thesis. By contextualising postoperative management strategies within a comprehensive understanding of surgical trauma and wound healing, this chapter establishes the rationale for evaluating the effects of different local therapeutic adjuncts.

The integration of biological insights with clinical practice represents a key aspect of translational research in oral and maxillofacial surgery. Studies aimed at reducing postoperative discomfort following mandibular third molar extraction contribute not only to improved patient care but also to the broader understanding of tissue regeneration and inflammatory modulation.

Aim of the Study

The primary aim of the present study is to evaluate the effectiveness of different therapeutic strategies in reducing postoperative discomfort following surgical extraction of mandibular third molars. Postoperative discomfort is intended as a multidimensional outcome, encompassing pain intensity, facial swelling, trismus, and the occurrence of local postoperative complications.

Secondary objectives include the assessment of soft tissue healing quality and the incidence of inflammatory or infectious sequelae in relation to the adopted postoperative management protocols. Particular attention is directed towards the role of local therapeutic adjuncts and biologically active materials in modulating the inflammatory response and promoting physiological socket healing.

The overarching purpose of this investigation is to identify clinically effective, biologically sound, and reproducible strategies that may improve patient comfort, reduce postoperative morbidity, and enhance overall clinical outcomes following mandibular third molar surgery.

Materials and Methods

Study Setting and Ethical Considerations

The study was conducted at the Unit of Odontostomatological Surgery of the "G. d'Annunzio" University of Chieti–Pescara. A total of 60 patients presenting with clinical and radiological indications suitable for surgical extraction of a mandibular third molar were recruited. Prior to surgery, all patients were informed about the study and, after fully understanding the aim and nature of the procedure, were given the opportunity to ask any questions they deemed necessary. Patients were made aware of the potential risks, complications, and possible benefits associated with the intervention. Written informed consent was obtained from all participants before randomisation.

The study was conducted in accordance with the Declaration of Helsinki and followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Association, 2013). All patients received detailed information about the study prior to signing the informed consent forms.

Study Design

A single-centre randomised clinical trial was conducted. Although a monocentric study design may limit generalisability to other populations or clinical settings, it provides detailed information on treatment efficacy within a specific research centre. Sample randomisation was performed using a computer-generated randomisation code created with Microsoft Office Excel 2010, which employs the Mersenne Twister (MT19937) algorithm for random number generation.

Inclusion Criteria

Patients meeting the following criteria were included in the study:

- Age between 18 and 50 years;
- Indication for unilateral extraction of a mandibular third molar;
- Non-smokers;
- ASA (American Society of Anesthesiologists) physical status I, defined as patients without organic, biochemical, or psychiatric alterations;
- Mandibular third molars classified as Class 1A, 1B, 2A, or 2B according to the Pell and Gregory classification;
- Absence of hormonal therapy;
- Indication limited to extraction of mandibular third molars only;
- Unilateral extraction;
- Surgical duration shorter than 30 minutes;
- Complete crown formation confirmed radiographically;
- Absence of carious lesions on the distal surface of the second molar;
- Willingness and ability to provide written informed consent.

Exclusion Criteria

Patients were excluded if any of the following conditions were present:

- Allergy to local anaesthetics or known hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs);
- Ongoing generalised infectious diseases;
- Metabolic systemic diseases;
- Neoplastic diseases;
- Cardiovascular diseases;
- Hepatic diseases;
- Renal diseases;
- Gastrointestinal diseases;
- Haematological disorders and coagulopathies;
- Autoimmune diseases;
- Diabetes mellitus;
- HIV, HBV, or HCV infection;
- Psychiatric disorders;
- Pregnancy;
- Presence of carious processes;
- Use of medications that may interfere with wound healing, such as anticoagulants, corticosteroids, or immunosuppressive agents;
- Failure to provide informed consent;

- History of severe internal organ diseases that could affect drug absorption, distribution, or metabolism (e.g. peptic ulcer disease, gastrectomy).

Blinding

In this study, the operator responsible for analysing the final clinical data was different from both the surgeon who performed the surgical procedures and the operator who assigned patients to the treatment or control groups through randomisation using Microsoft Office Excel 2010.

Clinical Procedure

During the initial visit, each patient underwent a comprehensive clinical evaluation based on scientific and rational criteria. A complete medical record was compiled, including personal data, medical, pharmacological, recent and remote pathological history, and dental history. By signing the consent form, patients authorised the Department of Odontostomatological Sciences of the "G. d'Annunzio" University of Chieti–Pescara to use the provided personal data for the present investigation and for future medico-scientific procedures.

Subsequently, a thorough extraoral and intraoral clinical examination was performed. Prior to surgery, all participants underwent first- or second-level radiographic examinations, depending on clinical indications.

Pharmacological Protocol

All patients received prophylactic antibiotic coverage with amoxicillin trihydrate (875 mg amoxicillin and 125 mg clavulanic acid), one tablet every 12 hours starting the evening before surgery and continuing for six days postoperatively, for a total of 12 tablets. In patients allergic to penicillins, antibiotic therapy was replaced with azithromycin, a macrolide antibiotic.

Postoperative inflammation was controlled through the administration of NSAIDs and glucocorticoids. Ketoprofen 80 mg, in the form of granules dissolved in water, was prescribed as the non-steroidal anti-inflammatory drug, to be taken one hour before surgery

after a meal. Patients were advised to take ketoprofen in the days following surgery only in cases of severe pain. Corticosteroid therapy consisted of dexamethasone (4 mg) infiltrated into the buccinator muscle immediately after extraction, followed by oral dexamethasone 4 mg daily for the subsequent two days. Patients were instructed to perform mouth rinses with 0.2% chlorhexidine twice daily for one minute every 12 hours for 15 days.

