University of Helsinki
Dissertationes Universitatis Helsingiensis 174/2024

Department of Oral and Maxillofacial Diseases
Faculty of Medicine
University of Helsinki
Helsinki, Finland

Division of Oral and Maxillofacial Surgery
Department of Oral and Maxillofacial Diseases
Helsinki University Hospital
Helsinki, Finland

Perioperative surgical options and medications in mandibular fracture patients

Marko Oksa

ACADEMIC DISSERTATION

Doctoral Program in Clinical Research, Oral and Maxillofacial Surgery
To be presented for public examination, with the permission of the Faculty of Medicine of the University of Helsinki, in Lecture Hall Kruununhaka, Bridge Hospital, Helsinki University Hospital, Haartmaninkatu 4, Helsinki, on the 30th of August 2024 at 12 o'clock.

Helsinki 2024

Supervisors

Associate Professor (tenure-track) Johanna Snäll, PhD, MD, DDS
Department of Oral and Maxillofacial Diseases, Faculty of Medicine, University of Helsinki, Helsinki, Finland, and Division of Oral and Maxillofacial Surgery, Department of Oral and Maxillofacial Diseases, Helsinki University Hospital, Helsinki, Finland

Doctor Aleksi Haapanen, PhD, DDS
Department of Oral and Maxillofacial Diseases, Faculty of Medicine, University of Helsinki, Helsinki, Finland, and Division of Oral and Maxillofacial Surgery, Department of Oral and Maxillofacial Diseases, Helsinki University Hospital, Helsinki, Finland

Reviewers

Professor Jari Kellokoski, PhD, DDS
Institute of Dentistry, University of Eastern Finland, Kuopio, Finland, and Department of Oral and Maxillofacial Diseases, Kuopio University Hospital, Kuopio, Finland

Docent Leena Ylikontiola, PhD, MD, DDS
Research Unit of Oral Health Sciences, Faculty of Medicine, University of Oulu, Oulu, Finland, and Department of Oral and Maxillofacial Surgery, Oulu University Hospital, Oulu, Finland

Opponent

Professor honoris causa Pekka Laine, PhD, DDS
Patient Insurance Centre, Helsinki, Finland

Cover illustration by Osmo Lintervo.

The Faculty of Medicine uses the Ouriginal system (plagiarism recognition) to examine all doctoral dissertations.

Publisher: University of Helsinki
Series: Dissertationes Universitatis Helsingiensis 174/2024

ISBN 978-951-51-9912-6 (print)
ISBN 978-951-51-9911-9 (online)
ISSN 2954-2898 (print)
ISSN 2954-2952 (online)
PunaMusta, Joensuu 2024

To my family and friends

ABSTRACT

Background and purpose

Postoperative complications are common after mandibular fracture surgery. Antibiotics as well as glucocorticoids like dexamethasone (DXM) are typically used as part of surgical treatment of these fractures. Nonetheless, antibiotic use and surgical protocols for infected mandibular fractures tend to vary significantly between surgeons. The aim of this study was to evaluate medications and perioperative technical aspects to prevent postoperative complications in patients with fractures in the dentate part of the mandible. Additionally, patient-related factors predisposing to complications were evaluated.

Patients and methods

This study comprises three retrospective studies (I – III) and one prospective study (IV). Study I comprised patients who had undergone intraoral surgery for a single fracture of the dentate part of the mandible (n=107). The primary outcome variable was postoperative surgical site infection (SSI) and the primary predictor variable was duration of postoperative antibiotic treatment. Study II included patients with an infected fracture of the mandible without preceding surgery (n=41). The primary outcome variable was postoperative surgical site complication. Patient-, fracture-, and surgery-related variables were investigated and predictors for postoperative complications were analysed. Study III comprised patients with one or two fractures of the dentate part of the mandible treated surgically via an intraoral approach (n=232 patients with 270 mandibular fractures). The primary outcome variable was postoperative surgical wound dehiscence (SWD). Associations between patient-, fracture-, and surgery-related variables and SWD were studied. In Study IV, patients with one or two non-comminuted fractures of the dentate part of the mandible treated surgically via intraoral approach (n=34) were included. Patients in the study group received perioperative DXM. The control group received neither steroids nor placebo. The primary outcome variables were postoperative visual analogue scale (VAS) score, postoperative opioid medication, maximal mouth opening, and postoperative facial swelling.

Results

SSI occurred in 18 patients (16.8%) in Study I. None of the studied patient-, fracture-, or surgery related variables showed significant differences between the groups.

In Study II, postoperative surgical site complication was observed in 13 patients (31.7%). No significant differences in patient- and fracture-related variables or treatment-related variables were found between patients with and without postoperative complication. Recurrent infection was the most common surgical site complication (n=9, 69.2%). SWD without infection occurred only with intraoral approach (p=0.0380).

Twenty-two SWDs were detected, occurring in 9.5% of patients and in 8.1% of fractures in Study III. A significantly greater SWD rate was observed only among smokers (p=0.0410). In surgery-related variables, night-time surgery showed a significantly higher SWD rate than daytime surgery (p=0.012).

In Study IV, the VAS score was significantly lower in the study group 18 hours postoperatively (p=0.0330). No significant difference in the postoperative opioid medication, difference in percentage decrease in facial swelling, or mouth opening were found between the study and control groups.

Conclusions

Postoperative surgical site complications are common in mandibular fracture patients. A significantly greater SWD rate was observed among smokers and patients treated at night-time. SSIs can occur despite adequate fracture treatment and antibiotic regimen. The duration of antibiotic treatment showed no significant difference between patients with or without SSI. Thus, short antibiotic treatment as part of the surgical treatment of mandibular fracture seems to be sufficient.

Patient-related factors and delay caused by health care professionals for missed fracture were the most common reasons for infected mandibular fractures. Postoperative surgical site complications are common in patients with infected mandibular fracture. SWD without infection occurred exclusively with an intraoral approach. Both intraoral and extraoral approaches can be used, but patients should be selected with care and SWD risk in intraoral approach should be noted.

The use of perioperative DXM reduces postoperative pain significantly in mandibular fracture patients 18 hours postoperatively. No significant effect on postoperative trismus or oedema was found. The analgesic effect seems to be short-term, and potential disadvantages of glucocorticoids should be considered.

TIIVISTELMÄ (ABSTRACT IN FINNISH)

Taustaa

Leikkauksen jälkeiset komplikaatiot ovat yleisiä alaleukaluun murtumaleikkauspotilailla. Antibiootteja ja glukokortikoideja, kuten deksametasonia, käytetään yleisesti osana alaleukaluun murtumien kirurgista hoitoa. Antibioottien käyttö vaihtelee huomattavasti kirurgien välillä. Lisäksi infektoituneiden alaleukaluun murtumien kirurgisissa hoitomenetelmissä on huomattavaa vaihtelua. Tutkimuksen tavoitteena oli arvioida leikkaustekniikoita ja lääkehoitoa leikkauksen jälkeisten komplikaatioiden ehkäisemiseksi potilailla, joilla on murtuma alaleukaluun hampaallisessa osassa. Lisäksi tutkimuksessa arvioitiin komplikaatioille altistavia potilaaseen liittyviä tekijöitä.

Menetelmät

Tutkimus koostuu kolmesta retrospektiivisestä osatyöstä (I–III) ja yhdestä prospektiivisesta osatyöstä (IV). Osatyössä I tutkittiin potilaita, joilla oli alaleukaluun hampaallisen osan murtuma (n=107). Ensisijaisesti tutkittiin leikkauksen jälkeisen antibioottihoidon keston vaikutusta leikkausalueen infektioiden esiintymiseen. Osatyössä II tutkittiin potilaita, joilla oli infektoitunut alaleukaluun murtuma ilman edeltävää leikkausta (n=41). Tutkimme potilaisiin, murtumiin ja leikkauksiin liittyviä muuttujia sekä niiden vaikutusta leikkauksen jälkeisten komplikaatioiden esiintymiseen. Osatyössä III tutkittiin potilaita, joilla oli yksi tai kaksi alaleukaluun hampaallisen osan murtumaa (n = 232 potilasta, 270 alaleukaluun murtumaa). Analyyseissä vertailtiin potilaisiin, murtumiin ja leikkauksiin liittyvien muuttujien ja leikkaushaavan aukeamisen välistä yhteyttä. Osatyössä IV tutkittiin potilaita, joilla oli yksi tai kaksi alaleukaluun hampaallisen osan murtumaa (n=34). Tutkimusryhmän potilaat saivat leikkauksen yhteydessä deksametasonia, kun taas kontrolliryhmä ei saanut steroideja eikä lumelääkettä. Ensisijaiset muuttujat olivat leikkauksen jälkeinen kipujana, opioidilääkitys, suun maksimaalinen avautuminen ja kasvojen turvotus.

Tulokset

Leikkausalueen infektioita esiintyi 18 potilaalla (16,8 %) osatyössä I. Mitkään tutkituista potilaaseen, murtumaan tai leikkaukseen liittyvistä muuttujista eivät osoittaneet tilastollisesti merkitseviä eroja ryhmien välillä.

Osatyössä II leikkauksen jälkeisiä komplikaatioita havaittiin 13 potilaalla (31,7 %). Leikkauksen jälkeen komplikaatioita saaneiden ja ilman komplikaatioita selvinneiden potilaiden välillä ei havaittu tilastollisesti merkitseviä eroja

potilaaseen, hoitoon tai murtumaan liittyvissä muuttujissa. Uusiutuva infektio oli yleisin leikkausalueen komplikaatio (n=9, 69,2 %). Leikkaushaavan aukeamista ilman infektiota esiintyi yksinomaan suun sisäkautta tehdyissä leikkauksissa (21,1 %, p = 0,0380).

Osatyössä III leikkaushaavan aukeamista esiintyi 9,5 %:lla potilaista ja 8,1 %:lla murtumista. Tupakoitsijoilla havaittiin tilastollisesti merkitsevä ero leikkaushaavan aukeamisen esiintymisessä (p=0,0410). Yölliset leikkaukset johtivat useammin leikkaushaavan aukeamiseen verrattuna päiväsaikaan tehtyihin leikkauksiin (p=0,012).

Osatyössä IV kipujanan arvo oli merkittävästi alhaisempi tutkimusryhmässä 18 tuntia leikkauksen jälkeen (p=0,0330). Tutkimus- ja kontrolliryhmien välillä ei havaittu merkitsevää eroa leikkauksen jälkeisessä opioidilääkityksessä, kasvojen turvotuksessa tai suun maksimaalisessa avautumisessa.

Johtopäätökset

Leikkauksen jälkeiset leikkausalueen komplikaatiot ovat yleisiä alaleukamurtumapotilailla. Leikkaushaavan aukeamista havaittiin enemmän tupakoitsijoilla ja yöaikaan leikatuilla potilailla. Asianmukaisesta leikkaus- ja antibioottihoidosta huolimatta leikkausalueen infektioita esiintyy. Antibioottihoidon kesto ei vaikuttanut komplikaatioiden esiintyvyyteen potilaiden välillä. Näin ollen lyhyt antibioottihoito osana alaleukaluun murtuman kirurgista hoitoa vaikuttaa riittävältä.

Yleisimmät syyt alaleukaluun murtumien infektoitumiseen olivat potilaaseen liittyvät tekijät sekä terveydenhuollon ammattilaisista johtuva viive murtuman jäädessä diagnosoimatta potilaan ensimmäisellä lääkäri- tai hammaslääkärikäynnillä vamman jälkeen. Leikkauksen jälkeiset komplikaatiot ovat yleisiä potilailla, joilla on infektoitunut alaleukaluun murtuma. Leikkaushaavan aukeamista esiintyi yksinomaan potilailla, joilla murtuma oli hoidettu suun sisäkautta leikkaamalla. Sekä suun sisäistä että suun ulkopuolista leikkausavausta voidaan käyttää infektoituneiden alaleukaluun murtumien hoidossa, mutta potilasvalinta tulee tehdä huolella huomioiden riski haavan aukeamiselle suun sisäkautta toteutetuissa leikkauksissa.

Deksametasonin käyttö vähentää leikkauksen jälkeistä kipua tilastollisesti merkitsevästi alaleukaluun murtumapotilailla 18 tuntia leikkauksen jälkeen. Tilastollisesti merkitsevää vaikutusta suunavausrajoitukseen tai turvotukseen ei havaittu. Kipua lievittävä vaikutus näyttää kuitenkin olevan lyhytaikainen, ja glukokortikoidien mahdolliset haitat on otettava huomioon niitä käytettäessä.

CONTENTS

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications:

I Oksa M, Haapanen A, Marttila E, Snäll J. Simple dentate area fractures of the mandible – can we prevent postoperative infections? Acta Odontologica Scandinavica. 2022;80(7):494–500.

II Oksa M, Haapanen A, Kannari L, Furuholm J, Snäll J. Surgical treatment of clinically infected mandibular fractures. Oral and Maxillofacial Surgery. 2024;28(2):839-847.

III Oksa M, Haapanen A, Marttila E, Furuholm J, Snäll J. Postoperative wound dehiscence in mandibular fractures. Acta Odontologica Scandinavica. 2023;81(7):555–561.

IV Oksa M, Haapanen A, Furuholm J, Thorén H, Snäll J. Effect of Perioperative Systemic Dexamethasone on Pain, Edema, and Trismus in Mandibular Fracture Surgery: A Randomized Trial. Journal of Craniofacial Surgery. 2021; 32(8): 2611–2614.

The publications are referred to in the text by their roman numerals.

ABBREVIATIONS

ACTH, adrenocorticotropic hormone
CBCT, cone-beam computed tomography
CHX, chlorhexidine
CN, cranial nerve
CNS, central nervous system
COX, cyclooxygenase
CRH, corticotropin releasing hormone
CRP, C-reactive protein
CT, computer tomography
DPR, dental panoramic radiograph
DXM, dexamethasone
GCs, glucocorticoids
IAN, inferior alveolar nerve
MMF, mandibulo-maxillary fixation
NSAIDs, nonsteroidal anti-inflammatory drugs
ORIF, open reduction and internal fixation
PGE2, prostaglandin E2
SSI, surgical site infection
SWD, surgical wound dehiscence
TDI, modified total dental index
TXB2, thromboxane B2
VAS, visual analogue scale

1. INTRODUCTION

Mandibular fractures, together with nasal and orbital fractures, are the most frequent fractures in the maxillofacial area[1–3]. The aim in surgical treatment of mandibular fractures is to restore aesthetics and function and make the patient pain-free. However, postoperative complications are common, occurring in 25.0–61.1% of mandibular fracture surgeries[4–8]. The most typical complications are surgical site infection (SSI), hardware failure, non-union, surgical wound dehiscence (SWD) and malocclusion[4,6,9–14]. Furthermore, complications can predispose to other complications. For example, SWD can contribute to complications such as hardware failure. Postoperative complications can cause the need for reoperation and increase the requirement for control visits[4]. Additionally, associated injuries such as brain injury are common among facial bone fracture patients[15–17] which should be considered when treating these patients.

Antibiotics are commonly used as part of the treatment of mandibular fracture patients[18]. While benefits of prophylactic antibiotic treatment are well established[19], antibiotic treatment practices vary widely among surgeons[20]. Mandibular fracture may be infected already before surgical treatment, so antibiotics are often also used as part of the treatment of purulent infection at the fracture site. Surgical treatment practices differ between infected and non-infected mandibular fractures[21]. However, there is no clear evidence on whether these infected fractures should be treated intraorally or extraorally.

Glucocorticoids (GCs), especially dexamethasone (DXM), are widely used in maxillofacial surgeries[22,23]. GCs have been shown to prevent oedema[24–30], pain[24,27,28] and trismus[25] after orthognathic and third-molar surgeries. However, perioperative use of systemic DXM in mandibular fracture surgeries and its effect on oedema, pain relief, and trismus reduction have previously been unclear.

The aim of this study was to evaluate medications, including antibiotics and DXM, as well as perioperative surgical technical aspects to prevent postoperative complications in patients with fractures of the dentate part of the mandible.

2. REVIEW OF THE LITERATURE

2.1. Mandibular fractures

2.1.1. Mandible

The mandible 'lower jaw' is a U-shaped bone that articulates with temporal bones via the temporomandibular joint allowing biting and chewing motions. It consists of a horizontal (body) and two vertical (ramus) parts that meet posteriorly at the angle of the mandible (Figure 1). Muscles of mastication comprise the masseter, as well as temporal, medial, and lateral pterygoid muscles, and they have attachment points in the mandible. These muscles are innervated by the mandibular nerve that is the third division of the trigeminal nerve (fifth cranial nerve, CN V). Additionally, suprahyoid muscles (digastric, stylohyoid, mylohyoid, and geniohyoid muscles) and infrahyoid muscles (sternohyoid, sternothyroid, thyrohyoid, and omohyoid muscles) can depress the mandible, although gravity is mainly responsible for this movement[31,32].

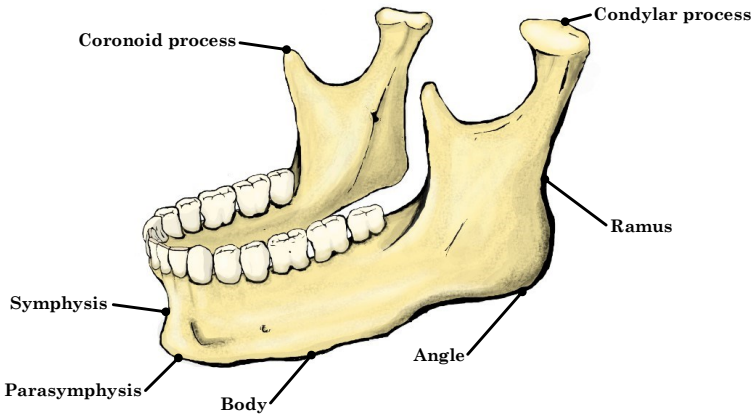


Figure 1 Anatomy of the mandible. Designed by Marko Oksa and illustrated by Osmo Lintervo.

2.1.2. Mandibular fracture aetiology and epidemiology

Condyle, angle, body, and symphysis/parasymphysis are the most common locations of the mandibular fracture[33,34]. In the dentate part of the mandible, the most common fracture location is angle[12,13,35], and mandibular third molar has been found to increase the risk of angle fracture over three-fold[36]. The injury often causes two (or more) fractures (29.7%–64.0%)[4,34,37], typically bilaterally of the mandible[37].

Mandibular fractures occur considerably more often in men compared to women[38,39]; a previous American study showed that men have a four-fold higher incidence of mandibular fractures compared with women. However, this trend is reversed in older patients, and women at least 85 years-of-age had a higher incidence of mandibular fracture than men[40]. The highest incidence of mandibular fracture has been observed for both men and women in their third decade[34,40].

The most frequent mechanisms of injury are shown in Table 1. Assault is clearly the most dominant cause of mandibular fracture in men, while falls are a slightly more common injury mechanism in women[34]. Additionally, falls are the primary mechanism of injury in the ageing population[40]. Clear differences in the aetiology of the mandibular fractures have been observed in different countries[41]. These are due, for example to differences in the traffic and alcohol culture and sports. The mechanism of injury may also affect the location of the mandibular fracture – an assault is typically found to result fractures in the angle region[42,43].

Table 1 Most frequent mechanism of injury in mandibular fracture patients.

Injury mechanism	%
Assault	11.6–71.6 [34,40–42,44]
Motor vehicle accident	4.2–55.4 [34,40–42,44]
Falls	12.8–21.9 [34,40–42]
Sports	3.9–16.4 [34,41,42,44]
Bicycle	2.0–3.6 [34,40]

Alcohol is a major etiological factor in mandibular fractures[45–47] and it has shown to increase the severity of the fracture[48]. Alcohol is involved often in assault-related fractures. Substance abuse is also common in this patient population[46,49].

Concomitant maxillofacial fractures are observed in 5.2–27.7% patients with mandibular fracture[42,46,50]. Associated injuries such as limb, brain, and chest injuries, are also common among patients with facial bone fractures[15–17].

2.1.3. Signs and symptoms in mandibular fracture patients

Mandibular fracture causes several different symptoms that depend on the location and type of the fracture (Table 2).

Table 2 Typical signs and symptoms in mandibular fracture patients[50–53].

Signs and symptoms in mandibular fracture patients	
Dental malocclusion	Gingival tear
Diminished sensation to the lower lip	Oedema
Displacement or step in the teeth	Pain
Ecchymosis	Trismus
Facial asymmetry	

The injury causes damage in the tissues triggering a complex cascade causing some of the symptoms mentioned above. Damaged tissues release several substances, including, for example, bradykinin, serotonin, prostaglandins, and substance P, triggering inflammation reaction and causing hyperalgesia, oedema, and redness. Additionally, mast cells release histamine. These substances activate nociceptors that are free nerve endings transducing painful stimuli through fast Aδ-fibers and slow C-fibers finally to the central nervous system (CNS) where it is sensed as pain[54].

Submucosally and subcutaneously extravasated blood might cause a bruise in the tissues which is known as ecchymosis. It is more common in older patients due to weaker cellular attachment and decreased tissue tone[55].

Trismus is a condition where mouth opening is restricted. After trauma, it can be caused by, for example, haematoma, muscle spasm, inflammation of the muscles of mastication, or the fractured structure itself[56].

Changes in the sensation of the lower lip are caused by inferior alveolar nerve (IAN) injury[57].

2.1.4. Diagnostic imaging in mandibular fracture patients

Different imaging modalities are used to support fracture diagnostics, including dental panoramic radiograph (DPR), computer tomography (CT), cone-beam computed tomography (CBCT), and anteroposterior, lateral, and oblique x-rays of the mandible[58–61]. Different projections are used to identify all fracture lines and the level of displacement[58]. However, CT is the initial imaging modality of choice today having an increased sensitivity in detecting mandibular fractures. It also enables a reconstructed 3D view of the bony structures[58]. When comparing CT and

DPR in mandibular fracture patients, CT is found to be sufficient in identifying mandibular fractures and dental injuries[62]. However, DPR has a significantly lower radiation dose compared to CT[63] and it represents entire dentition and bony structures of the mandible[64], which is also beneficial for further treatment of the dentition.

