An Analysis of Etiological Factors for Traumatic Mandibular Osteomyelitis

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Key words: *mandibular fracture; traumatic osteomyelitis; etiology of osteomyelitis.*

Summary. *Objective. The aim of this study was to analyze the factors that were associated with the development of osteomyelitis during the treatment of mandibular fractures.*

Material and Methods. The data of 3188 patients with mandibular fractures treated during 2002–2009 were analyzed. Traumatic osteomyelitis of the mandible was diagnosed in 207 patients. The background factors of complications were studied and compared with the control group (100 patients) not having complications after treatment of mandibular fractures. The data of clinical, roentgenologic, microbiological, and immunological investigations were analyzed. A logistic regression model was developed to identify the factors for osteomyelitis development.

Results. The treatment in 6.5% of patients was complicated with osteomyelitis; 88.5% of these patients were men, and more than 80% of patients were younger than 50 years. In 86.8% of cases, Staphylococcus species were isolated, with Staphylococcus aureus accounting for 69.1% of cases. The following factors were found to be associated with osteomyelitis development: immunity dysfunction, caries-affected teeth at the fracture line, mobile fractured bones, bone fixation after more than 7 days following trauma, healthy teeth at the fracture line, insufficient bone reposition, and bone fixation after 3–7 days following trauma.

Conclusion. Comparative analysis of factors influencing the treatment results revealed a great importance of immunological and dental status and microflora at the affected site. Insufficient or late reposition and fixation of fractured bone fragments play a significant role in the healing process.

Introduction

Face region is very susceptible to trauma as it is the most exposed part of the body (1). Fractures of the mandible account for 63.0%–95.0% of all fractures occurring in the face region (2–5). The overall rate of mandibular fractures is reported to be more than 11 cases per 100 000 person-years (6).

Traumatic osteomyelitis is one of the most severe complications after mandibular fracture, with an incidence being 2.9% to 14.0% (7–9). The majority of patients with traumatic osteomyelitis are aged between 20 and 50 years (10). For these reasons, the traumatic osteomyelitis of the mandible is a relevant problem in medical, socioeconomic, and psychological aspects (11, 12), because able-bodied population at their best age becomes temporarily disabled, and this leads to limited professional and social activities.

Rational prophylaxis of this disease is possible only with good knowledge of predisposing factors. Unfortunately, there is a lack of literature data with integrated analysis on this topic. Many authors just mention the frequency of this complication after various treatment methods of a fractured mandible (13), while others give the percentage of all treated cases (14, 15).

Thus, the aim of this study was to analyze the possible factors that may predispose osteomyelitis during the treatment of mandibular fractures.

Material and Methods

A total of 3188 patients with mandibular fractures were treated during 2002–2009, and in 207 cases (6.5%), the fracture healing process was complicated with osteomyelitis. The study group comprised 207 patients with osteomyelitis (OST group), and 100 randomly selected patients were enrolled in the control group (control group). The patients in the control group did not have any complications of mandibular fracture healing.

The following factors, which may have had an impact on the development of traumatic mandibular osteomyelitis, were analyzed: patient gender and age, fracture localization, time from trauma to treatment, teeth relation to the fracture site, the condition of teeth not involved in a fracture, quality of fractured bone reposition, method of fractured bone fixation, and concomitant diseases. Immunological investigation (flow cytometry with monoclonal antibodies) was performed in 50 randomly selected

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patients in both the groups with a dual-laser flow cytometer FACScabibub (Bectron Dickinson, US). All the patients in the OST group underwent microbiological testing to determine aerobes and anaerobes. Because this study focused on traumatic osteomyelitis, no bacterioscopic analysis to determine actinomycetes was performed. All the patients were evaluated for orthopantomography data.

Statistical analysis was performed, and the results were tested for statistical significance using SPSS 15.0 for Windows. Statistical analysis included descriptive statistics; the Student *t* test was used to compare two groups. The level of significance was set at $P<0.05$. A logistic regression binary model was developed to identify the factors associated with osteomyelitis development.

Results

Age and Gender. The distribution of patients by gender and age did not differ significantly. The data in Table 1 show that 88.4% of patients in the OST group were male compared with 89.0% of male patients in the control group, where no complications occurred during healing.

In the OST and control groups, the distribution of patients aged less than 60 years by age was similar. Even though there were more patients older than 60 years in the OST group (9.4%) compared with the control group (5%), this difference was not statistically significant ($P>0.05$).

Fracture Localization. Patients in the OST group with double fractures in the body of the mandible or both the body of the mandible and ascending ramus accounted for 85.0% of cases (Table 2), while 15.0% of patients had a single fracture in the body of the mandible.