Surgical Technique

All surgical procedures were performed by the same oral surgeon. Interventions were carried out under local anaesthesia, achieving blockade of the inferior alveolar, lingual, and buccal nerves. The local anaesthetic used was 4% articaine with adrenaline 1:200,000.

A standardised surgical protocol was applied to all patients, regardless of group allocation. A full-thickness triangular mucoperiosteal flap was raised. Flap design was planned preoperatively, taking into account the depth of impaction and position of the third molar, in order to ensure adequate visual and instrumental access while maintaining a safe distance from adjacent anatomical structures. To minimise the risk of lingual nerve injury, the distal incision was directed diagonally at approximately 45° towards the buccal side relative to the line connecting the central fossae of the molars.

After flap elevation, osteotomy was performed to remove a portion of the alveolar bone and expose the impacted tooth, allowing access for odontotomy and tooth mobilisation. Osteotomy was carried out using tungsten carbide round burs of various diameters mounted on a straight handpiece under copious irrigation.

Following osteotomy, odontotomy was performed to section the tooth and facilitate extraction. A straight elevator was inserted into the osteotomy site, and gentle rotational movements were applied to complete controlled fracture of the remaining dental tissue. Once sufficient mobilisation was achieved, coronal and radicular fragments were removed using curved haemostatic forceps.

Post-Extraction Socket Management

For each study group (L-PRF, Glt, Glt-Chl), a different topical agent was placed within the post-extraction socket. In the control group, no material was applied, and the socket was irrigated with sterile saline solution only.

In all groups, wounds healed by primary intention, as the flaps were repositioned and sutured using non-resorbable 3-0 polyamide sutures (ASSUMID), which were removed on postoperative day 7. All patients, regardless of group allocation, were instructed to apply cold packs to the surgical site at 10-minute intervals for at least six hours following extraction. Patients were also advised to consume soft and cold foods and to avoid oral hygiene procedures at the surgical site and adjacent areas for 24 hours after surgery. Subsequently, the use of a soft-bristled toothbrush was recommended.

Preparation of PRF

Leukocyte- and platelet-rich fibrin (L-PRF) was prepared according to the protocol described by Choukroun et al., immediately prior to the surgical procedure. Preparation of the concentrate involved venous blood collection using a butterfly needle and sterile 8 mL syringes, obtained by venipuncture from the antecubital vein. In general, needles with a gauge of 20 or 21 G are recommended (grade A recommendation), while the use of smaller-gauge needles is reserved for blood collection from small or particularly fragile veins (grade B recommendation).

The key factor in obtaining a clinically viable product is the limited time interval between blood collection and subsequent centrifugation. If this time threshold is not respected, the fibrinogen present in the blood will be converted into fibrin, which will then be uniformly distributed throughout the entire sample within the tube. As a result, following centrifugation, only a minimal amount of L-PRF (platelet-rich fibrin) with poor consistency will be obtained, rendering it unsuitable for clinical use.

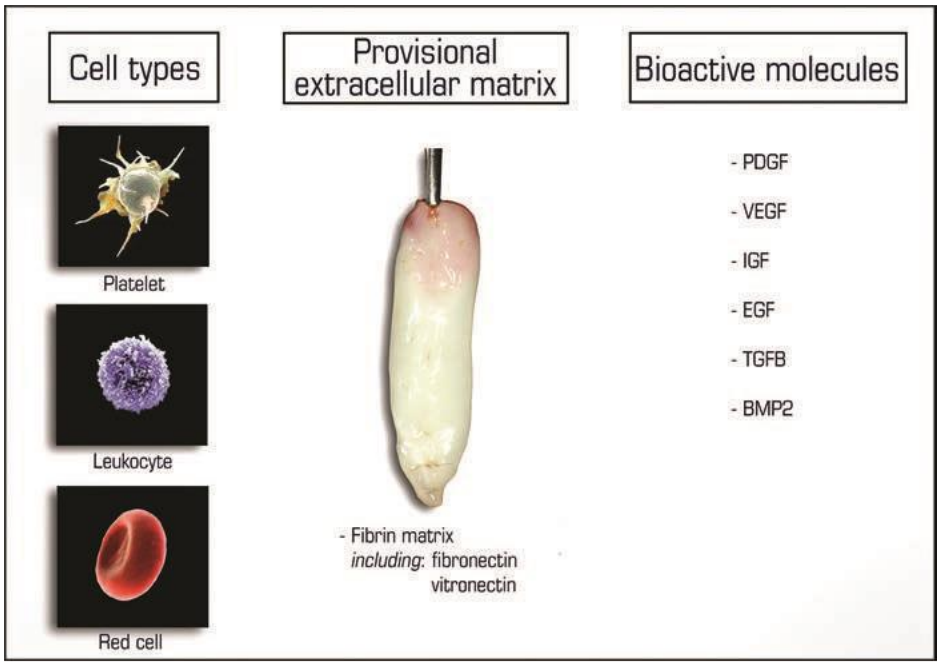
The blood was subsequently collected into 4 mL VACUETTE tubes (13 × 75 mm) containing a separator gel and a coagulation activator composed of silica microparticles. The collected blood was placed into a centrifuge using the EBA 200 bench-top centrifuge

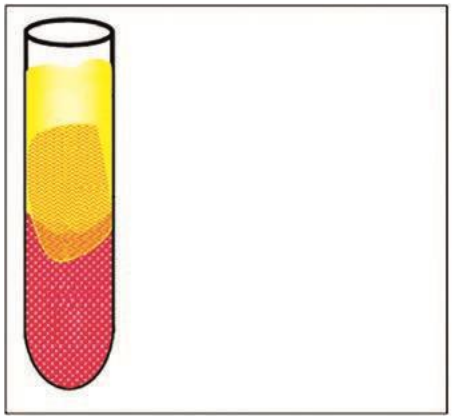
(Hettich Italia), with the centrifugation speed manually set at 2700 rpm for a duration of 12 minutes.