2.2. Treatment of mandibular fractures

The appropriate treatment for mandibular fracture patients depends on the type, location, and comminution of the fracture, dentition, patient's age and patient compliance. The management of these fractures includes closed treatment and/or open reduction and internal fixation (ORIF)[33,65]. However, some mandibular fractures do not require surgical treatment. Non-surgical treatment is indicated in non-displaced, favourable fractures if the occlusion is maintained[33]. Soft diet and careful follow-up are required.

Muscles of mastication might have a displacing effect in the fracture line of the mandible. Favourable fractures are those that are nondisplaced by muscular pull. (Figure 2). In unfavourable fracture, muscle forces lead to displacement of the bony fragment. These forces should be considered when planning the treatment method[33].

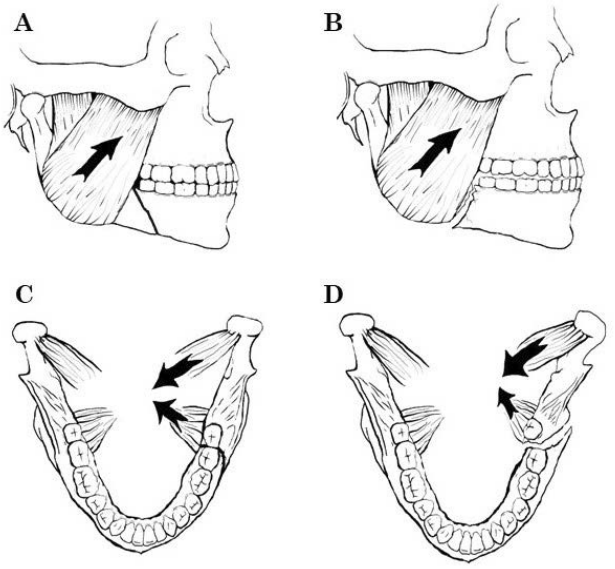


Figure 2 Muscle forces and their impact on fracture lines can lead to favourable (A&C) or unfavourable (B&D) fractures. Designed by Marko Oksa and illustrated by Osmo Lintervo.

2.2.1. Closed reduction

Closed treatment is defined as a treatment of the fracture without visualization of fractured bone through skin or mucous membrane. It can usually be used in nondisplaced and favourable mandibular fractures, grossly comminuted fractures, and in fractures in children with developing dentition. Additionally, closed treatment is used in most of the condylar and coronoid process fractures. Sometimes reduction of the fracture is implemented. Closed treatment covering mandibulomaxillary fixation (MMF) is accomplished using, for example, arch bars (e.g., Erich arch bar), wires and intermaxillary fixation screws combined with wires. Additionally, splints are sometimes used in children with mixed dentition[33,65].

2.2.2. Open reduction and internal fixation

Surgical treatment of mandibular fractures comprises ORIF. It is indicated especially for patients with displaced unfavourable mandibular fracture, multiple fractures, or contraindication to MMF even if it was the primary treatment option. Reduction can be obtained, for example, by approximating fracture fragments with bone pliers. After reduction of the fracture, fixation can be achieved using plates and/or lag screws[33,65]. Titanium plating is the standard method in mandibular fracture treatment. However, resorbable materials are also used[66].

Internal fixation is conducted using rigid or nonrigid methods. Fixation is considered rigid when the bone fixation used prevents interfragmentary movement between segments during active loading of the bone[67] using, for example, a reconstruction plate, two miniplates, or lag screws. Nonrigid fixation allows movements between the bone fragments[68,69]. One of the most important nonrigid fixation techniques today is the treatment of angle fractures using Champy method, where a single miniplate is placed on the superior border of angle[70]. Plates are placed along the ideal lines of osteosynthesis which depend on the forces on the mandible (Figure 3). In the symphysis and parasymphysis regions, torsional forces also exist. Thus, two parallel plates are used in the fractures located between the two canines[70,71]. In patients with multiple mandibular fractures, only one of the fractures can be treated with nonrigid methods. In other fractures, rigid fixation should be used[69].

Fixation can also be classified as load-bearing or load-sharing. Load-bearing osteosynthesis is a form of rigid fixation. It takes place when reconstruction plates with bicortical screws are used to bear all mandibular functional load especially in severe complex and comminuted fractures, in chronically infected fractures, and in patients with an atrophic mandible[69,72]. Load-sharing osteosynthesis is when

smaller plates with screws or lag screws are used to share functional loads with bone in fractures that have a healthy bone contact[69,72–74].

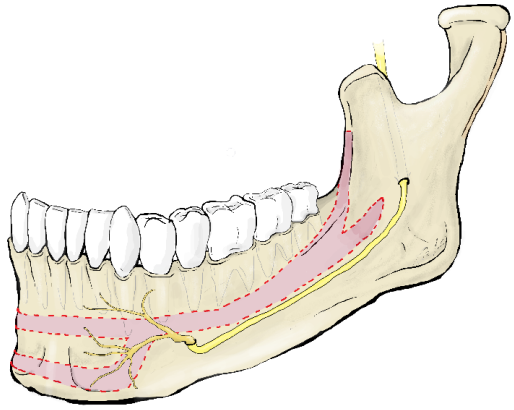


Figure 3 Ideal lines of osteosynthesis according to Champy et al. (Champy M, Lodde JP. Mandibular synthesis. Placement of the synthesis as a function of mandibular stress. *Rev Stomatol Chir Maxillofac*. 1976;77(8):971-976) Designed by Marko Oksa and illustrated by Osmo Lintervo.

Lag screws can be used in noncomminuted vertically oriented fractures and short oblique fractures, especially in the anterior mandible. Typically, two lag screws are crisscrossed across the fracture line[33,75]. MMF is sometimes used after ORIF-treatment, for example in cases where a concomitant condylar fracture exists or if the stability of the internal fixation is suspicious[33].

During mandibular fracture surgery, the need for tooth removal should be assessed carefully. Indications for tooth removal in the fracture line during surgery may be teeth that have fractured roots, teeth that interfere with reduction of the fracture, teeth with a periapical lesion or extensive periodontal damage, and teeth with pericoronitis. In children, tooth buds in the fracture line should be left to the fracture site. Careful clinical and radiological follow up for at least one year is recommended for all teeth in the fracture line[76].

An intraoral or an extraoral approach can be used in mandibular fracture surgery. Noncomminuted angle, body, and symphysis/parasymphysis fractures are usually treated intraorally. An extraoral approach is used, for example, in condylar and atrophic mandibular fractures[72]. A recent systematic review and meta-analysis showed no significant difference in infection rates between intraoral and extraoral approaches[77]. Surgical incision can be conducted using a scalpel or electrosurgery[78].

Mandibular fracture surgery is recommended soon after the injury. However, no higher complication rates are found in mandibular fracture surgeries if there has been a short delay between the injury and surgery[11,79–81].

Surgical treatment of infected mandibular fractures

Treatment of infected mandibular fractures differs from non-infected fractures. Injury during intoxication, a delay in seeking treatment due to a low level of patient compliance, and lack of understanding of the consequences of the mandibular fracture are the main factors which contribute to infection in patients without preceding mandibular fracture surgery[35]. Infected mandibular fractures are usually stabilized with rigid internal fixation combined with abscess incision and drainage, debridement, and reduction of the fracture[82]. Additionally, immediate bone grafting seems effective even in presence of infection in the fracture site[83].

2.3. Mechanisms of mandibular fracture healing

2.3.1. Wound healing

Wound healing begins immediately after the injury with haemostasis including vascular constriction, platelet aggregation, and fibrin clot formation. After haemostasis, wound healing has three overlapping phases: inflammation, proliferation, and remodelling. The inflammatory phase (days 1–4) involves clinically noted signs including heat, pain, redness, and swelling. Neutrophils and monocytes are recruited to the wound site by cytokines to ingest microorganisms and tissue debris by phagocytosis. Monocytes differentiate to macrophages and release growth factors stimulating and directing wound healing to the proliferation phase (up to three weeks). The proliferative phase involves formation of extracellular matrix, angiogenesis, collagen synthesis, and re-epithelialization. Fibroblasts produce collagen, glycosaminoglycans, and proteoglycans forming extracellular matrix. Keratinocytes provide re-epithelialization to form a protective outside barrier to the wound. Finally, the remodelling phase begins, including collagen remodelling and vascular maturation and regression, and this phase can last for years[84,85].

Multiple factors can disturb wound healing such as infection, foreign bodies, smoking, ischemia and several medications and diseases[85–87].

2.3.2. Bone healing

Bone healing includes similar phases as wound healing. Fracture healing can be direct (primary) or indirect (secondary). Indirect healing is the most common type of healing and occurs especially in non-operative fracture treatment. After the injury, a haematoma is formed that further forms a template for callus formation. The inflammatory response involves secretion of several cytokines that promote angiogenesis and the production of the collagen-rich primary cartilaginous callus.

Specific mesenchymal stem cells are also recruited to differentiate into osteogenic cells. The primary soft cartilaginous callus is then resorbed and replaced with hard bony callus as extracellular matrix becomes calcified. Finally, the remodelling process begins 3–4 weeks after the injury. Hard callus is resorbed by osteoclasts and new bone is formed by osteoblasts.

Direct (primary) healing occurs if fracture ends are closely reapproximated and stabilized rigidly. Osteoclasts produce cutting cones filled with bone produced by osteoblasts[88,89]. Thus, there are differences in bone healing in mandibular fractures treated with load-sharing and load-bearing methods depending on the rigidity of the fixation and gap between the segments[65]. Additionally, some special features regarding bone formation in the mandible are observed. For example, high masticatory muscle activity increases the amount and density of the cortical and trabecular bone[90]. Disturbance in bone healing in the fracture site can lead to a non-union[91].

2.4. Postoperative complications in mandibular fracture surgery

2.4.1. Surgical site infection

Infectious complications are the most common complication types after mandibular fracture surgery[5,6]. A postoperative SSI-rate of 7.5–17.9% has been reported for mandibular fracture surgery[10–14]. Clinical signs of SSI are purulent discharge, granulation tissue with fistula, erythema, pain, and swelling[4,92]. Several patient-related factors can contribute to SSI, such as smoking, alcohol and drug abuse, infected tooth in the fracture site, and patients immunocompromised status[4,5,93]. Furthermore, alcohol and drug abusers with tooth decay[94] as well as patients with severe periodontal disease[95] have shown higher SSI rates after mandibular fracture surgery. Angular location and comminuted fractures have shown higher SSI-rates[35]. Adequate use of prophylactic antibiotics is necessary to reduce the incidence of SSIs[18,96], but the optimal duration of the antibiotic treatment remains unclear.

2.4.2. Wound dehiscence and scarring

SWD is described as a mechanical failure of the surgical wound postoperatively (Figure 4). Clinically, it is observed as hardware and/or bone exposure and the presence of granulation tissue. SWD has been detected in 3.0–13.4%[4,6,97] of mandibular fracture patients and it is often associated with local infection[4] and especially miniplate fixation techniques[6]. SWD can lead to hardware failure and

SSI. Properly positioned hardware and adequate closure of the wound should be considered to avoid SWD[4].

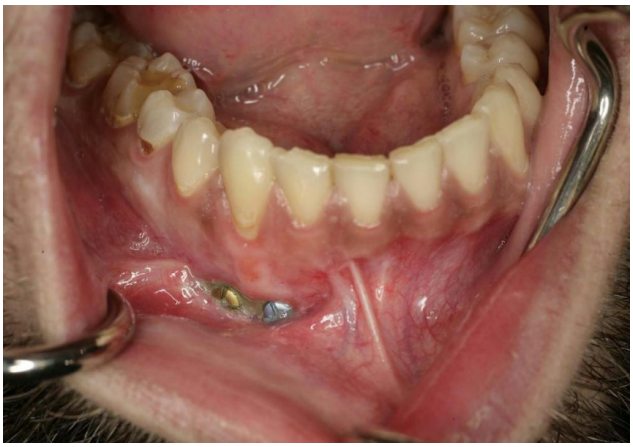


Figure 4 Surgical wound dehiscence after surgery for mandibular parasymphysis fracture.

Additionally, hypertrophic, or wide scarring may occur in the wound area when an extraoral approach is used[98,99]. Meticulous planning of the incision, atraumatic tissue handling, prevention of infection, and careful placement of the dermal sutures are essential in preventing scarring[100].

2.4.3. Neurosensory disturbance

Neurosensory disturbance caused by IAN injury is common in mandibular fracture patients, both before and after fracture treatment. It is observed in 33.7–42.3% of mandibular fracture patients and even after treatment in 53.8% of the patients[57,101]. However, Bede et al reported that 90.9% of patients experienced an IAN recovery [101]. IAN-injury is more common in angle and body regions, and especially in comminuted and displaced fractures. Fracture repositioning, drilling, and screwing can cause compression, stretching and/or transection of the IAN. Thus, mandibular canal location should be considered when screw placement is planned[57,101]. Caution should be exercised when incision is performed due to the location of the mental nerve. In submandibular approach, risk for injury in the mandibular branch of the facial nerve (CN VII) should also be considered[102,103].

2.4.4. Hardware failure

Hardware failure has been found in 7.4–15.4%[4,9] of mandibular fracture patients. Early excessive mastication, poor oral hygiene, and bruxism predispose to hardware failure. Hardware failure can be detected clinically as a loose plate or screw, dislodged screw, and broken or exposed plate. Malunion and non-union can also be observed. Hardware failure is often associated with infection which can cause loosening of the osteosynthesis material[9]. On the other hand, hardware failure can lead to infection at the fracture site. Inadequate fixation technique during surgery predisposes to hardware failure, which can lead to the need for hardware removal[4].

2.4.5. Non-union

Clinical signs of non-union are mobility of fractured segments and/or increased radiolucency at the fracture site. It is observed postoperatively in 2.8–5.8% of the mandibular fracture patients. Patient noncompliance, preoperative infection, and improper reduction and fixation can contribute to non-union, and it can lead to reoperation[4,6,104]. Non-union can be treated surgically with debridement of bony edges, rigid fixation and using bone grafting depending on bony defect size and infection status[105].

2.4.6. Malocclusion and temporomandibular dysfunction

Malocclusion has been detected postoperatively in 2.9–8.0%[4,6] of the mandibular fracture patients. It is observed as an improper bite by a clinician and/or patient and it might lead to reoperation[4]. The use of reconstruction plates in comminuted mandibular fractures may predispose to malocclusion. Malocclusion can be in most cases treated with occlusal equilibration or elastics. However, orthognathic surgery is sometimes indicated[106].

Temporomandibular dysfunction includes symptoms like sounds, fatigue, luxation, and locking of the jaw. Additionally, difficulty in mouth opening and pain can be presented. In a study by Rajantie et al.[107] including mandibular fractures not involving the condyle, 12.9% of the patients had severe symptoms of temporomandibular dysfunction postoperatively. Temporomandibular dysfunction is common already after the injury especially in patients with a condylar fracture and a contralateral body or angle fracture[108].

2.5. Medications in mandibular fracture surgery

2.5.1. Antibiotics

Antibiotics are used as prophylactic therapy as well as treatment of preoperative and postoperative infections in mandibular fracture surgeries. Prophylactic antibiotics are used preoperatively, perioperatively, and postoperatively to reduce the incidence of SSIs[18,96]. Antibiotic prophylaxis protocols differ between oral and maxillofacial surgeries. In maxillofacial trauma surgeries, the use of antibiotic prophylaxis depends on the type of the fracture (open or closed), the location of the fracture mandibular fractures being more likely to become infected, and planned treatment (open or closed reduction)[96].

Preoperative single dose antibiotic prophylaxis is recommended for patients having an orthognathic surgery[96,109]. However, in mandibular fracture patients, the tissue injury and microbial contamination have occurred already during the injury while in orthognathic surgery they occur during operative treatment.

In mandibular fracture surgeries, a three-fold decrease in the infection rate is found in antibiotic-treated groups compared with control groups[19]. However, there are major differences in antibiotic treatment practices between surgeons especially in duration of postoperative antibiotic regimen[20]. Pre- and perioperative use of antibiotics is beneficial[110]; however, previous studies have found that antibiotic treatment can be restricted to a maximum of 24 hours postoperative without higher risk of SSI[19,20]. The most used antibiotics are penicillin (G or V), cephalosporin (first or second generation), aminopenicillin (ampicillin or amoxicillin) and clindamycin[18,20,93]. Antibiotic target sites are presented in Figure 5.

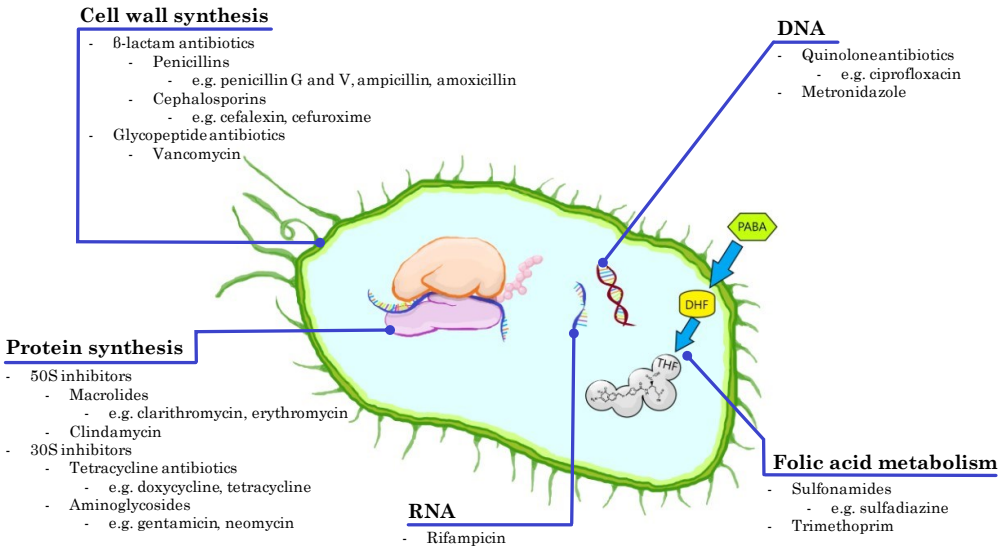


Figure 5 Antibiotic target sites in bacteria cell and example compounds. PABA, para-aminobenzoic acid; DHF, dihydrofolic acid; THF, tetrahydrofolic acid. Modified from the articles by Neu[111] and Cheesman et al.[112]. Designed by Marko Oksa and illustrated by Osmo Lintervo.

Oral microbiota

Mandibular fractures in the tooth bearing area are typically open fractures, and they can be considered contaminated with oral flora[33]. The oral cavity has a complex microbiome covering over 700 bacterial species[113,114]. Oral flora consists of a mix of aerobe and anaerobe bacteria[115]. Most common oral bacterial genera are listed in Table 3. Especially, alpha- and beta-haemolytic streptococcus are found in infected mandibular fractures[82]. Thus, antibiotic treatment should cover these most virulent bacteria. In infected mandibular fractures, antibiotic treatment is suggested and can be targeted after specimen culturing[82]. Additionally, fungal infections of the oral cavity such as candidiasis are observed and associated especially patients with immunosuppression. *Candida albicans* is the most common organism causing candidiasis[116–118].

Disadvantages

Antibiotic-related adverse events such as dysbiosis in the gut microbiota[119,120] should be considered at the patient level and antimicrobial resistance at the population level when antibiotics are used[96]. Antibiotics are also the most common cause of immune-mediated adverse events ranging from cutaneous reactions to anaphylaxis[121–125].

Table 3 Principal bacterial genera found in the oral cavity[115,126].

Table combined from original works by *Marsh PD. Role of the Oral Microflora in Health. Microbial Ecol Health Dis. 2000;12(3):130–137* and *Dewhirst FE, Chen T, Izard J, et al. The Human Oral Microbiome. J Bacteriol. 2010;192(19):5002–5017.*

Gram-positive bacteria		Gram-negative bacteria	
Cocci	**Rods**	**Cocci**	**Rods**
Abiotrophia *Peptostreptococcus* *Streptococcus*	*Actinomyces* *Bifidobacterium* *Corynebacterium* *Lactobacillus* *Propionibacterium* *Rothia*	*Moraxella* *Neisseria* *Veillonella*	*Campylobacter* *Capnocytophaga* *Desulfovibrio* *Eikenella* *Fusobacterium* *Haemophilus* *Leptotrichia* *Prevotella* *Selenomonas* *Simonsiella* *Treponema*

Chlorhexidine

Antiseptic chlorhexidine (CHX) mouthwash can be used to decrease plaque levels[127] to improve patient's oral hygiene postoperatively allowing adequate wound healing. CHX is a positively charged molecule that causes damage to the bacterial cell wall, causing an outflow of cytoplasmic components (bacteriostatic effect). Additionally, it causes bactericidal cytoplasmic precipitation and coagulation with, for example, nucleic acids and adenosine triphosphate[128]. CHX also has antifungal[129] and virucidal[130] effects. Tooth staining and taste alteration are the most common adverse effects of CHX[131]. Novel crystallized CHX-CaCl2 particles on maxillofacial appliances have shown an effective and sustained drug release compared to CHX mouthwash[132].

2.5.2. Analgesics

Postoperative pain is commonly relieved with administration of nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, paracetamol (acetaminophen), GCs, and their combinations[133,134].