Table 1. The Distribution of Patients by Age and Gender

Characteristic	All Patients N=3188	OST Group N=207	Control Group N=100
Gender			
Male	2828 (88.7)	183 (88.4)	89 (89.0)
Female	360 (11.3)	24 (11.6)	11 (11.0)
Age, years			
15–44	2563 (80.4)	157 (75.8)	80 (80.0)
45–59	469 (14.7)	31 (15.0)	15 (15.0)
60–74	156 (4.9)	19 (9.2)	5 (5.0)
>74	0 (0)	0 (0)	0 (0)

Values are number (percentage).

Wounds in the Face Region or Mouth. In the OST group, 7.4% of patients with osteomyelitis had wounds in their face or mouth mucosa (2 to 8 cm in size) (Table 3). The same type of wounds was also found in 6.0% of patients who did not develop complications during healing (control group).

Time of Bone Reposition and Permanent Fixation. Permanent fixation of fractured bones was performed more than two days after trauma in more than 90% of patients in the OST group (Table 3), while there were only 30.0% of such patients in the control group ($P<0.001$). Therefore, if appropriate treatment methods are applied more than two days after trauma, such patients are more likely to develop osteomyelitis development.

Quality of Fractured Bone Reposition. Reposition of a fractured bone was considered sufficient, if a fracture gap was not less than 1 mm and not greater than 3 mm, and bone dislocation in any direction was not greater than 3 mm. These values were chosen according to the experimental data from the study by Lavrisceva and Dubrov (16), which demonstrated that normal reparative regeneration of a fractured bone took place under previously mentioned conditions.

More than half (54.1%) of patients in the OST group had insufficient bone reposition, while there were only 10.0% of such cases in the control group ($P<0.001$).

Fractured Bone Fixation Method. A total of 25 patients in the OST group did not have any bone fixation applied, and there were no such patients in the control group ($P<0.001$). Fractured bones were fixated with intermaxillary wiring, Kirschner wire combined with intermaxillary wiring, or miniplate osteosynthesis. The distribution of patients according to the fractured bone fixation method in the OST and control groups did not differ significantly (Table 3).

Teeth Relation to Fracture Line. At the beginning of the treatment, caries-affected teeth were not removed from the fracture line for 17 patients, and

Table 2. The Distribution of Patients by Fracture Type and Localization

Fracture Type and Localization	All Patients N=3188	OST Group N=207	Control Group N=100
Single fracture			
Body of the mandible	1677 (52.6)	31 (15.0)	39 (39.0)
Ascending ramus	140 (4.4)	0 (0)	7 (7.0)
Double fracture			
Body of the mandible	995 (31.2)	151 (72.9)	42 (42.0)
Ascending ramus	67 (2.1)	0 (0)	0 (0)
Body of the mandible and ramus	252 (7.9)	25 (12.1)	12 (12.0)
Multiple fracture	57 (1.8)	0 (0)	0 (0)

Values are number (percentage).

Table 3. Incidence and Influence of Factors to Osteomyelitis Development

Factor	OST Group	Control group	P value
Wounds in the face or mouth	15 (7.4)	6 (6.0)	>0.05
Time of fractured bone reposition after trauma			
1–2 days	19 (9.2)	70 (70.0)	<0.001
2–7 days	151 (72.9)	28 (28.0)	<0.001
>7 days	37 (17.9)	2 (2.0)	<0.001
Reposition quality			
Good	95 (45.9)	90 (90.0)	<0.001
Insufficient	112 (54.1)	10 (10.0)	<0.001
Fractured bone fixation methods			
Not fixated	25 (12.2)	0 (0)	<0.001
Intermaxillary wiring	89 (43.2)	40 (40.0)	>0.05
Kirschner wire	46 (22.3)	30 (30.0)	>0.05
Miniplate osteosynthesis	71 (34.5)	30 (30.0)	>0.05
Dental status			
Caries-affected teeth at the fracture line	17 (8.1)	12 (12.0)	>0.05
Not removed	17 (8.1)	0 (0)	<0.001
Intact teeth at the fracture line	70 (33.8)	28 (28.0)	>0.05
Not removed	45 (21.6)	4 (4.0)	<0.001
Caries-affected teeth not at the fracture line	54 (26.3)	25 (25.0)	>0.05
Not removed	15 (7.4)	5 (5.0)	>0.05
Concomitant diseases			
Cardiovascular	13 (6.1)	7 (7.1)	>0.05
Respiratory	4 (2.0)	3 (3.0)	>0.05
Gastrointestinal	15 (7.4)	9 (9.0)	>0.05
Urogenital	4 (2.0)	0 (0)	>0.05
Oncologic	0 (0)	1 (10)	>0.05
Tuberculosis	6 (2.7)	0 (0)	>0.05
Diabetes mellitus	3 (2.0)	0 (0)	>0.05

Values are number (percentage).

they all developed osteomyelitis (Table 3, OST group). Twelve patients in the control group had their caries-affected teeth removed from the fracture site before applying bone reposition and permanent fixation; however, the difference was not significant. Moreover, there were no significant differences in the percentage of patients having intact teeth at the fracture line or having caries-affected teeth not at the fracture line comparing the groups ($P>0.05$).