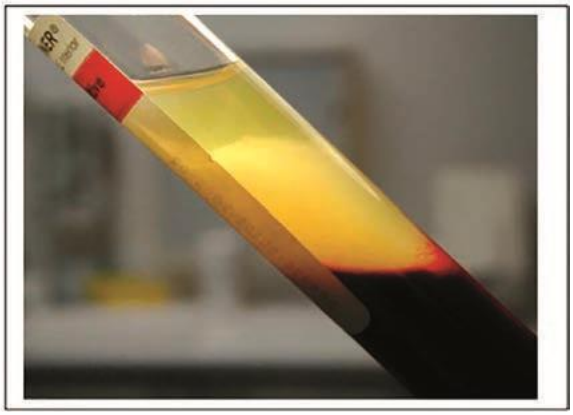
During the centrifugation process, when the blood comes into contact with the inner surface of the tube, platelet activation occurs, triggering the initiation of the coagulation cascade and resulting in separation into three distinct layers: the upper layer consists of acellular plasma poor in platelets, the intermediate layer contains an L-PRF clot, and the lower layer contains red blood cells. During centrifugation, contact between blood and the tube walls leads to platelet activation and initiation of the coagulation cascade. Initially, fibrinogen is concentrated in the upper portion of the tube; however, upon contact with thrombin, which is physiologically present in the blood, it is converted into fibrin and becomes located in the central portion of the tube, between the cellular blood components at the bottom and the acellular plasma at the top. Consequently, platelets become entrapped within the fibrin network.

At the end of the centrifugation cycle, the yellow-coloured platelet concentrate was gently removed from the tube using sterile surgical forceps and separated from the lower red layer containing a high concentration of red blood cells.

L-PRF is an extremely versatile material that can be prepared in different forms depending on the clinical application: it may be obtained as membranes, fragments, or plugs for extraction sites. In the present study, the obtained concentrate was placed into a dedicated surgical kit known as the “PRF Box” (Dental Ant), allowing the production of L-PRF plugs using the Teflon cylinders contained within the box. The resulting so-called “plug” can be easily shaped and placed within the extraction socket.


Cell types
Provisional extracellular matrix
Bioactive molecules
Platelet
Leukocyte
Red cell
- Fibrin matrix
including: fibronectin
vitronectin
- PDGF
- VEGF
- IGF
- EGF
- TGFB
- BMP2





Outcome Measures

The study was designed to evaluate clinical outcomes, both objective and subjective, at three postoperative time points: T1 (first day), T2 (third day), and T3 (seventh day) following the surgical procedure. Patient allocation and monitoring were carried out at the Dental Clinical Facility of the University of Chieti–Pescara.

This study included a total sample of 60 patients. The recruited patients were randomly divided into four groups of 15 patients each:

- **Group 1:** Application of a fibrin sponge (L-PRF) within the post-extraction socket.
- **Group 2:** Application of a haemostatic gelatin sponge soaked with chlorhexidine gel (Spongostan® with Corsodyl® gel).
- **Group 3:** Application of a haemostatic gelatin sponge without chlorhexidine (Spongostan®).
- **Control Group:** No topical application within the post-extraction socket, with irrigation performed using sterile saline solution only.

Data were recorded at three time points: T1 (day 1), T2 (day 3), and T3 (day 7). The evaluated parameters included:

- Bleeding
- Pain
- Swelling
- Soft tissue healing

Bleeding

Bleeding was evaluated using a four-point visual analogue scale:

- **Grade 0:** Absence of bleeding
- **Grade 1:** Mild bleeding
- **Grade 2:** Moderate bleeding
- **Grade 3:** Severe haemorrhage

Pain

Postoperative pain was assessed using a six-point Visual Analogue Scale (VAS) (Delgado DA, 2018):

Score	Pain intensity	Patient experience
0	No pain	The patient feels well
1	Mild pain	Pain is not perceived if the patient is distracted
2	Moderate pain	Pain is perceived even if the patient is engaged in an activity
3	Severe pain	The patient is considerably disturbed by pain but can still perform normal activities
4	Very severe pain	The patient is forced to discontinue normal activities
5	Extremely severe pain	The patient must discontinue all activities and is debilitated due to pain

Swelling

Postoperative follow-up also included the assessment of swelling, which typically develops a few hours after surgery, reaches its maximum intensity on the second or third postoperative day, and subsequently decreases over the following days. Swelling represents an inflammatory process that frequently occurs after surgical extractions.

This parameter was evaluated as any clinical swelling observed during the first seven postoperative days.