Nonsteroidal anti-inflammatory drugs

Most used NSAIDs are ibuprofen, diclofenac, naproxen, aspirin, and ketorolac. NSAIDs decrease pain as well as fever and inflammation by inhibiting cyclooxygenase (COX) enzymes COX-1 and COX-2, which are involved to convert

arachidonic acid into prostaglandins, thromboxanes, and leukotrienes[135–137]. COX-1 participates, for example in cytoprotection of gastric mucosa and platelet thrombogenesis, while COX-2 contributes to inflammation and normal function of the vascular endothelium. Thus, COX-2 selective NSAIDs, such as celecoxib and etoricoxib, are anti-inflammatory and analgesic drugs lacking gastrointestinal adverse effects[138]. However, COX-2 selective NSAIDs are associated with an increased risk for cardiovascular events because they could cause an imbalance in the thromboxane and prostacyclin ratio favouring thromboxane leading to vasoconstriction and thrombi formation[138–140]. To reduce gastrointestinal adverse effects such as peptic ulcer, NSAIDs can be used with proton pump inhibitors (e.g., omeprazole, lansoprazole), H2-receptor antagonists (e.g., ranitidine), and prostaglandin analogues (e.g., misoprostol), which work as gastroprotective agents[141]. Additionally, renal circulation and function are independent of the prostaglandin system. Thus, NSAIDs can impair kidney function[136].

Paracetamol

Paracetamol (acetaminophen) is an analgesic and antipyretic drug, the mechanism of which is partly unclear. However, it acts through COX inhibition in the brain and with its metabolite N-arachidinoyl-phenolamine that enhances the activity of the endocannabinoid system[142,143]. Paracetamol is mostly a safe analgesic, but hepatotoxicity can occur with excessive dosing and even at therapeutic doses if the patient has history of chronic alcohol use[142,144].

Opioids

Opioids are effective analgesics that are used to relieve moderate to severe pain[145]. They act through opioid receptors that are found in the peripheral nervous system, spinal cord, and brain. Opioids acting on μ-opioid receptor are the most effective as well as the most used analgesics. Opioid receptor activation by endogenous agonist, such as endorphin or exogenous agonist, inhibits neurons opening potassium channels and preventing the opening of calcium channels finally inhibiting pain transmission in pain modulating pathways. Additionally, they activate dopamine reward pathways causing euphoria. Opioids cause several adverse effects such as nausea, vomiting, sedation, hypotension, constipation, urinary retention, itching, and sweating[146]. Additionally, they can cause respiratory depression that can be fatal[147]. Prolonged opioid use should be restricted as it causes tolerance reducing the analgesic effect and leading to the need for higher dosing. Several causes for opioid tolerance have been identified but changes in opioid receptors causing decreasing receptor activation (desensitization) is the best-known mechanism[148]. Codeine and tramadol are commonly used weak opioids, whilst fentanyl, morphine, oxycodone, and methadone are common strong opioids. Opioids can be combined with NSAIDs and/or paracetamol[149].

Polymorphism in cytochrome P450 2D6 (CYP2D6) metabolism should be considered when opioids are prescribed. Weak opioids are metabolized through CYP2D6 to their active metabolites: codeine to morphine and tramadol to O-desmethyltramadol. Enzymatic activity of the CYP2D6 ranges from nonfunctional (poor metabolizer) to increased function (ultrarapid metabolizer). Thus, concentration of the active metabolites is low in poor metabolizers and high in ultrarapid metabolizers[150] and these high concentrations might cause intoxication or even death[151,152].

Local anaesthetics

Postoperative pain can also be suppressed with preventive analgesia by local anaesthetics. The use of local anaesthetics has shown to reduce postoperative pain scores and analgesic consumption in orthognathic surgeries[153] as well as in orthopaedic surgeries[154]. They interrupt neural conduction by blocking voltage-gated Na^+ channels inhibiting action potential in nociceptive fibres. Lidocaine and ropivacaine with a longer half-life are examples of local anesthetics[155,156].

Glucocorticoids

GCs might have analgesic effects. Decrease in COX-2 levels and prostaglandin E2 (PGE2) production are found after GC administration[157,158].

2.5.3. Glucocorticoids

GCs are steroid hormones that have numerous effects on metabolism and the immune system, and behavioural effects on the CNS. Cortisol is the principal GC in humans, and it is synthesized in the adrenal cortex. Its effects are mediated by a glucocorticoid receptor that either diminishes or enhances gene expression. GCs increase glucose production via gluconeogenesis, inhibit the uptake of glucose to tissues, and promote lipolysis. GCs suppress the immune response diminishing lymphocyte count, cause lysis of lymphocytes, and suppress the inflammatory response by decreasing leukocyte, leukotriene, and prostaglandin levels. Additionally, GCs impair the ability of osteoblasts to produce new bone and have behavioural effects on the CNS. The hypothalamic-pituitary-adrenocortical axis is responsible for regulating cortisol concentration. The hypothalamus secretes corticotropin releasing hormone (CRH) that stimulates the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary. ACTH stimulates the production and secretion of cortisol, which in turn regulates the release of ACTH and CRH with negative feedback. Numerous synthetic GCs, such as prednisone, methylprednisolone and DXM are developed having longer half-life and better selectivity in GC actions[54,159]. DXM has the longest biological half-life (36–72 hours)[160].

Glucocorticoids in oral and maxillofacial surgery

The use of GCs is common among oral and maxillofacial surgeons, especially in orthognathic surgery and facial fracture surgeries[22,23]. GCs reduce postoperative oedema and pain after oral and orthognathic surgeries[24]. Benefits in neurosensory recovery are not visible after GC administration in facial fracture surgeries[161,162] and orthognathic surgeries[163]. DXM prevents postoperative nausea and vomiting in surgical patients in general[164], but does not significantly reduce them in facial fracture patients[165]. GCs can be administered in oral and maxillofacial surgeries in oral, intravenous, intramuscular[135] and submucosal[28] routes. In a study by Antunes et al.[166], the difference in local injection and systemic use of DXM was studied in third molar surgery showing similar efficacy in both routes.

Disadvantages

GCs are linked to several adverse effects especially when high doses are used and/or when the treatment is long-term. Significant metabolic adverse effects include dyslipidaemia, weight gain, and diabetes mellitus. In the cardiovascular system, hypertension and cardiovascular events are detected[167]. In the upper gastrointestinal tract, the risk of bleeding or perforation increases with GC use[168]. Additionally, an increased risk of adrenal suppression, steroid-induced psychosis, and avascular osteonecrosis are observed in oral and orthognathic surgeries after GC administration[24]. Leukocytosis[169] and decrease in blood C-reactive protein (CRP) levels[170] in facial fracture patients, as well as a higher risk for disturbance in surgical wound healing in zygomatic complex fracture patients[171] are observed in patients who have received perioperative DXM. In facial-fracture patients, disturbance in surgical wound healing after GC administration is linked especially to an intraoral approach[172]. Changes in leukocyte and CRP levels may challenge clinical decision making as GCs affect these results regardless of the clinical infection status and on the other hand, they predispose to infections. In head and neck cancer patients with microvascular reconstruction, DXM has been shown to predispose to infections[173] and cause higher short-term mortality[174] without providing a benefit.

3. AIMS OF THE STUDY

The aim of this study was to evaluate perioperative technical aspects and medications in mandibular fracture surgery to prevent complications and disadvantages postoperatively. Additionally, patient-related factors predisposing to complications were investigated.

Specific aims were as follows:

1. To clarify the occurrence and predisposing factors for post-operative SSI and SWD in intraorally treated mandibular fractures (Studies I and III).

2. To assess the benefit of antibiotic treatment considering the occurrence of SSI in patients with intraorally treated mandibular fracture(s) (Study I).

3. To clarify occurrence and predisposing factors of postoperative surgical site complications and to evaluate antibiotic treatment in infected mandibular fractures without preceding surgery (Study II).

4. To determine the analgesic effect of the perioperative use of systemic DXM and its impact on trismus and oedema in mandibular fracture surgery (Study IV).

4. PATIENTS

All mandibular fracture patients in studies I–IV were treated surgically at the Department of Oral and Maxillofacial Diseases, Helsinki University Hospital, Helsinki, Finland.

4.1. Study populations

This study comprises three retrospective studies (I, II, and III) and one prospective study (IV). Patient records in retrospective studies were collected from the hospital's electronic medical database.

Study I included patients aged at least 18 years who had undergone intraoral surgery for a single fracture of the dentate part of the mandible between January 2018 and October 2020. Patients with angle fractures and those with infection (i.e. pus in the fracture site) at the time of the primary surgery were excluded, as were those lacking an available DPR, who developed endodontic infection of a tooth in the fracture line, and who needed a reoperation due to a suboptimal reduction. A follow-up at least four weeks was required for patients to be included in the analysis.

Patients included to Study II suffered an infected fracture of the mandible without preceding fracture surgery between 2012 and 2022. To be infected, one or more of the following signs were required in the fracture site preoperatively: abscess, pus formation, and/or draining fistula (intraoral or extraoral).

Patients included to Study III suffered one or two fracture(s) of the dentate part of the mandible that was treated surgically via an intraoral approach between January 2017 and December 2021. Patients with infection at the time of primary surgery, patients who had infection-associated SWD, and those with no available DPR were excluded. A follow-up of at least three weeks was required for patients to be included in the analysis.

Study IV comprised patients with one or two non-comminuted fractures of the dentate part of the mandible treated surgically via intraoral approach. Patients were recruited to participate between June 2006 and June 2010. Patients in the study population were at least 18 years old. Patients who were pregnant or breastfeeding, as well as those with a history of peptic ulcer, psychosis due to GC use, kidney or liver dysfunction, or allergy to any constituent of the DXM preparation were excluded. Similarly, patients who conflicted with the study protocol, offered inadequate data, or experienced postoperative infection were excluded. A follow-up of at least seven days was required for patients to be included in the analysis.

4.2. Surgical technique and approaches

All mandibular fractures were treated surgically under general anaesthesia with ORIF.

In studies I and III, an intraoral approach was used with non-reconstruction plate and/or lag screw fixation.

In Study II, intraoral or extraoral approach was used. Reconstruction and non-reconstruction plates with or without lag screw(s) were used, and drainage and debridement of the infected fracture site was combined to the surgery.

In Study IV, patients underwent surgery for intraoral miniplate fixation.

Miniplate fixation was mainly performed according to the technique introduced by Champy and Lodde[175].

4.3. Perioperative dexamethasone protocol and randomization (Study IV)

Patients in Study IV were randomized into the DXM+ and DXM- groups with closed envelopes. The envelopes were mixed and picked from a vertical stack randomly by researchers or hospital staff. Thus, the randomization was confirmed twice.

Patients in the study group were given 10 mg of intravenous DXM (Oradexon®, 5 mg/ml injection solution, Orion Pharma, Espoo, Finland) during anaesthesia induction and 10 mg of DXM intramuscularly to deltoid or gluteal muscle every 8 hours for 16 hours with a total DXM dose of 30 mg. Patients in the control group received neither steroids nor placebo. Fentanyl was used as analgesic during anaesthesia. Paracetamol was postoperatively used as analgesic. Additionally, opioids (fentanyl, oxycodone or tramadol) were administered if the analgesic effect of paracetamol was insufficient. NSAIDs were not used as analgesics since they reduce swelling.

4.4. Clinical evaluation

4.4.1. Evaluation of surgical site infection or recurrent infection (Studies I and II)

In Study I, SSI was defined as antibiotic-requiring postoperative infection with clinically confirmed pus formation in the fracture site. Additionally, one or more of the following infection signs had to also appear: pain, cellulitis, or swelling after the initial stage of healing. The presence of granulation tissue with fistula in the fracture site was not considered SSI as being managed without antibiotics.

In Study II, recurrent infection was one of the postoperative surgical site complications. Here, recurrent infection is defined similarly as SSI in Study I.

4.4.2. Evaluation of surgical wound dehiscence (Studies II and III)

In studies II and III, SWD was defined as clinically observed partial or complete opening of the wound. Additionally, hardware and/or bone exposure was required for SWD diagnosis.

4.4.3. Evaluation of postoperative pain, oedema, and mouth opening (Study IV)

Postoperative pain, oedema, and trismus were evaluated as follows in Study IV:

Pain evaluation
Pain was evaluated preoperatively and 6, 12, 18, and 24 hours postoperatively using a visual analogue scale (VAS). VAS is a scale between "no pain" (VAS=0) and "worst pain" (VAS=10). The number of adjunct postoperative opioid medication was also collected.

Swelling evaluation
Facial swelling (oedema) was evaluated measuring the distance in centimetres from the tragus of the ear to the symphysis of the mandible on both sides of the face by an investigator who was blinded for DXM use. A permanent marker pen was used to indicate the measurement points on the skin. Two successive measurements with the same results were required. Measurement was conducted preoperatively and at 24 hours, 48 hours, 7 days, and 1 month postoperatively, and the swelling was assessed as percentage change comparing postoperative results with the results preoperatively.

Mouth opening evaluation (trismus)
Limits of mouth opening were evaluated as the difference in maximal mouth opening by measuring interincisal distance in millimetres preoperatively and at 24 hours, 48 hours, 7 days, and 1 month postoperatively.

5. METHODS

5.1. Outcome variables

The primary outcome variables were postoperative SSI (Study I), postoperative surgical site complication covering SWD or recurrent infection (Study II) and postoperative SWD (Study III). In Study IV, the primary outcome variables were postoperative visual analogue scale (VAS) score, the number of times that a patient needed postoperative opioid medication, maximal mouth opening in millimetres and relative difference in postoperative facial swelling.

5.2. Predictor variables

The primary predictor variable in Study I was duration of postoperative antibiotic treatment. Additional predictor variables were use of postoperative CHX mouth rinse, use of preoperative antibiotics, use of antibiotics in anaesthesia induction, use of postoperative antibiotics, and total postoperative duration and total duration of antibiotic medication. Patient-, fracture-, and surgery related variables in studies I–III are presented below.

In Study IV, the primary predictor variable was the perioperative use of DXM. Explanatory variables were treatment delay from accident to surgery, duration of the surgery and age of the patient.

Patient-related variables

Patient-related variables in Studies I–III were age, sex, substance abuse including evident heavy alcohol use and/or abuse of other drugs and smoking. Alcohol use was classified as heavy if the weekly doses of alcohol were ≥23 for men and ≥12 for women according to Finnish Current Care Guidelines[176]. One dose contains 12 grams of pure alcohol. Additionally, information of immunosuppressive condition (Studies I and III) and records of postoperative CHX mouthwash use (Study III) were collected. Immunosuppressive condition comprised immunosuppressive disorder(s) and/or immunosuppressive drug therapy. Furthermore, treatment delay from injury to surgery in days and factors contributing to delayed surgery were evaluated in Study II.

The level of patients' oral hygiene described as modified total dental index (TDI) [177,178] was collected in Study I as a patient related variable. Scores for TDI including caries, periodontitis, apical periodontitis, and furcation lesions were collected from

the DPRs. TDI is a value between 0 and 10; higher values indicate higher infection loads in the oral cavity (Table 4).

Table 4 Modified Total Dental Index[177,178].

Modified Total Dental Index defined by *Mattila K, Nieminen M, Valtonen V, et al.: Association between dental health and acute myocardial infarction. BMJ. 1989; 298(6676):779–781* and *Virtanen E, Nurmi T, Söder P-Ö, et al. Apical periodontitis associates with cardiovascular diseases: a cross-sectional study from Sweden. BMC Oral Health. 2017;17(1):1*.

Type of disease	Score
Caries	
No caries	0
1–3 carious lesions	1
4–7 carious lesions	2
≥ 8 carious lesions or infected roots or no teeth	3
Periodontitis	
None	0
1–3 deep vertical pockets	1
4–7 deep vertical pockets	2
≥ 8 deep vertical pockets	3
Apical periodontitis	
None	0
1 tooth	1
2 teeth	2
≥ 3 teeth	3
Furcation lesions	
Absent	0
Present	1

Fracture-related variables

Fracture-related variables were comminution of the fracture and fracture site (Studies I–III). Fractures were defined as non-comminuted or having minor or major comminution. Fracture was non-comminuted if no fragmentation or fragments smaller than the size of the crown of a premolar existed. Fracture was minorly comminutioned if one or more fragments larger than the size of the crown of a premolar not involving the full vertical height of the mandibular arch were observed. In fractures with major comminution, fragments involved the full height of the mandibular arch[179].

In study II, fractures were also divided into severely and mildly infected fractures. Severely infected fractures included cases with abscess, cellulitis, and/or extraoral fistula.

Surgery-related variables

Surgery-related variables in Study I were treatment delay from injury to surgery and the number of miniplates and/lag screws used. Patients with tooth extractions due to poor dental condition or due to location in fracture line were also analysed.

In Study II, surgery-related factors were surgical approach (intraoral or extraoral), fixation method, bone grafting, and use of a drain. Additionally, occurrence of postoperative surgical site complications, duration of postoperative antibiotic course and delay from surgery to postoperative surgical site complication in days were recorded.

Surgery-related predictor variables in Study III were treatment delay from injury to surgery, postoperative MMF, time of surgery (specified as night-time surgery if surgery began between 10pm and 6am), surgeons experience (resident or consultant), incision technique (scalpel or electrosurgery), fixation technique (miniplates, lag screws, or combined) and suturing technique (simple interrupted sutures, continuous sutures, or a combination of these sutures).

5.3. Statistics

Statistical analyses were performed using GraphPad Prism (version 5.00, GraphPad Inc. San Diego, CA, USA) in Study I and SPSS for Macintosh, IBM in studies II–IV (version 27 in Studies III and IV and version 28 in Study II). Differences between study groups in continuous variables were analysed with Mann-Whitney U test (Studies I-IV for non-normally distributed data) and t test (Studies II and III for normally distributed data). Categorical variables were analysed with Pearson Chi-squared test or Fisher's exact test if expected values were below 5 in studies I–III. Additionally, a binomial logistic regression model was used in Study III. P-values <0.050 were considered statistically significant.

5.4. Ethical considerations

The protocols in studies I–III were approved by the internal board of the Head and Neck Centre, Helsinki University Hospital, Helsinki, Finland (HUS/356/2017 and HUS/29/2022). Study IV was approved by the Ethics Committee of the Department of Surgery and the Internal Review Board of the Division of Musculoskeletal Surgery, Helsinki University Hospital, Helsinki, Finland (Dno33/E6/06). All patients in Study IV signed an informed written consent. All studies (I–IV) complied with the 1964 Declaration of Helsinki and amendments thereafter.

6. RESULTS

In Study I, data of 254 mandibular fracture patients was collected. Condyle and angle fracture patients (n=74) were excluded. Of these 180 patients with mandibular body, symphysis, or parasymphysis fracture, 73 were excluded due to strict inclusion criteria. Thus, 107 patients were accepted for the analysis.

In Study II, data from 908 patients with fracture in the dentate part of the mandible treated surgically during the eleven-year research period was collected. Infection in fractures without preceding surgery was observed in 41 patients, all of which were accepted for analyses.

In Study III, the data of 405 mandibular fracture patients was collected. Condyle fracture patients without dentate area fracture (n=49) were excluded. Additionally, 124 patients were excluded due to exclusion criteria. Finally, 232 patients were accepted for analysis with 270 mandibular dentate area fractures.

In Study IV, the use of DXM was studied in 49 patients. Four of these patients refused to participate. Additionally, 11 patients were excluded due to conflict with the study protocol, inadequate data, or postoperative infection. Thus, 34 patients were accepted for statistical analyses.

Patient inclusion in Studies I–IV is presented in Figure 6.

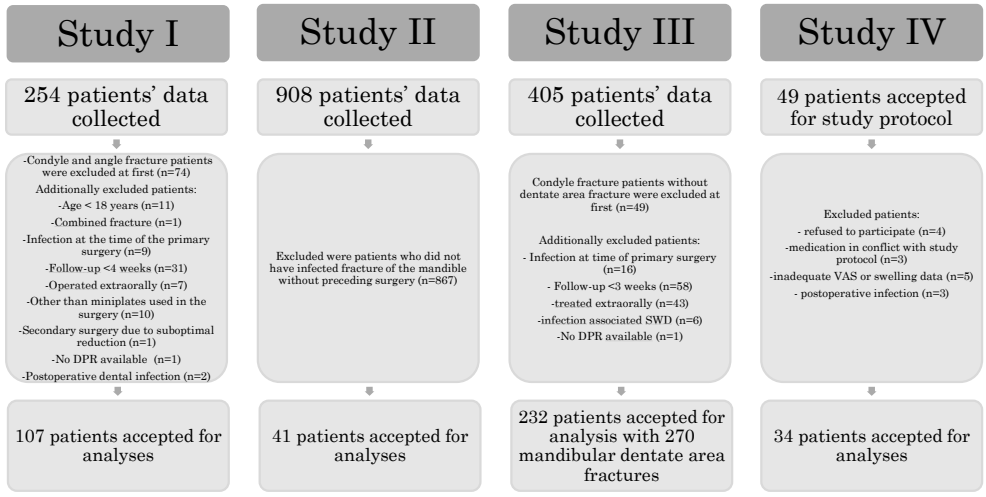


Figure 6 Patient inclusion in Studies I–IV. DPR, dental panoramic radiograph; SWD, surgical wound dehiscence; VAS, visual analogue scale.

6.1. Occurrence and causes of post-operative surgical site infection and wound dehiscence in intraorally treated mandibular fractures (Studies I and III)

6.1.1. Occurrence of surgical site infection and wound dehiscence

In Study I, 107 patients were included in the final analyses. SSI occurred in 18 patients (16.8%). The timing of SSIs varied between 5 and 106 days with a mean of 31.8 days and a median of 19.5 days.

In Study III, 232 patients with 270 mandibular fractures were included in the final analyses. Twenty-two SWDs were detected occurring in 9.5% of patients and in 8.1% of fractures. The timing of SWD varied between 7 and 130 days with mean 21.6 days and median 12 days.

6.1.2. Causes of postoperative surgical site infection

Patient-, fracture-, and surgery related variables were analysed to determine causes of SSIs (Tables 5, 6 and 7). None of the studied variables showed significant differences between the groups.

Effect of intoxicants, smoking, and poor oral hygiene on SSI
SSI occurrence was higher in alcohol and/or drug abusers and smokers, though not significantly. Additionally, TDI was higher in patients with SSI (median TDI 2 in SSI-group and 1 in control group). Thus, poor oral hygiene and intoxicants might predispose to SSIs.