Concomitant Diseases. There were no significant differences in the occurrence of concomitant diseases comparing both the groups.

Immunity. Cellular immunity was investigated in 50 patients with osteomyelitis and 50 patients in the control group (Table 4). All patients with osteomyelitis had some kind of immunity pathology: cellular immunity dysfunction and reduced phagocytosis.

Microflora. Aerobes and anaerobes were cultivated from the infected bone sites, and in most cases, staphylococcus and streptococcus species dominated (bacterioscopic examination was not performed). *Staphylococcus* spp. was found in 86.8% of patients with osteomyelitis, and 42.0% were streptococci. It should be noted that 69.1% of patients with osteomyelitis had *Staphylococcus aureus*; therefore, only resistance of this pathogen to antibiotics was tested (Table 5).

Table 6 shows various factors associated with osteomyelitis development after mandibular fractures, determined by logistic regression.

Table 4. Lymphocyte Phenotype Data

Lymphocyte Phenotype	OST Group N=50	Control Group N=50
CD3 (T lymphocytes)	66.4 (5.3)	50.2 (3.6)
CD4 (T helpers-inductors)	31.3 (2.8)	46.7 (2.8)
CD8 (T suppressors-cytotoxic)	24.6 (1.3)	29.3 (4.6)
CD19 (B lymphocytes)	4.2 (1.1)	12.1 (1.7)
CD56/16 (natural killers)	7.8 (2.4)	16.4 (2.9)
CD4/CD8 ratio	1.1 (0.4)	1.59 (0.4)
Phagocytosis index	42.9 (4.3)	80.6 (4.2)

Values are percentage (SD).

Discussion

A common complication of mandibular fractures is traumatic osteomyelitis. A total of 3188 patients with mandibular fractures were treated, and 6.5% developed osteomyelitis. These data are consistent with the data of other studies, showing a frequency of osteomyelitis to be 5.3% to 6.5% (13, 14, 17). However, some authors provide a very different frequency of traumatic mandibular osteomyelitis. According to Luhr and Hausmann (18), the frequency of this complication is 0.87%; Fox and Kellman (8), 2.9%; Patrocinio et al. (9) and Biller et al. (15), 10.0%–13.1%; and Gutwald (19), 20%–30%. This and almost all other studies show that the majority of patients with osteomyelitis are men younger than 50 years (20).

The development of osteomyelitis is influenced by local and systemic factors. Some of them are directly involved in etiopathogenesis; others predis-

Table 5. Resistance of *Staphylococcus Aureus* to Antibiotics

Antibiotic	Resistance, %
Ampicillin	80.0
Cefuroxime	18.5
Ciprofloxacin	18.5
Clindamycin	22.2
Erythromycin	25.9
Fucidin	0.0
Gentamycin	18.5
Methicillin	21.7
Oxacillin	25.0
Penicillin	100.0
Rifampicin	0.0
Tetracycline	37.0
Vancomycin	0.0

Table 6. Factors Associated with Osteomyelitis Development (Logistic Regression Analysis)

Factor	OR	95% CI
Immunity dysfunction	7.7	2.4–12.3
Caries-affected teeth at the fracture line	7.2	2.1–6.5
Not fixated fractured bone	6.3	1.8–7.2
Bone fixation after more than 7 days after trauma	5.1	2.7–5.3
Intact teeth at the fracture line	4.8	3.2–9.5
Insufficient bone reposition	3.1	1.9–6.4
Bone fixation after 3–7 days after trauma	1.5	1.8–3.4
Double fracture in a dental arch	1.3	1.1–5.3

OR, odds ratio; CI, confidence interval.

pose osteomyelitis development. There is no doubt that osteomyelitis etiopathogenesis is directly associated with microorganisms. This study showed a predominance of staphylococci (86.8% of cases) in the affected bone site, and the most common was *Staphylococcus aureus* (69.1%) resistant to several antibiotics. These results are similar to other studies. According to Calhoun et al. (21), polymicroflora causes 93% of cases of mandibular osteomyelitis. Sands et al. (22) found that in 80% of cases, staphylococci predominated at the affected bone site, and 56% of them were *Staphylococcus aureus*. According to latter authors, anaerobic bacteria are found in 59.9% of cases. Similar results on microflora in osteomyelitis-affected bone site were demonstrated in the studies by Brook (23), Lima et al. (24), and Vasconcelos et al. (12). For osteomyelitis to develop at the fracture site, not only the pathogenicity of microorganisms is important, but also some other local and systemic factors. One of the predisposing factors for osteomyelitis development is organism's inability to fight pathogenic bacteria, which invade the fracture site, when the immune system is weak. This study confirms such statement. Patients with osteomyelitis had cellular immunity dysfunction and reduced phagocytosis.