Swelling was assessed using a six-point VAS for swelling (Delgado DA, 2018):

Score	Swelling intensity	Patient experience
0	No swelling	—
1	Mild swelling	The patient notices slight, barely visible swelling
2	Moderate swelling	Swelling is evident but does not interfere with normal mastication and swallowing
3	Severe swelling	Pain interferes with normal masticatory activity
4	Very severe swelling	Pain is associated with reduced masticatory activity without trismus
5	Extremely severe swelling	Pain is clearly evident and associated with reduced mouth opening (trismus)

Soft Tissue Healing

Healing of the extraction socket begins with the formation of a blood clot within the first 24 hours following tooth extraction. Subsequently, granulation tissue forms to fill the tissue loss resulting from extraction.[100] Granulation tissue is then replaced by connective tissue before being substituted by bone. Healing of the extraction socket involves remodelling of both bone and soft tissues, which occurs during the first three months following extraction.[101]

The use of PRF is justified by the fact that platelets provide a reservoir of multiple growth factors that play a fundamental role in both hard and soft tissue healing processes. Neovascularisation is initiated by the presence of the PRF clot, and epithelial coverage develops over the surgical site. The postoperative soft tissue site heals by primary intention.[102] Consequently, it has been demonstrated that the PRF membrane used in extraction sockets stimulates local soft tissue healing and reduces the postoperative pain response.[103]

This parameter was assessed and documented according to the criteria described by Landry and Turnbull. Soft tissue healing was evaluated using a five-point scale:

Healing index	**Clinical signs**
Healing index 1: Very poor	Gingival colour: red gingiva ≥ 50% Response to palpation: bleeding present Granulation tissue: present Marginal incision: non-epithelialised with epithelial loss beyond the marginal incision Suppuration: present
Healing index 2: Poor	Gingival colour: red gingiva ≥ 50% Response to palpation: bleeding present Granulation tissue: present Marginal incision: non-epithelialised with exposed connective tissue Suppuration: present
Healing index 3: Good	Gingival colour: red gingiva ≥ 25% and < 50% Response to palpation: absence of bleeding Granulation tissue: absent Marginal incision: absence of exposed connective tissue
Healing index 4: Very good	Gingival colour: red gingiva < 25% Response to palpation: absence of bleeding Granulation tissue: absent Marginal incision: absence of exposed connective tissue
Healing index 5: Excellent	Gingival colour: completely pink tissue Response to palpation: absence of bleeding

Healing index	Clinical signs
	Granulation tissue: absent Marginal incision: absence of exposed connective tissue

Statistical Analysis

Statistical analysis was performed using SPSS software version 20.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as median values and interquartile ranges. The Kolmogorov–Smirnov test was performed to assess data normality.

The non-parametric Mann–Whitney test was used to compare the L-PRF, gelatin (Glt), gelatin with chlorhexidine (Glt-Chl), and control groups at the different postoperative time points. The non-parametric Friedman test was used to compare values across different time points within the same group. Statistical significance was set at $p < 0.05$.