Table 5 Patient-related variables in 107 mandibular fracture patients in Study I. Table modified from Oksa M, Haapanen A, Marttila E, Snäll J. Simple dentate area fractures of the mandible – can we prevent postoperative infections? Acta Odontol Scand. 2022;80(7):494–500.

	Surgical site infection		No surgical site infection		P
All (n)	18		89		
Age, years					
Range	18–61		18–89		0.660
Median	33		34		
Modified Total Dental Index (TDI)					
Range	0–5		0–8		0.220
Mean	2.2		1.8		
Median	2		1		
	n	**% of n**	**n**	**% of n**	
Sex					
Male	16	19.0	68	81.0	0.350
Female	2	8.7	21	91.3	
Smoking					
Yes	10	27.0	27	73.0	0.0567
No	8	11.4	62	88.6	
Alcohol and/or drug abuse					
Yes	7	28.0	18	72.0	0.124
No	11	13.4	71	86.6	
Immunosuppressive condition					
Yes	0	0.0	3	100.0	1
No	18	17.3	86	82.7	

Table 6 Fracture-related variables in 107 mandibular fracture patients in Study I. Table modified from Oksa M, Haapanen A, Marttila E, Snäll J. Simple dentate area fractures of the mandible – can we prevent postoperative infections? Acta Odontol Scand. 2022;80(7):494–500.

	Surgical site infection		No surgical site infection		P
Fracture site	**n**	**% of n**	**n**	**% of n**	
Body	2	18.2	9	81.8	1
Symphysis/parasymphysis	16	16.7	80	83.3	
Comminution of the fracture					
Non-comminuted	17	16.8	84	83.2	1
Comminuted	1	16.7	5	83.3	
Minor comminution	1	25.0	3	75.0	
Major comminution	0	0	2	100	

Table 7 Surgery-related variables in 107 mandibular fracture patients in Study I. Table modified from Oksa M, Haapanen A, Marttila E, Snäll J. Simple dentate area fractures of the mandible – can we prevent postoperative infections? Acta Odontol Scand. 2022;80(7):494–500.

	Surgical site infection		No surgical site infection		P
All (n)	18		89		
Treatment delay from accident to surgery, days					
Range	0–8		0–6		0.140
Mean	2.22		1.54		
Median	2		1		
No. of plates					
Range	0–2		0–2		0.970
Mean	1.78		1.75		
Median	2		2		
No. of lag screws					
Range	0–3		0–3		0.920
Mean	0.22		0.21		
Median	0		0		
No. of teeth extracted for poor dental condition (no trauma teeth)					
Range	0–3		0–12		0.900
Mean	0.33		0.53		
Median	0		0		
	n	**% of n**	**n**	**% of n**	
Tooth removal (any)					
Yes	3	15.8	16	84.2	1
No	15	17.0	73	83.0	
Tooth removal from fracture line					
Yes	1	100.0	0	0.0	0.170
No	17	16.0	89	84.0	
Tooth removal during surgery for poor dental condition					
Yes	3	15.8	16	84.2	1
No	15	17.0	73	83.0	

6.1.3. Causes of surgical wound dehiscence

Patient-, fracture-, and surgery related variables were analysed to determine causes of SWD. In patient-related variables (Table 8), a significantly greater SWD rate was observed only among smokers (p=0.0410).

Table 8 Patient-related variables in Study III. Table modified from Oksa M, Haapanen A, Marttila E, Furuholm J, Snäll J. Postoperative wound dehiscence in mandibular fractures. Acta Odontol Scand. 2023;81(7):555–561.

	All patients	Surgical wound dehiscence		No surgical wound dehiscence		P
		n	%	n	%	
All patients	232	22	9.5	210	90.5	
Age, years						
Range	5 – 89	16 – 77		5 – 89		0.985
Median	31	32		31		
		n	% of n	n	% of n	
Sex						
Male	187	20	10.7	167	89.3	0.264
Female	45	2	4.4	43	95.6	
Immunosuppressive condition						
Yes	6	0	0	6	100.0	1
No	226	22	9.7	204	90.3	
Smoking						
Yes	89	13	14.6	76	85.4	0.0410*
No	143	9	6.3	134	93.7	
Alcohol and/or drug abuse						
Yes	54	7	13.0	47	87.0	0.302
No	178	15	8.4	163	91.6	
Postoperative chlorhexidine mouthwash						
Yes	201	21	10.4	180	89.6	0.324
No	31	1	3	30	96.8	

*Statistically significant.

Fracture-related variables (Table 9) including fracture site and comminution of the fracture showed no significant difference between groups.

Table 9 Fracture-related variables in Study III. Table modified from Oksa M, Haapanen A, Marttila E, Furuholm J, Snäll J. Postoperative wound dehiscence in mandibular fractures. Acta Odontol Scand. 2023;81(7):555–561.

	Surgical wound dehiscence		**No surgical wound dehiscence**		**P**
	n	**%**	**n**	**%**	
All fractures	22	8.1	248	91.9	
	n	**% of n**	**n**	**% of n**	
Fracture site					
Symphysis/parasymphysis	13	7.7	156	92.3	0.262
Body	5	15.2	28	84.8	
Angle	4	5.9	64	94.1	
Comminution of fracture					
Non-comminuted	19	7.6	230	92.4	0.394
Comminuted	3	14.3	18	85.7	
Minor comminution	3	17.6	14	82.4	1
Major comminution	0	0	4	100.0	

In surgery-related variables (Table 10) a night-time surgery showed a significantly higher SWD rate than daytime surgery (p=0.0120). All nighttime surgeries were conducted by residents with or without an assistant consultant. Nighttime surgery was the only significant independent variable in a multivariate analysis (Table 11) with an odds ratio of 3.297 (95% CI 1.237 – 8.780, p=0.0170) for SWD. Only residents were included in the multivariate analysis because no SWDs were observed in fractures operated on by consultants.

Table 10 Surgery-related variables in Study III. Table modified from Oksa M, Haapanen A, Marttila E, Furuholm J, Snäll J. Postoperative wound dehiscence in mandibular fractures. Acta Odontol Scand. 2023;81(7):555–561.

	Surgical wound dehiscence		No surgical wound dehiscence		P
	n	**%**	**n**	**%**	
All fractures	22	8.1	248	91.9	
Treatment delay from accident to surgery, days					
Range	0 – 14		0 – 19		
Mean	2.0		1.8		0.629
Median	1		1		0.936
	n	**% of n**	**n**	**% of n**	
Incision technique					
Scalpel	7	9.9	64	90.1	0.539
Electrosurgery	15	7.5	184	92.5	
Fixation method					
Plate(s)	22	8.6	234	91.4	0.519
Lag screw(s)	0	0	10	100.0	
Combined	0	0	4	100.0	
Suturing technique					
Simple interrupted sutures	14	8.7	147	91.3	0.494
Continuous sutures	8	8.5	86	91.5	
Combined	0	0	15	100.0	
Additional mentalis muscle suturing in (para)symphysis fractures					
Yes	5	5.7	83	94.3	0.307
No	8	9.9	73	90.1	
Postoperative mandibulomaxillary fixation					
Yes	5	8.9	51	91.1	0.787
No	17	7.9	197	92.1	
Surgeon					
Resident with/without assistant consultant	22	8.6	234	91.4	0.613
Resident	17	9.3	165	90.7	0.504
Resident with assistant consultant	5	6.8	69	93.2	
Consultant	0	0	14	100.0	
Time of surgery					
Night-time	8	18.6	35	81.4	0.0120*
Daytime	14	6.2	213	93.8	

*Statistically significant.

Table 11 Logistic regression analysis with 95% confidence intervals for occurrence of surgical wound dehiscence after mandibular fracture surgery. Table modified from Oksa M, Haapanen A, Marttila E, Furuholm J, Snäll J. Postoperative wound dehiscence in mandibular fractures. Acta Odontol Scand. 2023;81(7):555–561.

Variable	Coefficient	SE	VIF	OR	95% CI	P
Smoker ref. non-smoker	0.905	0.470	1.018	2.472	0.983 – 6.214	0.054
Body fracture ref. angulus and symphysis fracture	1.027	0.598	1.037	2.793	0.864 – 9.025	0.086
Electrosurgery ref. scalpel incision	-0.243	0.512	1.015	0.785	0.287 – 2.141	0.636
Simple interrupted sutures ref. continuous and combined sutures	0.268	0.486	1.020	1.307	0.504 – 3.386	0.582
Comminuted fracture ref. non-comminuted fracture	0.689	0.703	1.023	1.992	0.502 – 7.906	0.327
Night-time surgery ref. daytime surgery	1.193	0.500	1.008	3.297	1.238 – 8.780	0.0170*

Abbreviations: SE, standard error; VIF, variance inflation factor; OR, odds ratio; CI, confidence interval

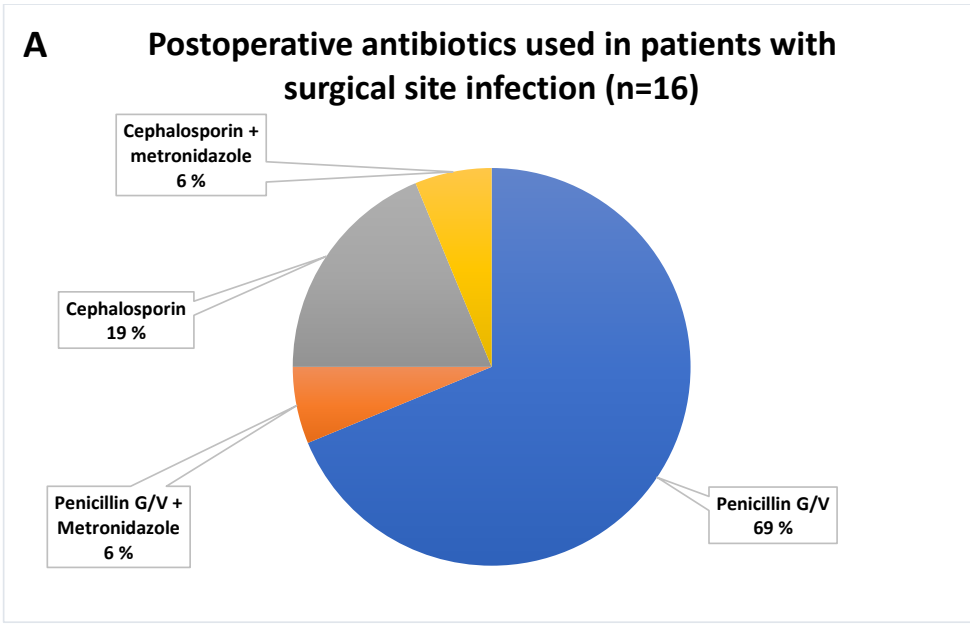
*Statistically significant.

6.2. Antibiotic treatment and occurrence of SSI in patients with intraorally treated mandibular fracture (Study I)

In Study I, SSIs occurred in 18 patients (16.8%) being more common in patients with a shorter antibiotic treatment (Table 12). However, no statistically significant difference was observed in duration or timing of antibiotic use and SSI. Additionally, the use of postoperative CHX mouthwash showed no significant difference (p=0.174) between patients with or without SSI. Penicillin G/V was the most prescribed antibiotic postoperatively (Figure 7).

Table 12 Antibiotic use in 107 mandibular fracture patients. Table modified from Oksa M, Haapanen A, Marttila E, Snäll J. Simple dentate area fractures of the mandible – can we prevent postoperative infections? Acta Odontol Scand. 2022;80(7):494–500.

	Surgical site infection		**No infection**		**P**
Duration of postoperative antibiotic course, days					
Range	0–9		0–26		0.0870
Mean	3.44		5.04		
Median	4		5		
Total duration of antibiotic course, days					
Range	1–11		1–27		0.230
Mean	5.17		6.34		
Median	5		6		
	n	**% of n**	**n**	**% of n**	
Preoperative antibiotics					
Yes	13	15.1	73	84.9	0.340
No	5	23.8	16	76.2	
Antibiotics in anesthesia induction					
Yes	18	17.0	88	83.0	1
No	0	0	1	100	
Postoperative antibiotics					
Yes	16	15.8	85	84.2	0.265
No	2	33.3	4	66.7	
Postoperative chlorhexidine mouthwash					
Yes	15	15.3	83	84.7	0.174
No	3	33.3	6	66.7	



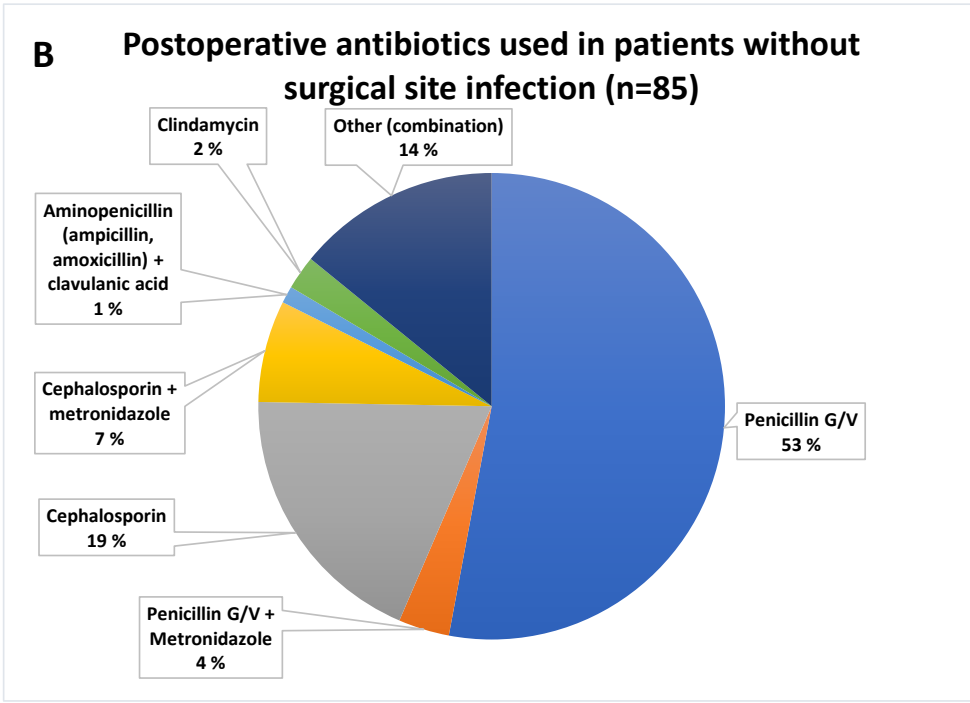


Figure 7 Postoperative antibiotics used in patients with (A) and without (B) surgical site infection.

6.3. Surgical techniques, antibiotic treatment, and occurrence of postoperative surgical site complications in infected mandibular fractures without preceding surgery (Study II)

Forty-one patients had clinically infected fracture in Study II. Most of the patients were males (n=35, 85.4%). Alcohol and/or drug abuse occurred in 46.3% of the patients, and smoking was also common in this patient population (58.5%). Demographics and substance abuse in patients with infected mandibular fracture are presented in Table 13. During the research period, infected mandibular fractures were located only in the dentate part of the mandible.

Table 13 Demographics and substance abuse in patients with infected mandibular fracture. Table modified from Oksa M, Haapanen A, Kannari L, Furuholm J, Snäll J. Surgical treatment of clinically infected mandibular fractures. Oral Maxillofac Surg. 2024;28(2):839-847.

All patients, n	41	
Age, years		
Range	17–73	
Median	38	
Treatment delay from injury to surgery, days*		
Range	2–76	
Mean	16	
Median	9	
	n	**% of 41 patients**
Sex		
Male	35	85.4
Female	6	14.6
Smoking		
Yes	24	58.5
No	17	41.5
Alcohol and/or drug abuse		
Yes	19	46.3
No	22	53.7

*Exact date of injury is missing in three cases (excluded from analyses).

Symphysis and parasymphysis were the most common fracture sites 46.3% (n=19). Patient-related factors were the most frequent reason for delayed surgery (n=30, 73.2%) following with delay caused by health care professionals for missed fracture (n=8, 19.5%). Initial non-surgical treatment decision preceded infection in three patients (Table 14).

Table 14 Infection aetiology in patients with infected mandibular fracture. Table modified from Oksa M, Haapanen A, Kannari L, Furuholm J, Snäll J. Surgical treatment of clinically infected mandibular fractures. Oral Maxillofac Surg. 2024;28(2):839-847.

	n	% of 41 patients
Factors contributing to delayed surgery		
Patient-related factors	30	73.2
Fracture not detected at first visit to health care professional	8	19.5
Initially planned non-surgical treatment, fracture infected during follow-up	3	7.3

6.3.1. Surgical techniques in infected mandibular fractures

Extraoral approach was chosen in 53.7% of the fractures (n=22) and intraoral in 46.3% of the fractures (n=19). Table 15 shows, that extraoral approach was associated with a longer treatment delay (p=0.0120). Drain usage was more common in extraorally treated patients (p=0.0140). Additionally, reconstruction plates were solely used in surgeries with extraoral approach (p<0.001).

Table 15 Patient-, fracture-, and treatment related variables in intraorally and extraorally treated patients (n=41). Table modified from Oksa M, Haapanen A, Kannari L, Furuholm J, Snäll J. Surgical treatment of clinically infected mandibular fractures. Oral Maxillofac Surg. 2024;28(2):839-847.

	Intraoral approach		Extraoral approach		P
All patients, n (%)	19 (46.3%)		22 (53.7%)		
Age, years					
Range	17–60		20–73		0.163
Median	35		44		
Treatment delay from injury to surgery, days*					
Range	2–26		3–76		0.0120**
Mean	8.5		19.9		
Median	6		10		
Duration of postoperative antibiotic course, days					
Range	2–15		2–33		0.0770
Mean	9.6		12.7		
Median	10		12		
	n	**% of n**	**n**	**% of n**	
Smoking					
Yes	9	37.5	15	62.5	0.177
No	10	58.8	7	41.2	
Alcohol and/or drug abuse					
Yes	7	36.8	12	63.2	0.257
No	12	54.5	10	45.5	
Fracture site					
Symphysis/parasymphysis	10	52.6	9	47.4	0.509
Body	5	55.6	4	44.4	
Angle	4	30.8	9	69.2	
Comminution of the fracture					
Non-comminuted	16	48.5	17	51.5	0.703
Comminuted	3	37.5	5	62.5	
	n	**% of comminuted fractures**	**n**	**% of comminuted fractures**	
Minor comminution	2	50.0	2	50.0	1.000
Major comminution	1	25.0	3	75.0	
	n	**% of n**	**n**	**% of n**	
Infection severity					
Mild	13	61.9	8	38.1	0.0620
Severe	6	30.0	14	70.0	
Fixation method					
Reconstruction plate	0	0	15	100.0	<0.001**
Non-reconstruction plate	19	86.4	3	13.6	
Combined	0	0	4	100.0	
Bone grafting					
Yes	0	0	1	100	1.000
No	19	47.5	21	52.5	
Use of drain					
Yes	2	16.7	10	83.3	0.0140**
No	17	58.6	12	41.4	

*Exact date of injury is missing in three cases (excluded from analyses).

**Statistically significant.

6.3.2. Occurrence of postoperative surgical site complications and antibiotic treatment in infected mandibular fractures

Postoperative surgical site complication was found in 13 patients (31.7%). No significant differences in patient- and fracture-related variables (Table 16) or treatment-related variables (Table 17) were found between patients with and without postoperative complication. Median duration of postoperative antibiotic course was 11 days in both groups. Postoperative antibiotics used are shown in Figure 8.

Table 16 Patient- and fracture-related variables in patients with and without surgical site complication (n=41). Table modified from Oksa M, Haapanen A, Kannari L, Furuholm J, Snäll J. Surgical treatment of clinically infected mandibular fractures. Oral Maxillofac Surg. 2024;28(2):839-847.

	Surgical site complication present		**Surgical site complication absent**		**P**
All patients, n (%)	13 (31.7%)		28 (68.3%)		
Age, years					
Range	21–72		17–73		0.488
Median	35		38		
	n	**% of n**	**n**	**% of n**	
Smoking					
Yes	8	33.3	16	66.7	0.790
No	5	29.4	12	70.6	
Alcohol and/or drug abuse					
Yes	6	31.6	13	68.4	0.987
No	7	31.8	15	68.2	
Fracture site					
Symphysis/parasymphysis	6	31.6	13	68.4	0.238
Body	1	11.1	8	88.9	
Angle	6	46.2	7	53.8	
Comminution of the fracture					
Non-comminuted	10	30.3	23	69.7	0.692
Comminuted	3	37.5	5	62.5	
	n	**% of comminuted fractures**	**n**	**% of comminuted fractures**	
Minor comminution	1	25.0	3	75.0	1.000
Major comminution	2	50.0	2	50.0	
	n	**% of n**	**n**	**% of n**	
Infection severity					
Mild	7	33.3	14	66.7	0.819
Severe	6	30.0	14	70.0	

Table 17 Treatment-related variables in patients with and without surgical site complication (n=41). Table modified from Oksa M, Haapanen A, Kannari L, Furuholm J, Snäll J. Surgical treatment of clinically infected mandibular fractures. Oral Maxillofac Surg. 2024;28(2):839-847.

	Surgical site complication present		**Surgical site complication absent**		**P**
All patients, n (%)	13 (31.7%)		28 (68.3%)		
Treatment delay from injury to surgery, days*					
Range	3–76		2–45		0.505
Mean	14.7		14.6		
Median	6		9		
Duration of postoperative antibiotic course, days					
Range	7–19		2–33		0.688
Mean	11.6		11.1		
Median	11		11		
	n	**% of n**	**n**	**% of n**	
Fixation method					
Reconstruction plate	5	33.3	10	66.7	1.000
Non-reconstruction plate	7	31.8	15	68.2	
Combined	1	25.0	3	75.0	
Bone grafting					
Yes	1	100.0	0	0	0.317
No	12	30.0	28	70.0	
Use of drain					
Yes	4	33.3	8	66.7	1.000
No	9	31.0	20	69.0	

*Exact date of injury is missing in three cases (excluded from analyses).

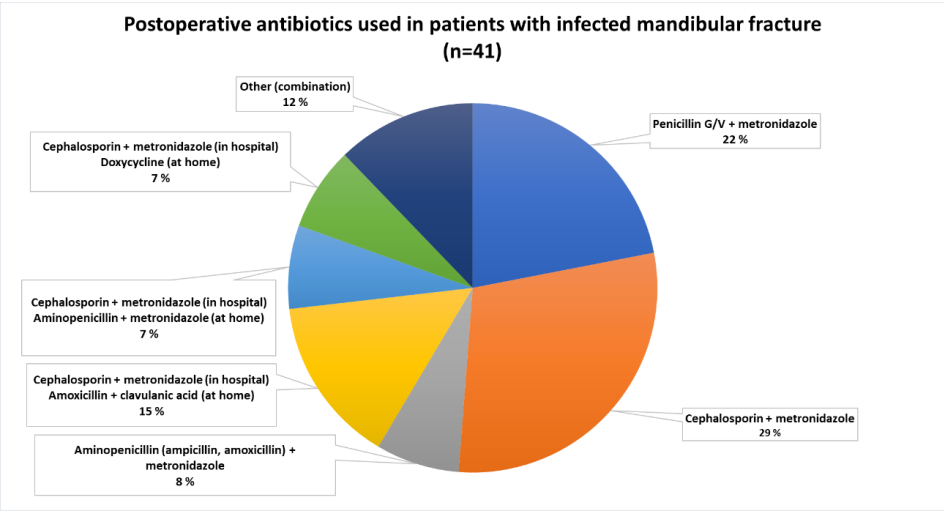


Figure 8 Postoperative antibiotics used in patients with infected mandibular fracture. Combinations of Penicillin G/V or Cephalosporin with metronidazole were the most used antibiotic treatment.

Surgical site complications in intraorally and extraorally treated patients with infected mandibular fracture are presented in Table 18. Recurrent infection was the most common surgical site complication (n=9, 69.2%). SWD without infection occurred exclusively with intraoral approach (21.1%, p=0.0380). Recurrent infections were slightly more often related to extraoral approach (27.3%), however, without statistical significance. Secondary osteosynthesis for non-union and recurrent infection was conducted for one patient treated intraorally.

Table 18 Surgical site complications in intraorally and extraorally treated patients with infected mandibular fracture. Table modified from Oksa M, Haapanen A, Kannari L, Furuholm J, Snäll J. Surgical treatment of clinically infected mandibular fractures. Oral Maxillofac Surg. 2024;28(2):839-847.

	Intraoral approach		Extraoral approach		P
All patients, n (%)	19	(46.3 %)	22	(53.7 %)	
Days between surgery and postoperative complication					
Range	7–129		4–93		0.445
Mean	34.2		31.7		
Median	28		17		
Postoperative complication					
Yes	7	36.8	6	27.3	0.511
No	12	63.2	16	72.7	
Recurrent infection					
Yes	3	15.8	6	27.3	0.466
No	16	84.2	16	72.7	
Wound dehiscence without infection					
Yes	4	21.1	0	0	0.038*
No	15	78.9	22	100.0	

*Statistically significant.

6.4. Analgesic effect of perioperative use of systemic dexamethasone and its impact on trismus and oedema in mandibular fracture surgery (Study IV)

6.4.1. Descriptive data of patients

Thirty-four patients were accepted for analysis. The study group (DXM+) and the control group (DXM-) consisted of 17 patients. Median age was 25 years in both groups. Treatment delay ranged from 0 to 5 days (median in DXM+ 2 days, DXM- 1 day). Median operation duration was 46 minutes in DXM+ group and 62 minutes in DXM- group. Both groups were comparable with respect to the study variables as shown in Table 19.

Table 19 Demographics of 34 mandibular fracture patients in Study IV. Table modified from Oksa M, Haapanen A, Furuholm J, Thorén H, Snäll J. Effect of Perioperative Systemic Dexamethasone on Pain, Edema, and Trismus in Mandibular Fracture Surgery: A Randomized Trial. J Craniofac Surg. 2021; 32(8): 2611–2614.

	DXM+	DXM-	P
No. of patients	17	17	
Age, years			
Median	25	25	0.838
Range	18–47	18–51	
Treatment delay from accident to surgery, days			
Median	2	1	0.586
Range	0–5	0–5	
Duration of surgery, min			
Median	46	62	0.760
Range	23–129	24–90	
Preoperative VAS			
Mean	3.5	3.3	0.812
Median	4	3	
Preoperative swelling in single fracture patients, cm			
Mean	32.2	32.0	0.833
Median	31.8	32.4	
Preoperative swelling in double fracture patients, cm			
Mean	32.2	31.9	0.429
Median	32.3	31.6	
Mouth opening preoperatively, mm			
Mean	25	28	0.357
Median	24	25	

DXM+ = study group; DXM- = control group; VAS = visual analogue scale

6.4.2. Analgesic effect of perioperative dexamethasone

The analgesic effect of DXM was evaluated with the number of times that a patient needed postoperative opioid medication and with VAS score. No significant difference in the postoperative opioid medication was observed between the groups. The VAS score was significantly lower in the DXM+ group 18 hours postoperatively (p=0.0330) but not in the other measurement points. Statistics of analgesic effect of DXM are shown in Table 20. Figure 9 shows the average VAS curve.

Table 20 VAS and opioid medication in study and control groups. Table modified from Oksa M, Haapanen A, Furuholm J, Thorén H, Snäll J. Effect of Perioperative Systemic Dexamethasone on Pain, Edema, and Trismus in Mandibular Fracture Surgery: A Randomized Trial. J Craniofac Surg. 2021; 32(8): 2611–2614.

		VAS 6 h post-operatively	VAS 12 h post-operatively	VAS 18 h post-operatively	VAS 24 h post-operatively	No. of times patient needed opioid analgesics
DXM+	No. of patients	17	17	15	7	17
	Mean	3.5	3.1	2.1	3.3	2.7
	Median	4	3	2	2	2
	Range	0–8	0–6	0–5.5	1–6	0–5
DXM-	No. of patients	16	17	13	12	17
	Mean	4.4	4.4	3.9	4.5	3.9
	Median	4	4	5	5	4
	Range	2–8.5	2–7.5	0–8	1–7	1–9
	P	0.231	0.0850	0.0330*	0.261	0.140

DXM+ = study group; DXM- = control group; VAS = Visual analogue scale
*Statistically significant

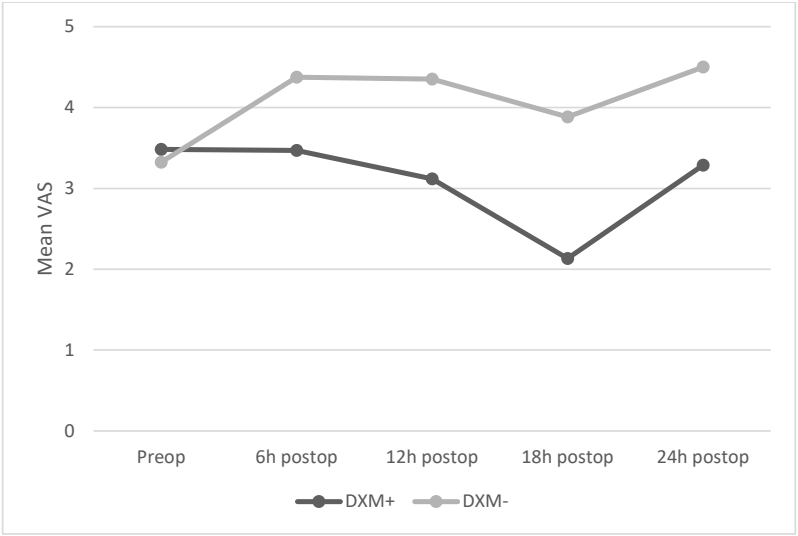


Figure 9 Average visual analogue scale curve. Note lower average VAS in DXM+ -group especially 18 hours postoperatively. DXM+, study group; DXM-, control group; VAS, Visual analogue scale. Figure modified from Oksa M, Haapanen A, Furuholm J, Thorén H, Snäll J. Effect of Perioperative Systemic Dexamethasone on Pain, Edema, and Trismus in Mandibular Fracture Surgery: A Randomized Trial. J Craniofac Surg. 2021; 32(8): 2611–2614.

6.4.3. Impact of perioperative dexamethasone on postoperative trismus and oedema

No significant differences in percentage decrease in facial swelling (Table 21) or mouth opening (Table 22) were found between the study and control groups. Thus, the use of perioperative DXM shows no impact on postoperative trismus or oedema.

Table 21 Percentage decrease in face swelling between study and control groups. Table modified from Oksa M, Haapanen A, Furuholm J, Thorén H, Snäll J. Effect of Perioperative Systemic Dexamethasone on Pain, Edema, and Trismus in Mandibular Fracture Surgery: A Randomized Trial. J Craniofac Surg. 2021; 32(8): 2611–2614.

		24 h postoperatively	48 h postoperatively *	7 days postoperatively	1 month postoperatively **
DXM+ (all mandibular fractures)	No. of patients	17	15	17	14
	Mean	-0.21	-0.06	1.62	1.22
	SD	1.16	1.62	1.92	1.69
	Median and range	0.00 (-3.15–1.78)	0.31 (-3.64–2.08)	1.93 (-2.98–5.28)	1.85 (-2,98–3,42)
DXM- (all mandibular fractures)	No. of patients	17	17	17	17
	Mean	-1.68	-1.92	0.90	1.91
	SD	1.54	2.08	2.01	1.60
	Median and range	-2.01 (-4.46–1.81)	-1.72 (-5.8–2.11)	1.23 (-2.61–4.28)	2.03 (-1,37–3,85)
	P	0.708	0.433	0.973	0.653

DXM+ = study group; DXM- = control group; SD = standard deviation.

* Two patients did not attend the 48-h follow-up visit

** Three patients did not attend the 1-month follow-up visit

Table 22 Mouth opening (mean, mm) between study and control groups. Table modified from Oksa M, Haapanen A, Furuholm J, Thorén H, Snäll J. Effect of Perioperative Systemic Dexamethasone on Pain, Edema, and Trismus in Mandibular Fracture Surgery: A Randomized Trial. J Craniofac Surg. 2021; 32(8): 2611–2614.

	24 h postoperatively	48 h postoperatively *	7 days postoperatively	1 month postoperatively **
DXM+	23 (n=17)	26 (n=15)	28 (n=17)	37 (n=14)
DXM-	22 (n=17)	24 (n=17)	28 (n=17)	40 (n=17)
P	0.865	0.655	0.919	0.518

DXM+ = study group; DXM- = control group.

* Two patients did not attend the 48-h follow-up visit

** Three patients did not attend the 1-month follow-up visit

7. DISCUSSION

The aim of this study was to investigate medications, including antibiotics and DXM, as well as perioperative technical aspects to prevent postoperative complications in mandibular fracture surgery.

7.1. Methodological considerations

Of the 254 mandibular fracture patients in Study I, 107 were included in the final analyses. SSI-group consisted of 18 patients and the control group of 89 patients. A follow-up duration of at least four weeks was required for inclusion. Thirty-one patients were excluded due to too short follow-up duration. The retrospective design of the study can be considered its main limitation. A prospective study protocol that included standardized antibiotic regimens and a clinical examination of patients' dentition could have provided more accurate knowledge of the use of antibiotics and the effect of oral hygiene level considering SSIs in mandibular fracture patients.

In Study II, 908 patients were evaluated with fractures in the dentate part of the mandible treated surgically during the research period, of which 41 had a clinically infected fracture during 11-year time-frame and were evaluated. A disadvantage of the study was the small population due to the low incidence of infected fractures and the design was retrospective.

In Study III, 405 mandibular fracture patients' data was collected. After exclusion, 232 patients with 270 mandibular fractures were included in the final analyses. A follow-up duration of at least three weeks was required for inclusion. Its retrospective design and the variation between patients and surgical methods may be considered disadvantages of the study. More differences could have emerged with standardized surgical techniques, especially considering the location of the incision.

Of the 49 patients accepted for the study protocol in Study IV, four refused to participate. Additionally, 11 patients were excluded due to strict inclusion criteria. Finally, 34 patients were accepted for analyses, both groups consisting of 17 patients (Figure 6). A follow-up duration of at least seven days was required for the analyses. The fact that the control group received no placebo might be considered a disadvantage of Study IV. This study was part of a large prospective facial fracture study organised in Helsinki University Hospital. Using placebo would have been demanding due to the scope of the whole study protocol and a wide timespan of the study. However, this sample size showed that the VAS score was significantly lower

in the DXM group than in the control group 18 hours postoperatively with a large effect size (Hedges' g = 0.908).

A strength of this study is its versatile design, including the effect of patient-related factors as well as medications (antibiotics and DXM) and surgical techniques to postoperative complications in mandibular fracture surgeries. This study revealed that postoperative complications, especially infectious complications, are common in this patient population despite antibiotic use. This highlights the importance of perioperative tissue handling. The impact of patients' oral hygiene level on postoperative complications is a new and significant perspective. In this study, both carious and periodontal diseases were evaluated.

7.1.1. Follow-up durations

Follow-up durations varied between our studies so that we could include as many patients as possible while maintaining reliable results.

In Study I, a follow-up duration of at least four weeks was required for inclusion in the analysis. We hypothesized that infections are diagnosed by the end of one month postoperatively. The timing of SSIs varied between 5 and 106 days (mean 31.8 days, median 19.5 days).

All patients with an infected mandibular fracture without preceding surgery were included in Study II due to the rather small study population. Thus, minor complications may have gone unrecorded in the data. As the department is the only emergency department treating these types of fractures in the region, patients would have most likely made contact had notable complications occurred. Thus, a short follow-up duration was not an exclusion criterion. However, median follow-up time was 90 (range 1–1008) days.

In Study III, a follow-up duration of at least three weeks was required for inclusion in the analysis. We hypothesized that SWDs typically occur earlier than SSIs. The timing of SWD occurrence varied between 7 to 130 days (mean 21.6 days, median 12 days).

In Study IV, a follow-up duration of at least seven days was required for the analysis as postoperative pain, oedema, and trismus are at peak during the first week after surgery.

7.2. Surgical site infection and wound dehiscence in mandibular fracture patients (Studies I and III)

7.2.1. Surgical site infection

SSI occurred in 18 patients (16.8%) in Study I. None of the studied patient, fracture, or surgery related variables showed significant differences between the groups. However, SSI occurrence was higher in alcohol and/or drug abusers and smokers without statistical significance. Postoperative SSI-rate has been reported 7.5%–17.9%[10–14]. Our study is in line with previous studies. SSI risk remained high in our study even though previously known risk factors such as angular region for infection were excluded. Thus, local and surgical factors for infection risk warrant further investigation.

Iatrogenic wound contamination may predispose to infections[4]. Additionally, postoperative complications may be linked to surgical experience[180]. A slightly suboptimal fixation was found in two patients. Careful wound closure and soft tissue management should be considered. SSIs occurred from five days to more than three months postoperatively suggesting several different aetiological causes.

Smoking, alcohol, and drug abuse, immunocompromised status and infected tooth in the fracture site can contribute to SSI[4,5,93]. In a study by Hall et al.[94], alcohol and drug abusers with tooth decay showed higher SSI rates after mandibular fracture surgery. In addition, severe periodontal disease has also shown to predispose to SSI[95]. In Study I, SSI occurrence was higher in smokers and alcohol and/or drug abusers than in other patients. Additionally, TDI was higher in patients with SSI though differences were not statistically significant. Thus, dental condition should be evaluated as part of mandibular fracture surgery. Affected teeth are recommended to be extracted during the surgery and patients should be motivated to maintain careful oral hygiene and to quit smoking.

7.2.2. Surgical wound dehiscence

In Study III, twenty-two SWDs were detected occurring in 9.5% patients and in 8.1% of fractures. A significantly greater SWD rate was observed among smokers. Additionally, night-time surgery showed a significantly higher SWD rate than daytime surgery. Postoperative SWD rate has been reported previously as 3.0–13.4%[4,6,97]. In our study, symphysis/parasymphysis, body, and angle fractures had different SWD rates being 7.7%, 15.2%, and 5.9%, respectively. In angle fractures, our result corresponds to the study by Fox and Kellman[97]. In mandibular body fractures, the mucosa and thin submucosa cover the intraorally placed plate fixation predisposing to the SWD. SWD occurrence was associated significantly with

smoking. SWD was also common in patients with alcohol/substance abuse history, although without statistical significance.

No difference was found between SWD occurrence and incision techniques in Study III. According to Nagargoje et al.[78], mucosal approaches made by a stainless-steel scalpel in anterior mandibular fracture surgery were more painful and bloody when compared with monopolar and bipolar diathermy. Diathermy was also faster to use than a scalpel; however, wound healing two days post-operatively was better in patients with the scalpel approach. Additionally, no difference was found between suturing technique and SWD. Surprisingly, separate closure of the mentalis muscle did not prevent SWD in the symphysis region. Thus, different closure techniques as well as scalpel and electrosurgery approach are equally good in mandibular fracture surgeries when estimating SWD. Heating power of the electrosurgical instrument should be considered. Special attention should be paid to the optimal approach level to prevent SWD (Figure 10). However, it is affected by several factors, such as the fixation method and the location and comminution of the fracture.

Nighttime surgery was significantly associated with SWDs and the experience of the surgeon diminished SWD occurrence in Study III. The impact of time of day affecting the result of surgery is controversial in previous studies. Increased risk to open surgery in nighttime cholecystectomy was found in a retrospective review by Wu et al.[181]. Additionally, an elevated risk of morbidity in surgical procedures performed later than 4pm was demonstrated in a previous study covering 144 740 patients[182]. However, two previous studies[183,184] showed that trauma surgeries at night-time were not associated with a higher complication rate. In Study III, residents were always involved in night-time surgeries. The surgeon's fatigue at night-time surgeries may increase the risk of complications. Previous studies have shown that a short delay is not associated with higher complication rates in mandibular fracture surgeries[11,79–81,185]. Thus, these fractures can be recommended to be postponed to daytime and this finding emphasizes the role of education and experience to reach an optimal result.

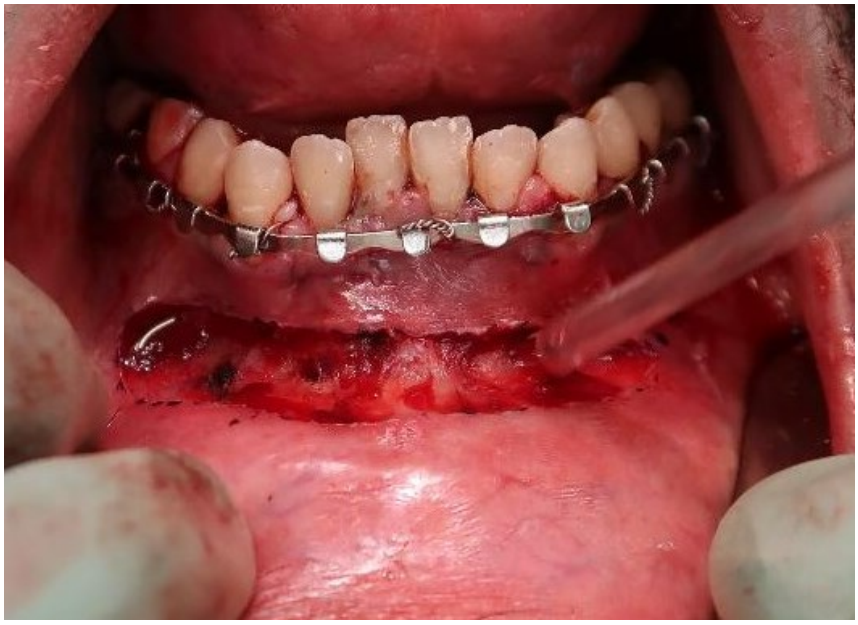


Figure 10 Picture of patient with mandibular symphysis fracture showing optimal site for incision considering the location of the fixation materials. The incision is made through the mucosa. Mentalis muscle is bisected after submucosal dissection to expose the fracture site.

7.2.3. Surgical site infection and wound dehiscence

Smoking, and alcohol/substance abuse is common in mandibular fracture patients. SSI rate was higher in patients with smoking and alcohol/substance abuse history, but without statistical significance. SWD occurrence was associated significantly with smoking and was common in patients with alcohol/substance abuse history, too, although without statistical significance. Substance abusers and patients with high risk for postoperative complications in general require special precision in treatment perioperatively and postoperatively. Despite adequate fracture treatment, SSIs can occur. Thus, attention should be drawn to the perioperative period, including fracture reduction and soft tissue handling.

7.3. Surgical techniques and occurrence of postoperative surgical site complications in patients with infected mandibular fracture (Study II)

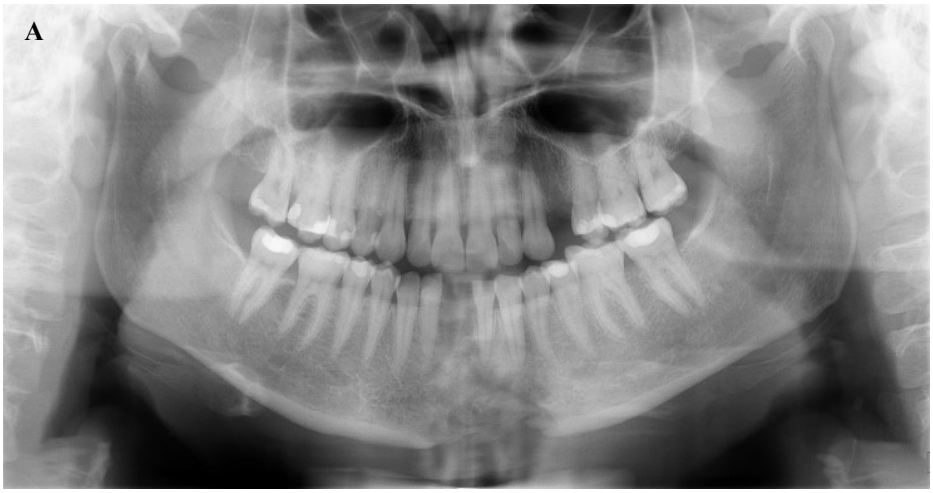
In study II, 41 patients had a clinically infected fracture (4.5%). Patient-related factors were the most frequent reason for delayed surgery followed by delay caused by health care professionals for missed fracture. Initial non-surgical treatment decision caused infection in three patients. Extraoral approach was chosen in 53.7% of the fractures and intraoral in 46.3% of the fractures. Postoperative surgical site complication was observed in 31.7% of patients.