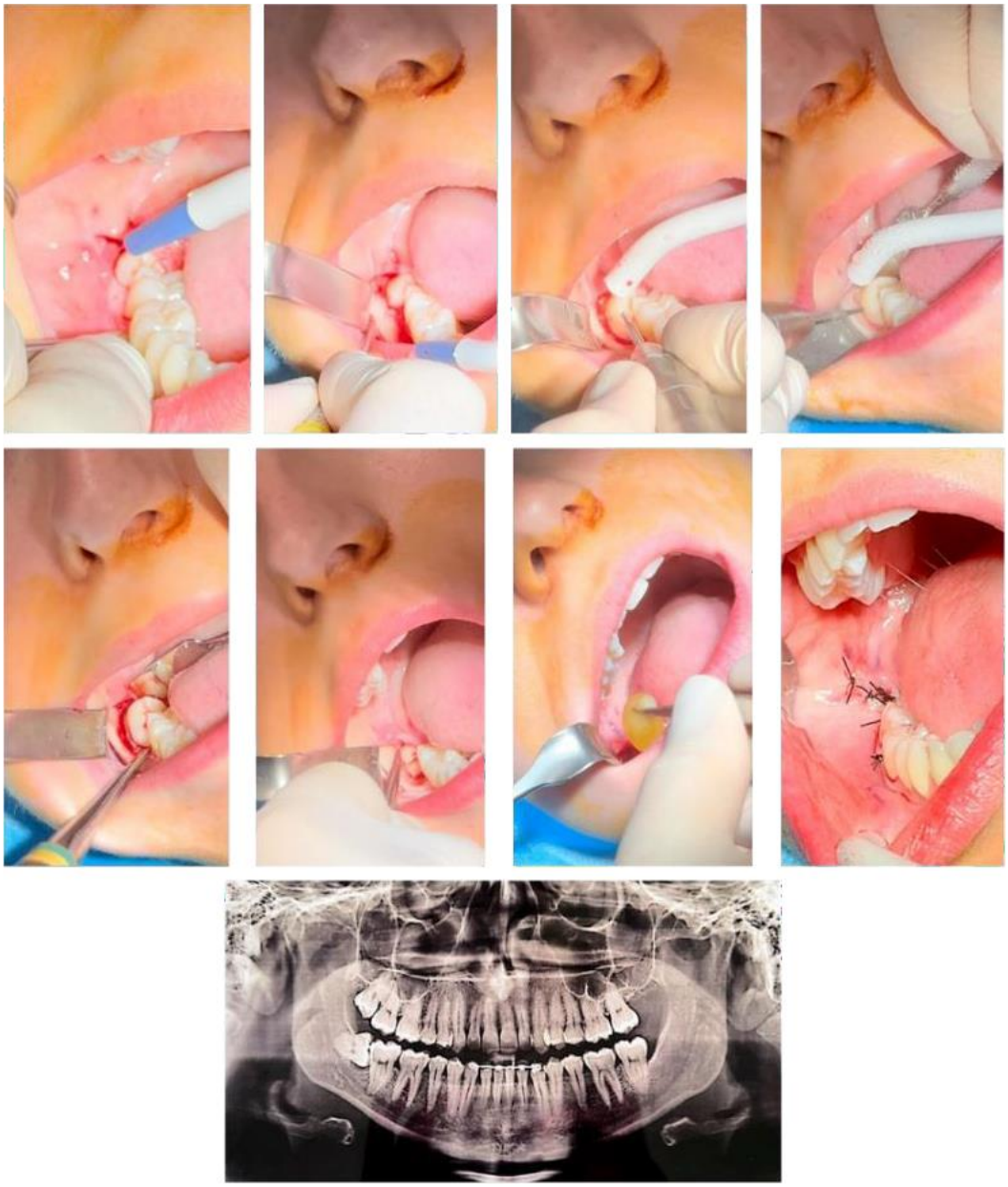


Fig. 1. Clinical case of extraction of element 4.8 (2A of Pell & Gregory) with insertion of L-PRF into the socket



Fig. 2. Insertion of Spongostan® into the post-extraction socket.

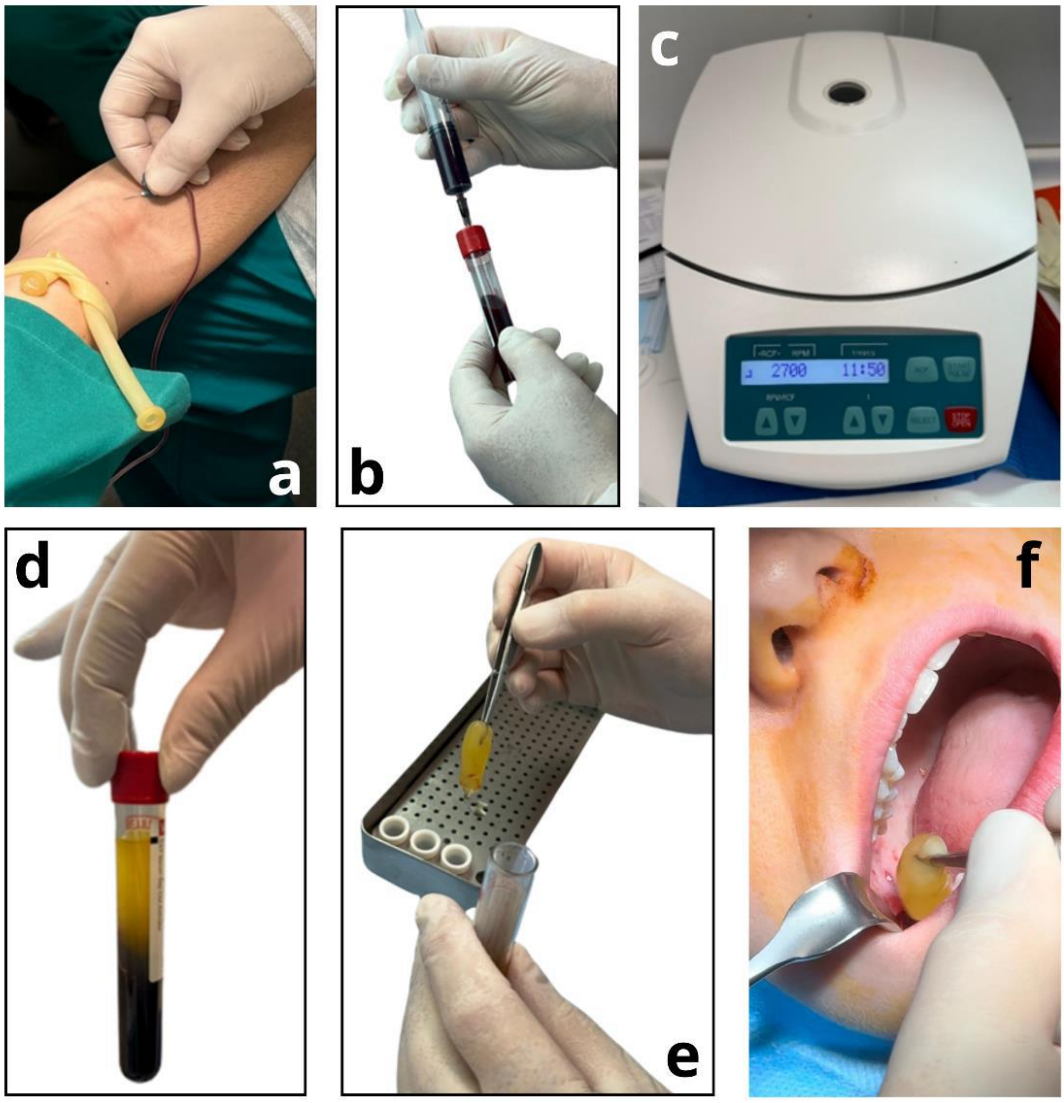


Fig. 3 L-PRF is prepared according to Choukroun et al. (Choukroun J D.A., 2006) immediately before surgery.