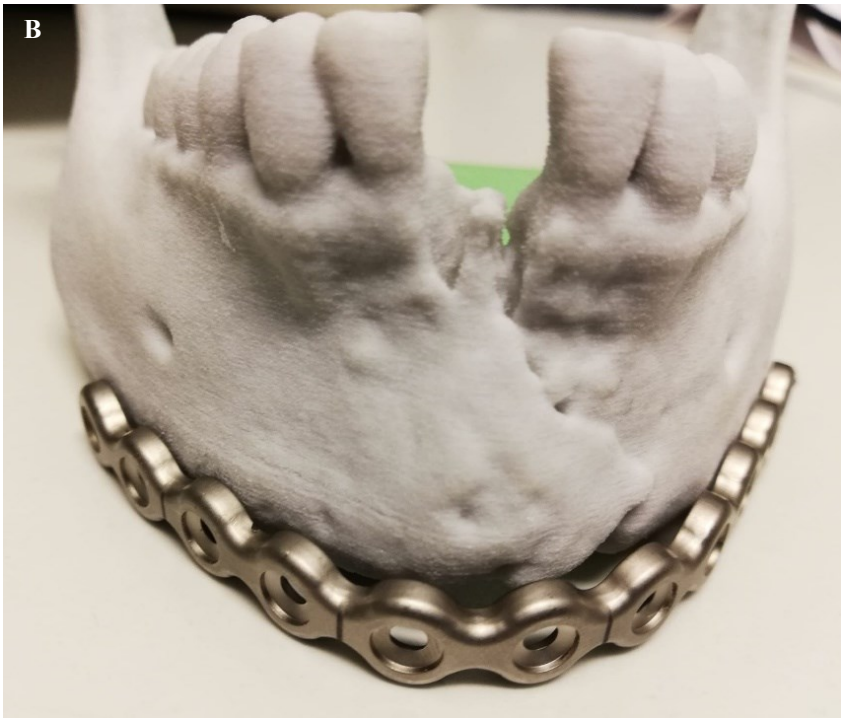
Patient compliance-related factors were the most important cause for delayed surgery. Substance and alcohol abuse was common in this patient population, which might explain the patient-related delay. However, a fifth of the patients had been evaluated by a health care professional, but the fracture was not detected at the first visit. In recent studies, mandibular fractures were missed in 14.8% of children (<20 years)[186] and in 20% of patients aged over 60 years[187] during patients' first health care assessments. Thus, an adequate clinical examination including imaging examinations (DPR and/or CT) are recommended for all patients with a recent facial injury. However, delay does not increase risk of postoperative complication in the present population. In addition, alcohol/drug abuse or smoking did not explain complication rates. Patients in this study had low treatment compliance and high surgical site complication risk. Thus, comprehensive treatment already in the primary phase is crucial, especially in this patient population.

Extraoral approach was chosen most often in severely infected fractures and in fractures with major comminution. However, postoperative complications occur regardless of the approach. Reconstruction plate with or without combined non-reconstruction plate was used in 19 patients (46.3%), and these patients had a complication rate of 31.6%. Thus, infection complications cannot be completely prevented by reconstruction plate or extraoral approach in clinically infected fractures. Additionally, extraoral approach causes a visible facial scar. In addition to plating technique, attention should be paid to the type, length, and stability of screws, tissue handling during surgery, the accuracy of the fracture reduction and the effect of teeth and occlusion on fracture site healing.

Only one patient received bone grafting in primary surgery. In a study by Benson et al.[83], immediate grafting in infected mandibular fracture was shown to be effective. They studied 50 infected fractures and reported that four patients developed recurrent infection and three had non-union with loss of graft. In

contrast, however, infected mandibular fractures with defects healed without bone grafting in Study II. Non-union was a rare complication (n=1). Figure 11 shows a patient case with bone grafting.





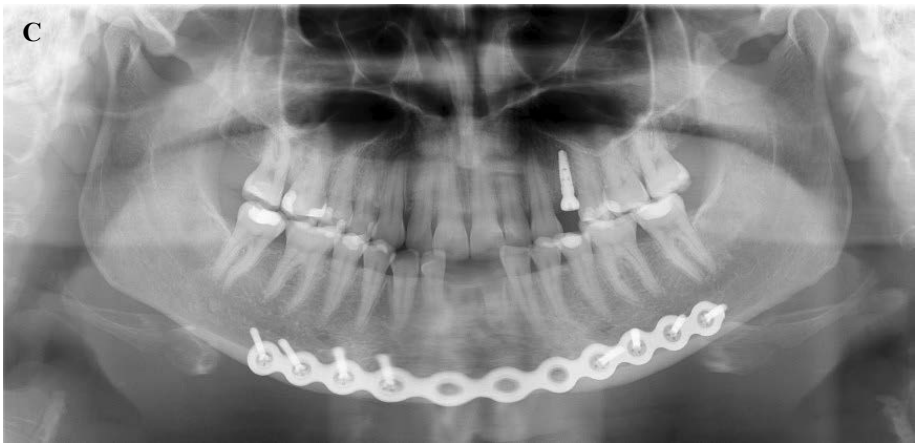


Figure 11 The patient was evaluated for an infected mandibular fracture two months after a traffic injury. Fracture was treated primarily non-surgically for other injuries and for local treatment options in another hospital. Patient had extraoral swelling and clinically non-union in the mandibular symphysis area. Osteolysis and chronic infection in the fracture line can be seen in the preoperative dental panoramic radiograph (A). The lower middle incisors were lost, but there were no fistula and the occlusion was acceptable. A reconstruction plate was pre-bent on a 3D-printed model (B) to ensure the comprehensive fit of the reconstruction plate on the lower border of the mandible. Extraoral approach was used for osteosynthesis. The reconstruction plate was first fitted and predrilled in place to ensure the correct occlusion. The osteosynthesis was removed while the fracture line underwent careful local debridement. A free iliac crest bone graft was harvested, and a separate cortical block was shaped and placed with cancellous bone in the area of the mandibular bone defect. Patient recovered without complications. Dental panoramic radiograph (C) confirms a favourable recovery process five weeks postoperatively.

7.4. Antibiotic treatment in patients with surgically treated mandibular fracture (Studies I and II)

7.4.1. Antibiotic treatment in patients with intraorally treated mandibular fracture(s) (Study I)

This study showed no significant difference between patients with or without SSI considering the duration of antibiotic treatment or the use of CHX mouth rinse. The use of antibiotics, especially postoperative regimen, varies significantly between surgeons. In our recent survey of oral and maxillofacial surgeons in the Nordic countries[20], the median reported duration for postoperative antibiotic treatment was 6 days (range 1–7 days). Literature review was implemented in the same study

showing that antibiotic regimen can be restricted to a maximum of 24 hours postoperatively without higher risk of SSI. Furthermore, a prospective study by Perepa et al.[188] showed that a one-day antibiotic regimen is as effective as a five-day regimen in reducing postoperative complications in mandibular fracture patients. Therefore, some surgeons prescribe an antibiotic course that is up to seven times longer than recommended. With these findings in antibiotic treatment, it can be stated that postoperative infections occur despite antibiotic treatment (Figure 12). Thus, the focus should be shifted from the antibiotic treatment to surgical techniques and local factors.

Use of CHX mouth rinse was common after mandibular fracture surgery, although it showed no significant difference between studied groups. However, CHX mouth rinse can be recommended to improve patients' oral hygiene[127] after mandibular fracture surgery. Extensive wound surfaces, sutures, and especially postoperative MMF weaken the maintenance of oral hygiene.

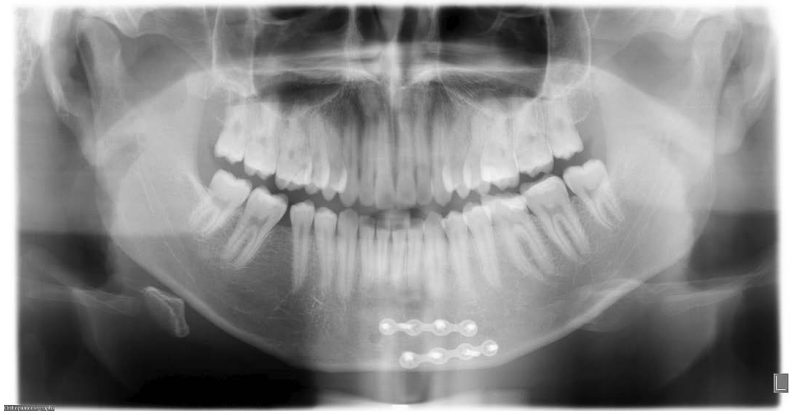


Figure 12 Postoperative dental panoramic radiograph of a healthy non-smoking 18-year-old male with a mandibular parasymphysis fracture after a traffic accident. Patient had no history of alcohol or substance abuse. Fracture was operated two days after injury intraorally with optimal fixation with two miniplates and screws. A four-day Penicillin V regimen was prescribed postoperatively. Despite adequate treatment, the patient had a surgical site infection with no significant cause.

7.4.2. Antibiotic treatment in patients with infected mandibular fracture (Study II)

Antibiotic therapy is indicated in infected mandibular fractures, and it can be targeted after specimen culturing. In a previous study by Mehra et al. [82], alpha- and beta-haemolytic streptococci were the most common pathogens isolated from the infected mandibular fracture sites. Viridans streptococci, especially *Streptococcus*

anginosus were the predominant bacteria cultured in infected fracture sites in our study. The duration of postoperative antibiotic regimen was clearly longer in this study than in mandibular fracture surgeries without infection. Antibiotic course varied between 2 and 33 days (mean 11.2 days, median 11 days) and several different antibiotics were used. Combinations of Penicillin G/V or Cephalosporin with metronidazole were the most used antibiotic treatment. Postoperative surgical site complications were not prevented by antibiotic medication; recurrent infection was found in 22.0% of patients. Patient-related factors, teeth in the fracture line, treatment delay, and difference in severity of the fractures challenge the evaluation of the antibiotic treatment. Thus, it is difficult to make general guidelines for antibiotic treatment in infected mandibular fractures.

7.5. Analgesic effect of perioperative systemic dexamethasone and its impact on trismus and oedema in mandibular fracture surgery (Study IV)

Study IV revealed that patients who received perioperative DXM in mandibular fracture surgery had less pain than patients without DXM 18 hours postoperatively but not in the other measurement points. No significant difference in the postoperative opioid medication was observed between the groups. Thus, the analgesic effect of DXM seems to be significant, but short-term. Additionally, the use of perioperative DXM showed no impact on postoperative trismus or oedema.

In a previous study by Dongol et al.[189], submucosal administration of DXM was found to reduce pain after mandibular fracture surgery with lower VAS score in the DXM+ group 72 hours postoperatively. Additionally, perioperative systemic DXM is found to reduce pain after zygomatic complex[190] and blowout[191] fracture surgeries. Thus, perioperative DXM has a significant analgesic effect in mandibular fracture surgeries as well as midfacial fractures surgeries. Surgery and even the injury itself cause inflammation cascade leading to pain. Decrease in COX-2 levels and prostaglandin E2 production[157] can explain the analgesic effect of GCs. However, in a study by Dionne et al.[158], lower PGE2 and thromboxane B2 (TXB2) levels at the third molar extraction site were found after systemic DXM administration (4 mg at 12 and 1 hours preoperatively) without analgesia. Subsequent NSAID administration (ketorolac 30 mg) reduced pain significantly and decreased PGE2 and TXB2 levels at the extraction site. Thus, the analgesic effect of DXM seems to be dose dependent.

We found no significant difference in trismus between DXM and control groups. Submucosal administration of DXM in a study by Dongol et al.[189] showed similar results. In third molar surgery, the results of GCs in controlling trismus are controversial. In a systematic review and meta-analysis by Almeida et al.[192], GCs

showed to be effective in controlling trismus. However, some previous studies[27,28] of third molar surgery showed no benefits in improving postoperative mouth opening after perioperative GC administration.

No significant difference in percentage decrease in facial swelling was found between the study and control groups in Study IV. In a previous study by Dongol et al.[189], a significant increase in swelling 24 hours postoperatively was observed in control group compared to group with submucosal DXM administration after mandibular fracture surgery. In third molar surgeries, a meta-analysis by Moraschini et al.[28] showed a reduction in postoperative oedema in the DXM groups. Additionally, a reduction in oedema in orthognathic surgeries are found after DXM administration[26,29,30]. However, third molar and orthognathic surgeries are not comparable with mandibular fracture surgeries. In orthognathic and third-molar surgeries, the injury is caused by the surgeon during the surgery, while in trauma surgeries, the primary injury is caused by the initial trauma itself. Different GCs might also have distinct responses. Alcantara et al.[25] found that DXM reduces oedema better than methylprednisolone. The mechanism of oedema reduction by GCs is the reduction in capillary permeability that lowers exudate formation[193,194].

Long-term use and high doses of GCs are linked to several adverse effects. These are metabolic changes[167], cardiovascular events[167], bleeding or perforation in upper gastrointestinal tract[168], leukocytosis[169], decrease in CRP[170], disturbance in surgical wound healing[171] and even steroid induced psychosis[24]. Thus, caution should be exercised when a high GC dosage is used. We used 30 mg DXM in this study. A lower DXM dose would reduce side effects of GCs. The clinician should consider the benefits and potential disadvantages of the GC administration. Based on this study, perioperative DXM has significant but short-term analgesic effect. Adequate postoperative pain management is necessary and can also be implemented with NSAIDs, paracetamol, and opioids.

7.6. Future aspects

Evidence-based international, as well as unit-level, guidelines for antibiotic treatment in mandibular fracture surgeries are needed to unify antibiotic treatment protocols and to avoid excessive antibiotic use. Numerous factors affect antibiotic treatment, so it is difficult to provide unambiguous instructions. On the other hand, our research shows that long antibiotic courses are not beneficial. Thus, guidelines limiting the duration of antibiotic treatment are appropriate.

Multicentre and prospective studies are needed to obtain larger populations to study infected mandibular fractures. Future studies should focus more on local factors instead of antibiotic medication.

The advantages and disadvantages of GCs and the necessity of their use in facial fracture surgery should be evaluated carefully. Some advantages have been observed, but it is reasonable to aim for the lowest possible dose due to the known disadvantages.

8. CONCLUSIONS

1. Postoperative surgical site complications are common in mandibular fracture patients. SSI occurred in 16.8% of patients and SWD in 9.5% of patients. None of the studied variables showed significant differences between the groups considering SSIs. A significantly greater SWD rate was observed among smokers and patients treated at night-time. Despite adequate fracture treatment, SSIs can occur. Attention should be drawn to surgical techniques including fracture reduction and soft tissue handling (Studies I and III).

2. The duration of antibiotic treatment showed no significant difference between patients with or without SSI. Thus, short antibiotic treatment as part of the surgical treatment of mandibular fracture seems to be sufficient. In infected mandibular fractures, postoperative surgical site complications were not prevented by antibiotic medication; recurrent infection was found in 22.0% of patients. (Studies I and II).

3. Patient-related factors and delay caused by health care professionals for missed fracture were the most common reasons for infected mandibular fractures. Postoperative surgical site complications are common in patients with infected mandibular fracture (31.7%). SWD without infection occurred exclusively with intraoral approach. Both intraoral and extraoral approaches can be used, but patients should be selected with care and SWD risk in intraoral approach should be noted (Study II).

4. The use of perioperative DXM reduces postoperative pain significantly in mandibular fracture patients 18 hours postoperatively. No significant effect on postoperative trismus or oedema was found. The analgesic effect of DXM seems to be short-term (Study IV).

ACKNOWLEDGMENTS

This project was carried out between 2019 and 2024 in the Department of Oral and Maxillofacial Diseases at the University of Helsinki, Finland and in the Department of Oral and Maxillofacial diseases in Helsinki University Hospital, Finland. I am deeply grateful to all the people who have been involved in this project. I would like to acknowledge:

Associate Professor Johanna Snäll, my supervisor whose passion for research has motivated me for years. Thank you for all the support and significant help during these past years. I greatly appreciate you as a surgeon and as a researcher. It has been an honour to work with you.

Doctor Aleksi Haapanen, my other supervisor whose constant encouragement and constructive feedback have pushed me forward as a researcher. With your excellent pedagogic skills in professional courses, you have also taught me a lot in my clinical work as a dentist.

I would like to warmly thank my co-authors Jussi Furuholm and Emilia Marttila especially regarding the statistical analyses, Professor Hanna Thorén for the opportunity to work with you on Study IV, and Leena Kannari for helping me with collecting patient data in Study II. Osmo Lintervo, thank you for the amazing illustrations!

The reviewers of the thesis, Professor Jari Kellokoski and Docent Leena Ylikontiola, are thanked for their critical evaluation and valuable insights to improving this thesis. Professor honoris causa Pekka Laine is thanked for accepting the invitation to be the opponent of this thesis.

I am grateful to my mother who has always supported me, let me follow my own paths, and loved me for who I am. I want to express gratitude to my marvellous sisters for their love and support. I thank all my friends and colleagues for giving joy to life.

Finally, thank you my dear spouse for all the love and support in daily life even on those challenging days. Thank you for understanding me during this project and all the help with this project. Thank you for giving meaning to everything.

Financial support from The Finnish Medical Foundation, the Finnish Dental Society Apollonia, and the Helsinki University Hospital Research Fund are gratefully acknowledged.

Helsinki, June 2024
Marko Oksa

REFERENCES

1. Boffano P, Roccia F, Zavattero E, et al. European Maxillofacial Trauma (EURMAT) project: A multicentre and prospective study. J Craniomaxillofac Surg. 2015;43(1):62-70. doi:10.1016/j.jcms.2014.10.011

2. Chukwulebe S, Hogrefe C. The Diagnosis and Management of Facial Bone Fractures. Emerg Med Clin N Am. 2019;37(1):137-151. doi:10.1016/j.emc.2018.09.012

3. Allareddy V, Allareddy V, Nalliah RP. Epidemiology of Facial Fracture Injuries. J Oral Maxillofac Surg. 2011;69(10):2613-2618. doi:10.1016/j.joms.2011.02.057

4. Gutta R, Tracy K, Johnson C, James LE, Krishnan DG, Marciani RD. Outcomes of Mandible Fracture Treatment at an Academic Tertiary Hospital: A 5-Year Analysis. J Oral Maxillofac Surg. 2014;72(3):550-558. doi:10.1016/j.joms.2013.09.005

5. Biller JA, Pletcher SD, Goldberg AN, Murr AH. Complications and the time to repair of mandible fractures. Laryngoscope. 2005;115(5):769-772. doi:10.1097/01.MLG.0000157328.10583.A7

6. Lamphier J, Ziccardi V, Ruvo A, Janel M. Complications of Mandibular Fractures in an Urban Teaching Center. J Oral Maxillofac Surg. 2003;61(7):745-749. doi:10.1016/S0278-2391(03)00147-2

7. Siddiqui A, Markose G, Moos KF, McMahon J, Ayoub AF. One miniplate versus two in the management of mandibular angle fractures: A prospective randomised study. Br J Oral Maxillofac Surg. 2007;45(3):223-225. doi:10.1016/J.BJOMS.2006.08.016

8. Beret M, Nicot R, Roland-Billecart T, Ramdane N, Ferri J, Schlund M. Impacted lower third molar relationship with mandibular angle fracture complications. J Stomatol Oral Maxillofac Surg. 2022;123(2):149-154. doi:10.1016/J.JORMAS.2021.05.004

9. Shurley CD, Abramowicz S, Manhan AJ, Roser SM, Amin D. Comprehensive analysis of patients with failure of mandibular hardware. Oral Surg Oral Med Oral Pathol Oral Radiol. 2022;134(1):15-19. doi:10.1016/J.OOOO.2021.11.011

10. Dodson TB, Perrott DH, Kaban LB, Gordon NC. Fixation of mandibular fractures: A comparative analysis of rigid internal fixation and standard fixation techniques. J Oral Maxillofac Surg. 1990;48(4):362-366. doi:10.1016/0278-2391(90)90431-Z

11. Czerwinski M, Parker WL, Correa JA, Williams HB. Effect of Treatment Delay on Mandibular Fracture Infection Rate. Plast Reconstr Surg. 2008;122(3):881-885. doi:10.1097/PRS.0b013e3181811a3c

12. Lee CC, Hajibandeh JT, Tannyhill RJ, Peacock ZS. Is Outpatient Management of Mandibular Fractures Associated with Inflammatory Complications? An

ACS-NSQIP study. J Oral Maxillofac Surg. 2021;79(12):2507-2518. doi:10.1016/j.joms.2021.03.018

13. Odom EB, Snyder-Warwick AK. Mandible fracture complications and infection: The influence of demographics and modifiable factors. Plast Reconstr Surg. 2016;138(2):282ee-2289e. doi:10.1097/PRS.0000000000002385

14. Gaal A, Bailey B, Patel Y, et al. Limiting Antibiotics When Managing Mandible Fractures May Not Increase Infection Risk. J Oral Maxillofac Surg. 2016;74(10):2008-2018. doi:10.1016/J.JOMS.2016.05.019

15. Thorén H, Snäll J, Salo J, et al. Occurrence and Types of Associated Injuries in Patients With Fractures of the Facial Bones. J Oral Maxillofac Surg. 2010;68(4):805-810. doi:10.1016/j.joms.2009.09.057

16. Alvi A, Doherty T, Lewen G. Facial Fractures and Concomitant Injuries in Trauma Patients. Laryngoscope. 2003;113(1):102-106. doi:10.1097/00005537-200301000-00019

17. Grunwaldt L, Smith DM, Zuckerbraun NS, et al. Pediatric Facial Fractures. Plast Reconstr Surg. 2011;128(6):1263-1271. doi:10.1097/PRS.0b013e318230c8cf

18. Kyzas PA. Use of antibiotics in the treatment of mandible fractures: A systematic review. J Oral Maxillofac Surg. 2011;69(4):1129-1145. doi:10.1016/J.JOMS.2010.02.059

19. Andreasen JO, Jensen SS, Schwartz O, Hillerup Y. A Systematic Review of Prophylactic Antibiotics in the Surgical Treatment of Maxillofacial Fractures. J Oral Maxillofac Surg. 2006;64(11):1664-1668. doi:10.1016/j.joms.2006.02.032

20. Oksa M, Haapanen A, Stråhlman F, Snäll J. Antibiotic use in mandibular fracture surgery – An international survey and a review of the literature. Stomatologija. 2022;24(2):35-42.

21. Alpert B, Kushner GM, Tiwana PS. Contemporary Management of Infected Mandibular Fractures. Craniomaxillofac Trauma Reconstr. 2008;1(1):25-29. doi:10.1055/s-0028-1098959

22. Kormi E, Snäll J, Törnwall J, Thorén H. A Survey of the Use of Perioperative Glucocorticoids in Oral and Maxillofacial Surgery. J Oral Maxillofac Surg. 2016;74(8):1548-1551. doi:10.1016/j.joms.2016.02.027

23. Assimes T, Lessard L. The Use of Perioperative Corticosteroids in Craniomaxillofacial Surgery. Plast Reconstr Surg. 1999;103(1):313-321.

24. Dan AEB, Thygesen TH, Pinholt EM. Corticosteroid Administration in Oral and Orthognathic Surgery: A Systematic Review of the Literature and Meta-Analysis. J Oral Maxillofac Surg. 2010;68(9):2207-2220. doi:10.1016/j.joms.2010.04.019

25. Alcântara CEP, Falci SGM, Oliveira-Ferreira F, Santos CRR, Pinheiro MLP. Pre-emptive effect of dexamethasone and methylprednisolone on pain, swelling, and trismus after third molar surgery: a split-mouth randomized triple-blind clinical trial. Int J Oral Maxillofac Surg. 2014;43(1):93-98. doi:10.1016/j.ijom.2013.05.016

26. Weber CR, Griffin JM. Evaluation of dexamethasone for reducing postoperative edema and inflammatory response after orthognathic surgery. J Oral Maxillofac Surg. 1994;52(1):35-39. doi:10.1016/0278-2391(94)90010-8

27. Bamgbose BO, Akinwande JA, Adeyemo WL, Ladeinde AL, Arotiba GT, Ogunlewe MO. Effects of co-administered dexamethasone and diclofenac potassium on pain, swelling and trismus following third molar surgery. Head Face Med. 2005;1(1):11. doi:10.1186/1746-160X-1-11

28. Moraschini V, Hidalgo R, Porto Barboza E dS. Effect of submucosal injection of dexamethasone after third molar surgery: a meta-analysis of randomized controlled trials. Int J Oral Maxillofac Surg. 2016;45(2):232-240. doi:10.1016/j.ijom.2015.09.008

29. Abukawa H, Ogawa T, Kono M, Koizumi T, Kawase-Koga Y, Chikazu D. Intravenous Dexamethasone Administration Before Orthognathic Surgery Reduces the Postoperative Edema of the Masseter Muscle: A Randomized Controlled Trial. J Oral Maxillofac Surg. 2017;75(6):1257-1262. doi:10.1016/j.joms.2016.12.048

30. Semper-Hogg W, Fuessinger MA, Dirlewanger TW, Cornelius CP, Metzger MC. The influence of dexamethasone on postoperative swelling and neurosensory disturbances after orthognathic surgery: a randomized controlled clinical trial. Head Face Med. 2017;13(1):19. doi:10.1186/s13005-017-0153-1

31. Drake RL, Vogl AW, Mitchell AWM. Gray's Anatomy for Students. 3rd ed. Churchill Livingstone; 2014.

32. Moore KL, Dalley AF, Agur AMR. Clinically Oriented Anatomy. 6th ed. Lippincott Williams and Wilkins; 2009.

33. Stacey DH, Doyle JF, Mount DL, Snyder MC, Gutowski KA. Management of Mandible Fractures. Plast Reconstr Surg. 2006;117(3):48e-60e. doi:10.1097/01.prs.0000209392.85221.0b

34. Lee KH. Epidemiology of mandibular fractures in a tertiary trauma centre. Emerg Med J. 2008;25(9):565-568. doi:10.1136/emj.2007.055236

35. Malanchuk V, Kopchak A. Risk factors for development of infection in patients with mandibular fractures located in the tooth-bearing area. J Craniomaxillofac Surg. 2007;35(1):57-62. doi:10.1016/J.JCMS.2006.07.865

36. Armond ACV, Martins CC, Glória JCR, Galvão EL, dos Santos CRR, Falci SGM. Influence of third molars in mandibular fractures. Part 1: mandibular angle—a meta-analysis. Int J Oral Maxillofac Surg. 2017;46(6):716-729. doi:10.1016/j.ijom.2017.02.1264

37. Moura LB, dos Santos Trento G, de Azambuja Carvalho PH, Granucci M, de Oliveira JCS, Pereira-Filho VA. Double unilateral, bilateral, and multiple mandibular fractures: an observational study. Oral Maxillofac Surg . 2018;22(3):315-321. doi:10.1007/S10006-018-0713-Y/METRICS

38. Ogundare BO, Bonnick A, Bayley N. Pattern of mandibular fractures in an urban major trauma center. J Oral Maxillofac Surg. 2003;61(6):713-718. doi:10.1053/joms.2003.50118

39. Simsek S, Simsek B, Abubaker AO, Laskin DM. A comparative study of mandibular fractures in the United States and Turkey. Int J Oral Maxillofac Surg. 2007;36(5):395-397. doi:10.1016/j.ijom.2006.11.010

40. Afrooz PN, Bykowski MR, James IB, Daniali LN, Clavijo-Alvarez JA. The Epidemiology of Mandibular Fractures in the United States, Part 1: A Review of 13,142 Cases from the US National Trauma Data Bank. J Oral Maxillofac Surg. 2015;73(12):2361-2366. doi:10.1016/j.joms.2015.04.032

41. Oikarinen K, Schutz P, Thalib L, et al. Differences in the etiology of mandibular fractures in Kuwait, Canada, and Finland. Dent Traumatol. 2004;20(5):241-245. doi:10.1111/j.1600-9657.2004.00243.x

42. Rashid A, Eyeson J, Haider D, van Gijn D, Fan K. Incidence and patterns of mandibular fractures during a 5-year period in a London teaching hospital. Br J Oral Maxillofac Surg. 2013;51(8):794-798. doi:10.1016/j.bjoms.2013.04.007

43. King RE, Scianna JM, Petruzzelli GJ. Mandible fracture patterns: A suburban trauma center experience. Am J Otolaryngol. 2004;25(5):301-307. doi:10.1016/j.amjoto.2004.03.001

44. Furr AM, Schweinfurth JM, May WL. Factors Associated with Long-Term Complications after Repair of Mandibular Fractures. Laryngoscope. 2006;116(3):427-430. doi:10.1097/01.MLG.0000194844.87268.ED

45. Lee K, Olsen J, Sun J, Chandu A. Alcohol-involved maxillofacial fractures. Aust Dent J. 2017;62(2):180-185. doi:10.1111/adj.12471

46. Munante-Cardenas JL, Facchina Nunes PH, Passeri LA. Etiology, Treatment, and Complications of Mandibular Fractures. J craniofac surg. 2015;26(3):611-615. doi:10.1097/SCS.0000000000001273

47. Lee K. Trend of alcohol involvement in maxillofacial trauma. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;107(4):e9-e13. doi:10.1016/j.tripleo.2008.12.020

48. O'Meara C, Witherspoon R, Hapangama N, Hyam D. Mandible fracture severity may be increased by alcohol and interpersonal violence. Aust Dent J. 2011;56(2):166-170. doi:10.1111/j.1834-7819.2011.01319.x

49. Serena-Gómez E, Passeri LA. Complications of Mandible Fractures Related to Substance Abuse. J Oral Maxillofac Surg. 2008;66(10):2028-2034. doi:10.1016/j.joms.2008.06.022

50. de Matos FP, Arnez MFM, Sverzut CE, Trivellato AE. A retrospective study of mandibular fracture in a 40-month period. Int J Oral Maxillofac Surg. 2010;39(1):10-15. doi:10.1016/j.ijom.2009.10.005

51. Schwab RA, Genners K, Robinson WA. Clinical predictors of mandibular fractures. Am J Emerg Med. 1998;16(3):304-305. doi:10.1016/S0735-6757(98)90108-5

52. Ceallaigh PO, Ekanaykaee K, Beirne CJ, Patton DW. Diagnosis and management of common maxillofacial injuries in the emergency department. Part 2: mandibular fractures. Emerg Med J. 2006;23(12):927-928. doi:10.1136/emj.2006.035956

53. Morrow BT, Samson TD, Schubert W, Mackay DR. Evidence-Based Medicine: Mandible Fractures. Plast Reconstr Surg. 2014;134(6):1381-1390. doi:10.1097/PRS.0000000000000717

54. Boron WF, Boulpaep EL. Medical Physiology. 2nd updated edition. Saunders; 2012.

55. Hupp JR, Ellis III E, Tucker MR. Contemporary Oral and Maxillofacial Surgery. Elsevier; 2013.

56. Luyk NH, Steinberg B. Aetiology and diagnosis of clinically evident jaw trismus. Aust Dent J. 1990;35(6):523-529. doi:10.1111/j.1834-7819.1990.tb04684.x

57. Tay ABG, Lai J Bin, Lye KW, et al. Inferior Alveolar Nerve Injury in Trauma-Induced Mandible Fractures. J Oral Maxillofac Surg. 2015;73(7):1328-1340. doi:10.1016/j.joms.2015.02.003

58. Naeem A, Gemal H, Reed D. Imaging in traumatic mandibular fractures. Quant Imaging Med Surg. 2017;7(4):469-479. doi:10.21037/qims.2017.08.06

59. Nardi C, Vignoli C, Pietragalla M, et al. Imaging of mandibular fractures: a pictorial review. Insights Imaging. 2020;11(1):30. doi:10.1186/s13244-020-0837-0

60. Wilson IF, Lokeh A, Benjamin CI, et al. Prospective Comparison of Panoramic Tomography (Zonography) and Helical Computed Tomography in the Diagnosis and Operative Management of Mandibular Fractures. Plast Reconstr Surg. 2001;107(6):1369-1375. doi:10.1097/00006534-200105000-00008

61. Aydin U, Gormez O, Yildirim D. Cone-beam computed tomography imaging of dentoalveolar and mandibular fractures. Oral Radiol. 2020;36(3):217-224. doi:10.1007/s11282-019-00390-5

62. Suskin JA, Rao V, Crozier JW, Yi T, Benz E, Woo AS. Re-evaluating the need for orthopantomography in the management of mandibular trauma: is computed tomography enough? Emerg Radiol. 2022;29(4):663-670. doi:10.1007/s10140-022-02049-x

63. Cohnen M, Kemper J, Möbes O, Pawelzik J, Mödder U. Radiation dose in dental radiology. Eur Radiol. 2002;12(3):634-637. doi:10.1007/s003300100928

64. Sklavos A, Beteramia D, Delpachitra SN, Kumar R. The panoramic dental radiograph for emergency physicians. Emerg Med J. 2019;36(9):565-571. doi:10.1136/emermed-2018-208332

65. Fonseca R, Barber D, Walker R, Powers M, Frost D. Oral and Maxillofacial Trauma. 4th ed. Saunders; 2012.

66. Bayram B, Araz K, Uckan S, Balcik C. Comparison of Fixation Stability of Resorbable Versus Titanium Plate and Screws in Mandibular Angle Fractures. J Oral Maxillofac Surg. 2009;67(8):1644-1648. doi:10.1016/j.joms.2009.03.011

67. Prein J, Kellman RM. Rigid internal fixation of mandibular fractures--basics of AO technique. Otolaryngol Clin North Am. 1987;20(3):441-456.

68. Ellis E. Open Reduction and Internal Fixation of Combined Angle and Body/Symphysis Fractures of the Mandible: How Much Fixation Is Enough? J Oral Maxillofac Surg. 2013;71(4):726-733. doi:10.1016/j.joms.2012.09.017

69. Ellis E. An Algorithm for the Treatment of Noncondylar Mandibular Fractures. J Oral Maxillofac Surg. 2014;72(5):939-949. doi:10.1016/j.joms.2013.11.026

70. Champy M, Loddé JP, Schmitt R, Jaeger JH, Muster D. Mandibular osteosynthesis by miniature screwed plates via a buccal approach. J Maxillofac Surg. 1978;6:14-21. doi:10.1016/S0301-0503(78)80062-9

71. Wong RCW, Tideman H, Kin L, Merkx MAW. Biomechanics of mandibular reconstruction: a review. Int J Oral Maxillofac Surg. 2010;39(4):313-319. doi:10.1016/j.ijom.2009.11.003

72. Ellis E, Miles BA. Fractures of the mandible: A technical perspective. Plast Reconstr Surg. 2007;120(7):76-89. doi:10.1097/01.prs.0000260721.74357.e7

73. Scolozzi P, Richter M. Treatment of severe mandibular fractures using AO reconstruction plates. J Oral Maxillofac Surg. 2003;61(4):458-461. doi:10.1053/joms.2003.50087

74. Sukegawa S, Kanno T, Masui M, et al. A retrospective comparative study of mandibular fracture treatment with internal fixation using reconstruction plate versus miniplates. J Craniomaxillofac Surg. 2019;47(8):1175-1180. doi:10.1016/j.jcms.2018.09.025

75. Forrest CR. Application of Minimal-Access Techniques in Lag Screw Fixation of Fractures of the Anterior Mandible. Plast Reconstr Surg. 1999;104(7):2127-2133. doi:10.1097/00006534-199912000-00028

76. Chrcanovic BR. Teeth in the line of mandibular fractures. Oral Maxillofac Surg. 2014;18(1):7-24. doi:10.1007/s10006-012-0369-y

77. Shah A, Perez-Otero S, Tran D, Aponte HA, Oh C, Agrawal N. Infection rates of an intraoral versus extraoral approach to mandibular fracture repairs are equal: A systematic review and meta-analysis. J Oral Maxillofac Surg. Published online January 2024. doi:10.1016/j.joms.2024.01.011

78. Nagargoje GL, Badal S, Mohiuddin SA, Balkunde AS, Jadhav SS, Bholane DR. Evaluation of Electrocautery and Stainless Steel Scalpel in Oral Mucoperiosteal Incision for Mandibular Anterior Fracture. Ann Maxillofac Surg. 2019;9(2):230-234. doi:10.4103/ams.ams_158_18

79. Barker DA, Oo KK, Allak A, Park SS. Timing for repair of mandible fractures. Laryngoscope. 2011;121(6):1160-1163. doi:10.1002/lary.21775

80. Hurrell MJL, David MC, Batstone MD. A prospective study examining the effects of treatment timing in the management of mandible fractures. Int J Oral Maxillofac Surg. 2018;47(9):1126-1131. doi:10.1016/j.ijom.2018.03.017

81. Lucca M, Shastri K, McKenzie W, Kraus J, Finkelman M, Wein R. Comparison of Treatment Outcomes Associated With Early Versus Late Treatment of Mandible Fractures: A Retrospective Chart Review and Analysis. J Oral Maxillofac Surg. 2010;68(10):2484-2488. doi:10.1016/j.joms.2010.01.024

82. Mehra P, Van Heukelom E, Cottrell DA. Rigid Internal Fixation of Infected Mandibular Fractures. J Oral Maxillofac Surg. 2009;67(5):1046-1051. doi:10.1016/j.joms.2008.12.036

83. Benson PD, Marshall MK, Engelstad ME, Kushner GM, Alpert B. The Use of Immediate Bone Grafting in Reconstruction of Clinically Infected Mandibular Fractures: Bone Grafts in the Presence of Pus. J Oral Maxillofac Surg. 2006;64(1):122-126. doi:10.1016/j.joms.2005.09.024

84. Shetty V, Schwartz HC. Wound Healing and Perioperative Care. Oral Maxillofac Surg Clin North Am. 2006;18(1):107-113. doi:10.1016/j.coms.2005.09.004

85. Guo S, DiPietro LA. Factors Affecting Wound Healing. J Dent Res. 2010;89(3):219-229. doi:10.1177/0022034509359125

86. Broughton G, Janis JE, Attinger CE. Wound Healing: An Overview. Plast Reconstr Surg. 2006;117:1e-S-32e-S. doi:10.1097/01.prs.0000222562.60260.f9

87. Silverstein P. Smoking and wound healing. Am J Med. 1992;93(1):S22-S24. doi:10.1016/0002-9343(92)90623-J

88. Marsell R, Einhorn TA. The biology of fracture healing. Injury. 2011;42(6):551-555. doi:10.1016/j.injury.2011.03.031

89. Phillips AM. Overview of the fracture healing cascade. Injury. 2005;36(3):S5-S7. doi:10.1016/j.injury.2005.07.027

90. Bresin A, Kiliaridis S, Strid KG. Effect of masticatory function on the internal bone structure in the mandible of the growing rat. Eur J Oral Sci. 1999;107(1):35-44. doi:10.1046/j.0909-8836.1999.eos107107.x

91. Wildemann B, Ignatius A, Leung F, et al. Non-union bone fractures. Nat Rev Dis Primers. 2021;7(1):57. doi:10.1038/s41572-021-00289-8

92. Iizuka T, Lindqvist C, Hallikainen D, Paukku P. Infection after rigid internal fixation of mandibular fractures: A clinical and radiologic study. J Oral Maxillofac Surg. 1991;49(6):585-593. doi:10.1016/0278-2391(91)90340-R

93. Domingo F, Dale E, Gao C, et al. A single-center retrospective review of postoperative infectious complications in the surgical management of mandibular fractures: Postoperative antibiotics add no benefit. J Trauma Acute Care Surg. 2016;81(6):1109-1114. doi:10.1097/TA.0000000000001232

94. Hall SC, Ofodile FA. Mandibular fractures in an American inner city: the Harlem Hospital Center experience. J Nati Med Assoc. 1991;83(5):421-423.