Results

A total of 60 patients were recruited, all of whom met the inclusion and exclusion criteria, for a total of 60 extractions. Patients were divided into four groups of 15 subjects each, and each group was treated with one of the three topical devices under investigation, except for the control group, in which no material was applied. All patients in each group fulfilled the study requirements, with a validity rate of 100%. No recruited patient was excluded from the evaluation.

In the L-PRF group, 15 patients were enrolled, of whom 53.3% were female and 46.7% were male. The median age of the patients was 25 years.
In the gelatin sponge group (Glt), 15 patients were enrolled, of whom 60% were female and 40% were male. The median age of the patients was 26 years.
In the gelatin sponge with chlorhexidine gel group (Glt-Chl), 15 patients were enrolled, of whom 66.7% were female and 33.3% were male. The median age of the patients was 26 years.
In the control group, 15 patients were enrolled, of whom 60% were female and 40% were male. The median age of the patients was 23 years.

Outcome data regarding bleeding, pain, swelling, and healing are reported in Tables 1–4.

Using the two non-parametric tests, Mann–Whitney and Kruskal–Wallis, the median values of the Landry and Turnbull healing index (Table 1) were compared among the L-PRF, Glt, Glt-Chl, and control groups at time points T1, T2, and T3. A statistically significant difference was observed, with better results in the group treated with L-PRF.

On the first postoperative day (T1), statistically significant differences were observed among the groups. The L-PRF group achieved a median value of 4 (IQR 3–4), whereas the Glt, Glt-Chl, and control groups all showed a median value of 3 (IQR 3–4, 2–3, and 2–3, respectively). With a p-value of 0.006, these differences were statistically significant. This suggests that patients in the L-PRF group experienced better initial healing compared with the other groups, indicating an early advantage of L-PRF treatment.

On the third postoperative day (T2), statistically significant differences among the groups were still present, although less pronounced than on the first day. The p-value of 0.036 confirms that these differences remained statistically significant. These data indicate that the L-PRF group continued to show an advantage over the other treatments at T2.

At T3, statistically significant differences were observed ($p = 0.009$), particularly for the L-PRF group, which demonstrated better healing compared with the other groups.

When healing was compared across postoperative days from T1 to T3, a statistically significant improvement ($p < 0.001$) was observed in all groups included in the study.

Table 1. Comparison of median Landry and Turnbull healing index values (five-point scale) among the L-PRF, gelatin (Glt), gelatin with chlorhexidine (Glt-Chl), and control groups

Time point	L-PRF Median (IQR)	Glt Median (IQR)	Glt-Chl Median (IQR)	Control Median (IQR)	p-value**
Day 1 (T1)	4 (3–4)	3 (3–4)	3 (2–3)	3 (2–3)	0.006
Day 3 (T2)	4 (3–5)	4 (3–4)	4 (2–4)	3 (3–4)	0.036
Day 7 (T3)	5 (5–5)	4 (4–5)	4 (3–4)	4 (4–5)	0.009
p-value*	<0.001	<0.001	<0.001	<0.001	

* p-value derived from Friedman test

** p-value derived from Mann–Whitney test

Statistical significance set at $p < 0.05$

Postoperative pain analysis was performed using a six-point Visual Analogue Scale (VAS), measuring scores on postoperative days 1, 3, and 7.

Overall, outcome data (Table 2) indicate that there were no statistically significant differences in pain scores among the different groups on the postoperative days analysed. Although the L-PRF and Glt groups tended to show slightly lower pain scores from the third postoperative day onwards, these differences did not reach statistical significance ($p < 0.001$). This may be attributed to individual variability in pain perception and to the overall effectiveness of all treatments in controlling postoperative pain.

The fact that pain was significantly reduced in all groups by the seventh postoperative day suggests that, regardless of the specific treatment applied, postoperative pain tends to decrease markedly within one week. However, treatment with L-PRF and gelatin sponges appeared to provide slightly better pain control compared with the other treatments, although the differences were not statistically significant.

Table 2. Comparison of pain scores (VAS, six-point scale) among the L-PRF, gelatin (Glt), gelatin with chlorhexidine (Glt-Chl), and control groups

Time point	**L-PRF Median (IQR)**	**Glt Median (IQR)**	**Glt-Chl Median (IQR)**	**Control Median (IQR)**	**p-value****
Day 1 (T1)	1 (1–1)	1 (0–2)	1 (1–3)	1 (1–2)	0.103
Day 3 (T2)	0 (0–1)	0 (0–1)	1 (0–2)	1 (0–1)	0.411
Day 7 (T3)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–1)	0.064
p-value*	<0.001	<0.001	0.044	0.002	

* p-value derived from Friedman test

** p-value derived from Mann–Whitney test

Statistical significance set at $p < 0.05$

Postoperative swelling analysis was conducted using a six-point VAS, with scores recorded on postoperative days 1, 3, and 7.

Outcome data for oedema (Table 3) revealed a statistically significant reduction in swelling values from T1 to T3 ($p < 0.001$) in all study groups. On the first postoperative day, significant differences in swelling were observed among the groups. The L-PRF group

reported a median value of 1 (IQR 1–1), whereas the Glt, Glt-Chl, and control groups showed median values of 2 (IQR 1–3). The p-value of 0.037 indicates that these differences were statistically significant, suggesting that patients in the L-PRF group experienced less swelling on the first postoperative day.