95. Janaphan K, Hashem I, Smith C, Holmes S, Chatzopoulou D. Periodontal disease as a primary cause of surgical site infection in fractures of the mandible: is smoking a confounding variable? Br J Oral Maxillofac Surg. 2022;60(10):1424-1429. doi:10.1016/j.bjoms.2022.08.001

96. Milic T, Raidoo P, Gebauer D. Antibiotic prophylaxis in oral and maxillofacial surgery: a systematic review. Br J Oral Maxillofac Surg. 2021;59(6):633-642. doi:10.1016/j.bjoms.2020.09.020

97. Fox AJ, Kellman RM. Mandibular angle fractures: Two-miniplate fixation and complications. Arch Facial Plast Surg. 2003;5(6):464-469. doi:10.1001/ARCHFACI.5.6.464

98. Ellis E, McFadden D, Simon P, Throckmorton G. Surgical complications with open treatment of mandibular condylar process fractures. J Oral Maxillofac Surg. 2000;58(9):950-958. doi:10.1053/joms.2000.8734

99. Hsueh WD, Schechter CB, Tien Shaw I, Stupak HD. Comparison of intraoral and extraoral approaches to mandibular angle fracture repair with cost implications. Laryngoscope. 2016;126(3):591-595. doi:10.1002/lary.25405

100. Chen MA, Davidson TM. Scar management: prevention and treatment strategies. Curr Opin Otolaryngol Head Neck Surg. 2005;13(4):242-247. doi:10.1097/01.moo.0000170525.74264.f8

101. Bede SYH, Ismael WK, Al-Assaf DA, Omer SS. Inferior Alveolar Nerve Injuries Associated With Mandibular Fractures. J Craniofac Surg. 2012;23(6):1776-1778. doi:10.1097/SCS.0b013e318266fda3

102. Iizuka T, Lindqvist C. Rigid internal fixation of mandibular fractures. Int J Oral Maxillofac Surg. 1992;21(2):65-69. doi:10.1016/S0901-5027(05)80533-8

103. Kanno T, Mitsugi M, Sukegawa S, Fujioka M, Furuki Y. Submandibular Approach Through the Submandibular Gland Fascia for Treating Mandibular Fractures Without Identifying the Facial Nerve. J Trauma Acute Care Surg. 2010;68(3):641-643. doi:10.1097/TA.0b013e31819ea15f

104. Mathog RH, Toma V, Clayman L, Wolf S. Nonunion of the mandible: An analysis of contributing factors. J Oral Maxillofac Surg. 2000;58(7):746-752. doi:10.1053/joms.2000.7258

105. Ostrander BT, Wang HD, Cusano A, Manson PN, Nam AJ, Dorafshar AH. Contemporary Management of Mandibular Fracture Nonunion—A Retrospective Review and Treatment Algorithm. J Oral Maxillofac Surg. 2018;76(7):1479-1493. doi:10.1016/j.joms.2018.01.027

106. Ellis E, Muniz O, Anand K. Treatment considerations for comminuted mandibular fractures. J Oral Maxillofac Surg. 2003;61(8):861-870. doi:10.1016/S0278-2391(03)00249-0

107. Rajantie H, Snäll J, Thorén H. Temporomandibular Dysfunction After Surgery of Mandibular Fractures Not Involving the Mandibular Condyle: A Prospective Follow-Up Study. J Oral Maxillofac Surg. 2019;77(8):1657-1662. doi:10.1016/j.joms.2019.03.034

108. Tabrizi R, Bahramnejad E, Mohaghegh M, Alipour S. Is the Frequency of Temporomandibular Dysfunction Different in Various Mandibular Fractures? J Oral Maxillofac Surg. 2014;72(4):755-761. doi:10.1016/j.joms.2013.10.018

109. Remschmidt B, Schwaiger M, Gaessler J, Wallner J, Zemann W, Schwaiger M. Surgical site infections in orthognathic surgery: prolonged versus single-dose antibiotic prophylaxis. Int J Oral Maxillofac Surg. 2023;52(2):219-226. doi:10.1016/j.ijom.2022.06.002

110. Miles BA, Potter JK, Ellis E. The efficacy of postoperative antibiotic regimens in the open treatment of mandibular fractures: A prospective randomized trial. J Oral Maxillofac Surg. 2006;64(4):576-582. doi:10.1016/J.JOMS.2006.01.003

111. Neu HC. The Crisis in Antibiotic Resistance. Science (1979). 1992;257(5073):1064-1073. doi:10.1126/science.257.5073.1064

112. Cheesman M, Ilanko A, Blonk B, Cock I. Developing new antimicrobial therapies: Are synergistic combinations of plant extracts/compounds with conventional antibiotics the solution? Pharmacogn Rev. 2017;11(22):57. doi:10.4103/phrev.phrev_21_17

113. Aas JA, Paster BJ, Stokes LN, Olsen I, Dewhirst FE. Defining the Normal Bacterial Flora of the Oral Cavity. J Clin Microbiol. 2005;43(11):5721-5732. doi:10.1128/JCM.43.11.5721-5732.2005

114. Deo P, Deshmukh R. Oral microbiome: Unveiling the fundamentals. J Oral Maxillofac Path. 2019;23(1):122. doi:10.4103/jomfp.JOMFP_304_18

115. Marsh PD. Role of the Oral Microflora in Health. Microbial Ecol Health Dis. 2000;12(3):130-137. doi:10.1080/089106000750051800

116. Hellstein JW, Marek CL. Candidiasis: Red and White Manifestations in the Oral Cavity. Head Neck Pathol. 2019;13(1):25-32. doi:10.1007/s12105-019-01004-6

117. Glick M, Siegel MA. Viral and fungal infections of the oral cavity in immunocompetent patients. Infect Dis Clin North Am. 1999;13(4):817-831. doi:10.1016/S0891-5520(05)70110-0

118. Coronado-Castellote L, Jimenez-Soriano Y. Clinical and microbiological diagnosis of oral candidiasis. J Clin Exp Dent. Published online 2013:e279-86. doi:10.4317/jced.51242

119. Lange K, Buerger M, Stallmach A, Bruns T. Effects of Antibiotics on Gut Microbiota. Dig Dis. 2016;34(3):260-268. doi:10.1159/000443360

120. McDonnell L, Gilkes A, Ashworth M, et al. Association between antibiotics and gut microbiome dysbiosis in children: systematic review and meta-analysis. Gut Microbes. 2021;13(1). doi:10.1080/19490976.2020.1870402

121. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. Lancet. 2019;393(10167):183-198. doi:10.1016/S0140-6736(18)32218-9

122. Gonzalez-Estrada A, Pien LC, Zell K, Wang XF, Lang DM. Antibiotics Are an Important Identifiable Cause of Perioperative Anaphylaxis in the United States. J Allergy Clin Immunol Pract. 2015;3(1):101-105.e1. doi:10.1016/j.jaip.2014.11.005

123. Bigby M. Rates of Cutaneous Reactions to Drugs. Arch Dermatol. 2001;137(6):765-770.

124. Kuruvilla M, Khan DA. Anaphylaxis to Drugs. Immunol Allergy Clin North Am. 2015;35(2):303-319. doi:10.1016/j.iac.2015.01.008

125. Gruchalla RS, Pirmohamed M. Antibiotic Allergy. N Engl J Med. 2006;354(6):601-609. doi:10.1056/NEJMcp043986

126. Dewhirst FE, Chen T, Izard J, et al. The Human Oral Microbiome. J Bacteriol. 2010;192(19):5002-5017. doi:10.1128/JB.00542-10

127. Brookes ZLS, Bescos R, Belfield LA, Ali K, Roberts A. Current uses of chlorhexidine for management of oral disease: a narrative review. J Dent. 2020;103:103497. doi:10.1016/J.JDENT.2020.103497

128. Poppolo Deus F, Ouanounou A. Chlorhexidine in Dentistry: Pharmacology, Uses, and Adverse Effects. Int Dent J. 2022;72(3):269-277. doi:10.1016/j.identj.2022.01.005

129. Fu J, Wei P, Zhao C, He C, Yan Z, Hua H. In vitro antifungal effect and inhibitory activity on biofilm formation of seven commercial mouthwashes. Oral Dis. 2014;20(8):815-820. doi:10.1111/odi.12242

130. Bernstein D, Schiff G, Echler G, Prince A, Feller M, Briner W. In vitro Virucidal Effectiveness of a 0.12%-Chlorhexidine Gluconate Mouthrinse. J Dent Res. 1990;69(3):874-876. doi:10.1177/00220345900690030901

131. Tartaglia GM, Tadakamadla SK, Connelly ST, Sforza C, Martín C. Adverse events associated with home use of mouthrinses: a systematic review. Ther Adv Drug Saf. 2019;10:204209861985488. doi:10.1177/2042098619854881

132. Alostath H, Chatzopoulou D, Holmes S, et al. A Novel Coating Onto Leonard Buttons; Surgical Site Infection Prevention In Mandibular Fractures. Int J Oral Maxillofac Surg. 2024;52:26. doi:10.1016/j.ijom.2023.10.080

133. DahlL JB, Nielsen R V., Wetterslev J, et al. Post-operative analgesic effects of paracetamol, NSAIDs, glucocorticoids, gabapentinoids and their combinations: a topical review. Acta Anaesthesiol Scand. 2014;58(10):1165-1181. doi:10.1111/aas.12382

134. Lovich-Sapola J, Smith CE, Brandt CP. Postoperative Pain Control. Surg Clin N Am. 2015;95(2):301-318. doi:10.1016/j.suc.2014.10.002

135. Kim K, Brar P, Jakubowski J, Kaltman S, Lopez E. The use of corticosteroids and nonsteroidal antiinflammatory medication for the management of pain and inflammation after third molar surgery: A review of the literature. Oral

Surg Oral Med Oral Pathol Oral Radiol. 2009;107(5):630-640. doi:10.1016/j.tripleo.2008.11.005

136. Katori M, Majima M. Cyclooxygenase-2: its rich diversity of roles and possible application of its selective inhibitors. Inflamm Res. 2000;49(8):367-392. doi:10.1007/s000110050605

137. Rao P, Knaus EE. Evolution of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): Cyclooxygenase (COX) Inhibition and Beyond. J Pharm Pharm Sci. 2008;11(2):81. doi:10.18433/J3T886

138. Chaiamnuay S, Allison JJ, Curtis JR. Risks versus benefits of cyclooxygenase-2-selective nonsteroidal antiinflammatory drugs. Am J Health-Syst Pharm. 2006;63(19):1837-1851. doi:10.2146/ajhp050519

139. Chen LC, Ashcroft DM. Risk of myocardial infarction associated with selective COX-2 inhibitors: Meta-analysis of randomised controlled trials. Pharmacoepidemiol Drug Saf. 2007;16(7):762-772. doi:10.1002/pds.1409

140. Jones SC. Relative Thromboembolic Risks Associated with COX-2 Inhibitors. Ann Pharmacother. 2005;39(7-8):1249-1259. doi:10.1345/aph.1E654

141. Scheiman JM. NSAID-induced Gastrointestinal Injury. J Clin Gastroenterol. 2016;50(1):5-10. doi:10.1097/MCG.0000000000000432

142. Ghanem CI, Pérez MJ, Manautou JE, Mottino AD. Acetaminophen from liver to brain: New insights into drug pharmacological action and toxicity. Pharmacol Res. 2016;109:119-131. doi:10.1016/j.phrs.2016.02.020

143. Ohashi N, Kohno T. Analgesic Effect of Acetaminophen: A Review of Known and Novel Mechanisms of Action. Front Pharmacol. 2020;11. doi:10.3389/fphar.2020.580289

144. Prescott LF. Paracetamol, alcohol and the liver. Br J Clin Pharmacol. 2000;49(4):291-301. doi:10.1046/j.1365-2125.2000.00167.x

145. Carr DB, Goudas LC. Acute pain. Lancet. 1999;353(9169):2051-2058. doi:10.1016/S0140-6736(99)03313-9

146. Al-Hasani R, Bruchas MR. Molecular Mechanisms of Opioid Receptor-dependent Signaling and Behavior. Anesthesiology. 2011;115(6):1363-1381. doi:10.1097/ALN.0b013e318238bba6

147. Lötsch J, Dudziak R, Freynhagen R, Marschner J, Geisslinger G. Fatal Respiratory Depression after Multiple Intravenous Morphine Injections. Clin Pharmacokinet. 2006;45(11):1051-1060. doi:10.2165/00003088-200645110-00001

148. Dang VC, Christie MJ. Mechanisms of rapid opioid receptor desensitization, resensitization and tolerance in brain neurons. Br J Pharmacol. 2012;165(6):1704-1716. doi:10.1111/j.1476-5381.2011.01482.x

149. Korff M Von, Saunders K, Thomas Ray G, et al. De Facto Long-term Opioid Therapy for Noncancer Pain. Clin J Pain. 2008;24(6):521-527. doi:10.1097/AJP.0b013e318169d03b

150. Crews KR, Gaedigk A, Dunnenberger HM, et al. Clinical Pharmacogenetics Implementation Consortium Guidelines for Cytochrome P450 2D6 Genotype and Codeine Therapy: 2014 Update. Clin Pharmacol Ther. 2014;95(4):376-382. doi:10.1038/clpt.2013.254

151. Stamer UM, Stüber F, Muders T, Musshoff F. Respiratory Depression with Tramadol in a Patient with Renal Impairment and CYP2D6 Gene

Duplication. Anesth Analg. 2008;107(3):926-929. doi:10.1213/ane.0b013e31817b796e

152. Ciszkowski C, Madadi P, Phillips MS, Lauwers AE, Koren G. Codeine, Ultrarapid-Metabolism Genotype, and Postoperative Death. N Engl J Med. 2009;361(8):827-828. doi:10.1056/NEJMc0904266

153. Alyahya A, Aldubayan A, Swennen GRJ, Al-Moraissi E. Effectiveness of different protocols to reduce postoperative pain following orthognathic surgery: A systematic review and meta-analysis. Br J Oral Maxillofac Surg. 2022;60(7):e1-e10. doi:10.1016/j.bjoms.2022.03.013

154. Barreveld A, Witte J, Chahal H, Durieux ME, Strichartz G. Preventive Analgesia by Local Anesthetics: The Reduction of Postoperative Pain by Peripheral Nerve Blocks and Intravenous Drugs. Anesth Analg. 2013;116(5):1141-1161. doi:10.1213/ANE.0b013e318277a270

155. Taylor A, McLeod G. Basic pharmacology of local anaesthetics. BJA Educ. 2020;20(2):34-41. doi:10.1016/j.bjae.2019.10.002

156. Becker DE, Reed KL. Essentials of local anesthetic pharmacology. Anesth Prog. 2006;53(3):98-108; quiz 109-110. doi:10.2344/0003-3006(2006)53[98:EOLAP]2.0.CO;2

157. Santini G, Patrignani P, Sciulli M, et al. The human pharmacology of monocyte cyclooxygenase 2 inhibition by cortisol and synthetic glucocorticoids. Clin Pharmacol Ther. 2001;70(5):415-424. doi:10.1016/S0009-9236(01)14130-5

158. Dionne RA, Gordon SM, Rowan J, Kent A, Brahim JS. Dexamethasone suppresses peripheral prostanoid levels without analgesia in a clinical model of acute inflammation. J Oral Maxillofac Surg. 2003;61(9):997-1003. doi:10.1016/S0278-2391(03)00310-0

159. Granner DK, Wang JC, Yamamoto KR. Regulatory actions of glucocorticoid hormones: From organisms to mechanisms. AdvExp Med Biol. 2015;872:3-31. doi:10.1007/978-1-4939-2895-8_1/COVER

160. Paragliola RM, Papi G, Pontecorvi A, Corsello SM. Treatment with Synthetic Glucocorticoids and the Hypothalamus-Pituitary-Adrenal Axis. Int J Mol Sci. 2017;18(10):2201. doi:10.3390/ijms18102201

161. Haapanen A, Thorén H, Apajalahti S, Suominen AL, Snäll J. Does Dexamethasone Facilitate Neurosensory Function Regeneration After Zygomatic Fracture? A Randomized Controlled Trial. J Oral Maxillofac Surg. 2017;75(12):2607-2612. doi:10.1016/j.joms.2017.08.009

162. Haapanen A, Thorén H, Apajalahti S, Suominen AL, Snäll J. Neurosensory recovery after trauma to the orbital floor: a prospective trial with dexamethasone. Br J Oral Maxillofac Surg. 2018;56(9):810-813. doi:10.1016/j.bjoms.2018.08.017

163. de Lima VN, Lemos CAA, Faverani LP, Santiago Júnior JF, Pellizzer EP. Effectiveness of Corticoid Administration in Orthognathic Surgery for Edema and Neurosensorial Disturbance: A Systematic Literature Review. J Oral Maxillofac Surg. 2017;75(7):1528.e1-1528.e8. doi:10.1016/j.joms.2017.03.039

164. Henzi I, Walder B, Tramèr MR. Dexamethasone for the Prevention of Postoperative Nausea and Vomiting: A Quantitative Systematic Review. Anesth Analg. 2000;90(1):186-194. doi:10.1097/00000539-200001000-00038

165. Haapanen A, Thorén H, Törnwall J, Suominen AL, Snäll J. Postoperative nausea and vomiting in facial fracture patients: A Randomized and controlled trial on the effect of dexamethasone. Int J Oral Maxillofac Surg. 2017;46(10):1267-1270. doi:10.1016/j.ijom.2017.03.026

166. Antunes AA, Avelar RL, Martins Neto EC, Frota R, Dias E. Effect of two routes of administration of dexamethasone on pain, edema, and trismus in impacted lower third molar surgery. Oral Maxillofac Surg. 2011;15(4):217-223. doi:10.1007/s10006-011-0290-9

167. Fardet L, Fève B. Systemic Glucocorticoid Therapy: a Review of its Metabolic and Cardiovascular Adverse Events. Drugs. 2014;74(15):1731-1745. doi:10.1007/s40265-014-0282-9

168. García Rodríguez LA, Hernández-Díaz S. The risk of upper gastrointestinal complications associated with nonsteroidal anti-inflammatory drugs, glucocorticoids, acetaminophen, and combinations of these agents. Arthritis Res. 2001;3(2):98. doi:10.1186/ar146

169. Snäll J, Törnwall J, Suominen AL, Thorén H. Postoperative leukocyte changes in facial fracture patients: a randomized prospective study with short-term dexamethasone. Oral Maxillofac Surg. 2017;21(2):241-246. doi:10.1007/s10006-017-0623-4

170. Snäll J, Törnwall J, Suominen AL, Thorén H. Behavior of C-reactive protein in association with surgery of facial fracture and the influence of dexamethasone. Oral Maxillofac Surg. 2018;22(2):129-134. doi:10.1007/s10006-018-0678-x

171. Snäll J, Kormi E, Koivusalo AM, et al. Effects of perioperatively administered dexamethasone on surgical wound healing in patients undergoing surgery for zygomatic fracture: a prospective study. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;117(6):685-689. doi:10.1016/j.0000.2014.02.033

172. Thorén H, Snäll J, Kormi E, et al. Does Perioperative Glucocorticosteroid Treatment Correlate With Disturbance in Surgical Wound Healing After Treatment of Facial Fractures? A Retrospective Study. J Oral Maxillofac Surg. 2009;67(9):1884-1888. doi:10.1016/j.joms.2009.04.089

173. Kainulainen S, Törnwall J, Koivusalo AM, Suominen AL, Lassus P. Dexamethasone in head and neck cancer patients with microvascular reconstruction: No benefit, more complications. Oral Oncol. 2017;65:45-50. doi:10.1016/j.oraloncology.2016.12.008

174. Kainulainen S, Aro K, Koivusalo AM, et al. Perioperative Dexamethasone Is Associated With Higher Short-Term Mortality in Reconstructive Head and Neck Cancer Surgery. J Oral Maxillofac Surg. 2020;78(10):1835-1845. doi:10.1016/j.joms.2020.05.004

175. Champy M, Lodde JP. Mandibular synthesis. Placement of the synthesis as a function of mandibular stress (in French). Rev Stomatol Chir Maxillofac. 1976;77(8):971-976.

176. Alcohol abuse. Current Care Guidelines. Working group appointed by the Finnish Medical Society Duodecim and the Finnish Society of Addiction Medicine: Treatment of alcohol abuse [Internet]. The Finnish Medical Society Duodecim. 2018. [cited 2024 Jan 15]. Available from: www.kaypahoito.fi/.

177. Mattila K, Nieminen M, Valtonen V, et al. Association between dental health and acute myocardial infarction. BMJ. 1989;298(6676):779-781. doi:10.1136/bmj.298.6676.779

178. Virtanen E, Nurmi T, Söder PÖ, Airila-Månsson S, Söder B, Meurman JH. Apical periodontitis associates with cardiovascular diseases: a cross-sectional study from Sweden. BMC Oral Health. 2017;17:1. doi:10.1186/s12903-017-0401-6

179. Cornelius CP, Audigé L, Kunz C, et al. The Comprehensive AOCMF Classification System: Mandible Fractures-Level 3 Tutorial. Craniomaxillofac Trauma Reconstr. 2014;7(1):31-43. doi:10.1055/s-0034-1389558

180. Jerjes W, El-Maaytah M, Swinson B, et al. Experience versus complication rate in third molar surgery. Head Face Med. 2006;2(14). doi:10.1186/1746-160X-2-14

181. Wu JX, Nguyen AT, de Virgilio C, et al. Can it wait until morning? A comparison of nighttime versus daytime cholecystectomy for acute cholecystitis. Am J Surg. 2014;208(6):911-918. doi:10.1016/j.amjsurg.2014.09.004

182. Kelz RR, Freeman KM, Hosokawa PW, et al. Time of Day Is Associated With Postoperative Morbidity. Ann Surg. 2008;247(3):544-552. doi:10.1097/SLA.0b013e31815d7434

183. Yaghoubian A, Kaji AH, Putnam B, de Virgilio C. Trauma Surgery Performed By "Sleep Deprived" Residents: Are Outcomes Affected? J Surg Educ. 2010;67(6):449-451. doi:10.1016/j.jsurg.2010.09.003

184. Busse J, Bhandari M, Devereaux PJ. The impact of time of admission on major complications and mortality in patients undergoing emergency trauma surgery. Acta Orthop Scand. 2004;75(3):333-338. doi:10.1080/00016470410001286

185. Sundheepkumar V, Saravanan R, Krishnan B. Infectious complications in compound mandibular fractures undergoing a delayed surgical intervention – a prospective observational study. Br J Oral Maxillofac Surg. 2023;61(4):302-308. doi:10.1016/j.bjoms.2023.03.008

186. Kannari L, Marttila E, Toivari M, Thorén H, Snäll J. Paediatric mandibular fracture—a diagnostic challenge? Int J Oral Maxillofac Surg. 2020;49(11):1439-1444. doi:10.1016/j.ijom.2020.06.008

187. Kannari L, Marttila E, Thorén H, Toivari M, Snäll J. Mandibular fractures in aged patients – Challenges in diagnosis. Dent Traumatol. 2022;38(6):487-494. doi:10.1111/edt.12778

188. Perepa A, Sinha R, Agarwal A, Khan TA. Protocol for Antibiotic Administration in Mandibular Trauma: A Prospective Clinical Trial. J Maxillofac Oral Surg. 2018;17(1):19-23. doi:10.1007/S12663-016-0964-9

189. Dongol A, Jaisani MR, Pradhan L, Dulal S, Sagtani A. A Randomized Clinical Trial of the Effects of Submucosal Dexamethasone After Surgery for Mandibular Fractures. J Oral Maxillofac Surg. 2015;73(6):1124-1132. doi:10.1016/j.joms.2014.12.042

190. Kormi E, Thorén H, Snäll J, Törnwall J. The Effect of Dexamethasone on Pain Severity After Zygomatic Complex Fractures. J Craniofac Surg. 2019;30(3):742-745. doi:10.1097/SCS.0000000000005188

191. Kormi E, Snäll J, Koivusalo AM, Suominen AL, Thorén H, Törnwall J. Analgesic Effect of Perioperative Systemic Dexamethasone on Blowout Fracture Surgery. J Oral Maxillofac Surg. 2017;75(6):1232-1237. doi:10.1016/j.joms.2016.09.026

192. Almeida R de AC, Lemos CAA, de Moraes SLD, Pellizzer EP, Vasconcelos BC. Efficacy of corticosteroids versus placebo in impacted third molar surgery: systematic review and meta-analysis of randomized controlled trials. Int J Oral Maxillofac Surg. 2019;48(1):118-131. doi:10.1016/j.ijom.2018.05.023

193. Perretti M, Ahluwalia A. The Microcirculation and Inflammation: Site of Action for Glucocorticoids. Microcirculation. 2000;7(3):147-161. doi:10.1080/mic.7.3.147.161

194. Nauck M, Karakiulakis G, Perruchoud AP, Papakonstantinou E, Roth M. Corticosteroids inhibit the expression of the vascular endothelial growth factor gene in human vascular smooth muscle cells. Eur J Pharmacol. 1998;341(2-3):309-315. doi:10.1016/S0014-2999(97)01464-7