At T2, a p-value of 0.010 confirmed statistically significant differences, with the L-PRF group continuing to show the lowest swelling scores among the groups. On the seventh postoperative day, swelling scores further decreased in all groups. The L-PRF group showed a median of 0 (IQR 0–0), indicating complete resolution of swelling in all patients. The Glt and Glt-Chl groups showed a median of 0 (IQR 0–1), while the control group showed a median of 1 (IQR 0–1). The p-value of 0.152 indicates that differences in swelling among the groups were no longer statistically significant on the seventh postoperative day, reflecting an overall reduction of swelling in all groups.

Table 3. Comparison of swelling scores (VAS, six-point scale) among the L-PRF, gelatin (Glt), gelatin with chlorhexidine (Glt-Chl), and control groups

Time point	L-PRF Median (IQR)	Glt Median (IQR)	Glt-Chl Median (IQR)	Control Median (IQR)	p-value**
Day 1 (T1)	1 (1–1)	2 (1–3)	2 (1–3)	2 (1–3)	0.037
Day 3 (T2)	0 (0–1)	1 (1–2)	2 (1–3)	1 (1–2)	0.010
Day 7 (T3)	0 (0–0)	0 (0–1)	0 (0–1)	1 (0–1)	0.152
p-value*	<0.001	<0.001	<0.001	<0.001	

* p-value derived from Friedman test

** p-value derived from Mann–Whitney test

Statistical significance set at $p < 0.05$

Postoperative bleeding analysis, measured on postoperative days 1, 3, and 7 using a four-point scale, showed similar results among the treatment groups: L-PRF, gelatin (Glt), gelatin with chlorhexidine (Glt-Chl), and the control group.

On the first postoperative day, the L-PRF group reported a median value of 0 (IQR 0–1), as did the Glt and Glt-Chl groups. The control group showed a median value of 0 (IQR 0–0). These low bleeding scores were maintained on subsequent days. On the third postoperative day, all groups continued to report a median value of 0 (IQR 0–0). Finally, on the seventh postoperative day, bleeding scores remained unchanged, with all groups showing a median value of 0 (IQR 0–0).

The p-values on postoperative days 1, 3, and 7 were 0.464, 0.284, and 1.000, respectively, indicating no statistically significant differences in bleeding among the groups on any of the analysed postoperative days.

Table 4. Comparison of bleeding grades (four-point scale) among the L-PRF, gelatin (Glt), gelatin with chlorhexidine (Glt-Chl), and control groups

Time point	**L-PRF Median (IQR)**	**Glt Median (IQR)**	**Glt-Chl Median (IQR)**	**Control Median (IQR)**	**p-value****
Day 1 (T1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–0)	0.464
Day 3 (T2)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.284
Day 7 (T3)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	1.000
p-value*	0.018	0.007	0.001	0.146	

* p-value derived from Friedman test

** p-value derived from Mann–Whitney test

Statistical significance set at $p < 0.05$

Discussions

The present study was designed to compare the postoperative clinical outcomes associated with different local therapeutic strategies following surgical extraction of mandibular third molars. Specifically, the effects of L-PRF, gelatin sponges with and without chlorhexidine, and the absence of any topical agent were evaluated with respect to bleeding control, postoperative pain, facial swelling, and soft tissue healing. These parameters were selected because they represent the most clinically relevant determinants of patient morbidity and quality of life after third molar surgery.

Postoperative Bleeding Control

The results demonstrated that postoperative bleeding was minimal and comparable among all study groups throughout the follow-up period. Bleeding scores remained close to zero from the first postoperative day onwards, indicating effective haemostasis irrespective of the topical material applied. These findings confirm that surgical technique, primary wound closure, and appropriate postoperative protocols play a predominant role in bleeding control, while the additional benefit of local haemostatic agents may be limited in healthy patients undergoing uncomplicated extractions.

The effectiveness of gelatin sponges in controlling postoperative bleeding has been widely documented, particularly in patients receiving anticoagulant therapy. Previous studies have shown that absorbable gelatin-based materials provide a stable matrix that promotes clot formation and protects the extraction socket from mechanical disruption. The present findings are consistent with these observations and suggest that, in systemically healthy patients, all evaluated topical approaches are sufficient to ensure haemostatic stability.

Postoperative Swelling and Inflammatory Response

In contrast to bleeding outcomes, significant differences were observed in postoperative swelling among the study groups. L-PRF demonstrated superior efficacy in reducing facial swelling, particularly during the early postoperative period. This effect may be attributed to the biological properties of L-PRF, which releases a sustained concentration of growth factors and cytokines that modulate the inflammatory response, promote angiogenesis, and accelerate tissue repair.

The reduced swelling observed in the L-PRF group aligns with previous studies reporting its anti-inflammatory and regenerative potential. Platelet-derived growth factors such as PDGF, TGF-β, and VEGF are known to regulate vascular permeability and inflammatory cell recruitment, thereby limiting excessive oedema formation. The gelatin sponge groups showed intermediate outcomes, while the control group exhibited the least favourable swelling profile, further supporting the beneficial role of local adjuncts in postoperative inflammation control.

The lack of a clear advantage associated with the addition of chlorhexidine suggests that antimicrobial activity alone may not be sufficient to modulate postoperative inflammation and may, in some cases, interfere with physiological healing processes.

Postoperative Pain

Pain assessment revealed no statistically significant differences among the study groups, although a trend towards lower pain scores was observed in the L-PRF and gelatin sponge groups. Pain perception is inherently subjective and influenced by multiple factors, including individual pain thresholds, psychological state, and surgical variables. The absence of statistically significant differences may therefore reflect interindividual variability rather than true equivalence among treatments.

Nevertheless, the overall reduction in pain over time across all groups suggests that standardised surgical protocols combined with appropriate pharmacological management remain effective in controlling postoperative pain. The potential analgesic benefit of L-

PRF observed in some studies may become more evident in larger samples or in patients undergoing more complex surgical procedures.

Soft Tissue Healing

The most pronounced differences among groups were observed in soft tissue healing outcomes. The L-PRF group exhibited significantly superior healing, characterised by rapid epithelialisation, minimal inflammation, and optimal gingival tissue quality. These findings support the regenerative role of L-PRF and are consistent with a growing body of evidence demonstrating its positive effects on soft tissue healing.

Leukocytes contained within L-PRF play a crucial role in immune regulation and antimicrobial defence, while platelet-derived growth factors promote fibroblast proliferation and extracellular matrix deposition. This biological synergy likely accounts for the improved healing observed in the L-PRF group.

The inferior healing outcomes observed in the chlorhexidine-containing gelatin group raise important considerations. Although chlorhexidine is widely used for its antiseptic properties, its cytotoxic effects on fibroblasts and osteoblasts have been reported in vitro. This may partially explain the less favourable healing outcomes when chlorhexidine is combined with gelatin sponges.

Clinical Implications and Study Limitations

From a clinical perspective, the present findings suggest that L-PRF represents a valuable adjunct for reducing postoperative morbidity and enhancing soft tissue healing following mandibular third molar extraction. Gelatin sponges alone remain effective haemostatic agents, while the routine addition of chlorhexidine does not appear to confer additional benefits and may even negatively affect healing.

The limitations of this study include the relatively small sample size, the exclusive inclusion of young and systemically healthy patients, and the use of concomitant pharmacological therapies, particularly corticosteroids, which may have masked differences among groups. Future studies involving larger and more heterogeneous

populations, as well as reduced pharmacological interference, are warranted to further elucidate the role of local therapeutic strategies in third molar surgery.

Conclusion

The findings of the present study provide meaningful clinical and biological insights into the management of postoperative morbidity following surgical extraction of mandibular third molars. Within the limitations of the study design, the application of leukocyte- and platelet-rich fibrin (L-PRF) in the post-extraction socket demonstrated a clear advantage over conventional management without topical adjuncts, particularly in terms of reducing postoperative swelling and enhancing soft tissue wound healing during the early and intermediate postoperative phases.

The superior performance of L-PRF may be attributed to its unique biological composition, which combines a dense fibrin matrix with platelets and leukocytes capable of releasing growth factors and cytokines in a sustained manner. These bioactive molecules promote angiogenesis, fibroblast proliferation, and epithelial regeneration while modulating the inflammatory response. As a result, L-PRF appears to support a more physiologically balanced healing process, limiting excessive inflammation and accelerating tissue repair. From a clinical perspective, this translates into improved wound quality, reduced oedema, and enhanced patient comfort during recovery.

The use of absorbable gelatin sponges (Spongostan®) also proved to be beneficial in reducing postoperative discomfort. Patients treated with gelatin sponges experienced a reduction in swelling and improved healing compared with the control group, confirming the haemostatic and scaffold properties of gelatin-based materials. By stabilising the blood clot and providing a temporary matrix for tissue ingrowth, gelatin sponges support early stages of socket healing and contribute to favourable clinical outcomes.

The combination of gelatin sponges with chlorhexidine did not result in additional clinical advantages compared with gelatin alone. Although chlorhexidine is widely recognised for its antimicrobial efficacy, its incorporation into the gelatin sponge did not further reduce postoperative discomfort or improve healing outcomes in the present study. These findings suggest that, in the absence of overt infection or high microbial risk, the routine addition of chlorhexidine to local haemostatic materials may be unnecessary and may not enhance

physiological healing. This observation underscores the importance of balancing antimicrobial strategies with tissue biocompatibility and regenerative potential.

With regard to postoperative bleeding and pain, no statistically significant differences were observed among the investigated groups. Bleeding was effectively controlled across all treatment protocols, likely reflecting the influence of standardised surgical technique, primary wound closure, and appropriate postoperative care. Similarly, postoperative pain decreased progressively over time in all groups, suggesting that systemic pharmacological management and individual variability in pain perception play a more prominent role than local topical agents in pain control following third molar surgery.

Despite these encouraging results, several limitations must be acknowledged. The relatively limited sample size and the inclusion of exclusively young and systemically healthy patients may restrict the generalisability of the findings. Additionally, the use of concomitant pharmacological therapies, particularly corticosteroids and non-steroidal anti-inflammatory drugs, may have attenuated differences among treatment groups. Pain assessment remains inherently subjective and cannot be fully standardised, representing another methodological constraint.

In light of these considerations, further well-designed randomised clinical trials with larger and more heterogeneous populations are warranted to confirm the present findings and to better define the role of L-PRF and other local therapeutic strategies in third molar surgery. Future research should also aim to explore long-term outcomes, patient-reported quality-of-life measures, and cost–benefit analyses to support evidence-based clinical decision-making.

In conclusion, the application of L-PRF represents a biologically sound and clinically effective adjunct in the postoperative management of mandibular third molar extraction, offering tangible benefits in terms of swelling reduction and wound healing enhancement. Gelatin-based haemostatic materials remain a valid alternative for reducing postoperative discomfort, while the routine addition of chlorhexidine does not appear to confer further advantages. These findings contribute to the growing body of evidence supporting the integration of biologically active materials into contemporary oral surgical practice.

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