A direct source of microorganisms is caries-affected teeth in a fracture site. Our study indicates that this factor is significant for osteomyelitis development. Intact teeth at the fracture site are also an important factor predisposing osteomyelitis. They are not only a direct source of infection at the fracture site, but also if not removed, make a pathway for infection and disturb normal reparative regeneration. Besides, developing pulp necrosis due to affected innervation and blood circulation may directly influence the development of inflammation at the fracture site. That is why we agree with an opinion that all teeth at the fracture line should be removed before permanent fractured bone immobilization (25). However, some authors suggest leaving intact teeth at the fracture site (26).

According to our study data, not fixated or improperly reponated and fixated fractured bone fragments are significant factors predisposing osteomyelitis. However, these are not direct factors determining this complication. To our knowledge, there are some clinical cases, when not fixated or improperly reponated fractured bone fragments heal without complications but incorrectly positioned.

According to Lukjanenko (27), when the necessary specialized treatment is given during the first day after trauma, osteomyelitis develops in 6% of patients. If patients are treated after 2–7 days, complications develop in 16% to 18% of cases. When a specialized aid is given after more than one week, a chance of developing osteomyelitis rises several times. We agree with this author's opinion, as according to our study data, one of the most important factors influencing the development of traumatic mandibular osteomyelitis was the reposition of bone fragments and fixation after more than two days following trauma.

The impact of fracture localization in the development of traumatic mandibular osteomyelitis was analyzed, and patients with double fractures in the mandibular body developed osteomyelitis more often than those with a single fracture.

According to our data, wounds in the face and mouth and concomitant diseases did not have a significant impact on osteomyelitis development. Some authors indicate that endocrine and other systemic diseases (28, 29) and trauma to surrounding tissue (30) slow the healing of a fractured bone down and increase the risk of infection. We agree with this opinion that severe systemic diseases may alter the immune system and predispose complications during fracture healing. However, the majority of our patients were young, and only some of them had systemic diseases in remission phase, thus this factor was not significant for osteomyelitis development.

Rudman et al. (31) performed a photoelastic analysis of osteosynthesis with a supraperiosteal miniplate for the fractured mandible and reported along with Champy et al. (32), who analyzed clinical data, that an excessive force holding the miniplate on bone with screws might be the main cause

of complications after osteosynthesis. However, our study did not show a significant difference in the occurrence of osteomyelitis after osteosynthesis with supraperiosteal miniplate versus intermaxillary wire or Kirschner wire fixation.

Our study data indicate that various factors determine the development of traumatic mandibular osteomyelitis. It is hard to tell which factor was responsible for development of osteomyelitis in a particular patient. Usually, every patient with traumatic osteomyelitis has several factors, which may have predisposed the development of such complication. Our logistic regression analysis showed that these factors were of different significance for osteomyelitis development.

Conclusions

Healing complications after mandibular fractures are an important problem not only medically, but also socially and economically. Various factors of different importance predispose the development of traumatic mandibular osteomyelitis. Logistic regression showed the following factors to be significant in the development of osteomyelitis in the fractured mandible: immunity dysfunction, oral microflora, caries-affected or intact teeth at the fracture line, mobile bone fragments, insufficient reposition, and late fixation of bone fragments after trauma.

Statement of Conflict of Interest

The authors state no conflict of interest.

Apatinio žandikaulio trauminio osteomielito etiologinių veiksnių analizė

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Raktažodžiai: apatinio žandikaulio lūžiai, trauminis osteomielitas, osteomielito etiologija.

Santrauka. *Tyrimo tikslas.* Šio tyrimo tikslas buvo išanalizuoti veiksnius, turinčius įtakos trauminiam apatinio žandikaulio osteomielitui išsivystyti.

Tyrimo medžiaga ir metodai. Išnagrinėti 3188 pacientų, gydytų dėl apatinio žandikaulio lūžių 2002–2009 m., duomenys. Trauminis apatinio žandikaulio osteomielitas diagnozuotas 207 pacientams. Išanalizuoti etiologiniai trauminio apatinio žandikaulio osteomielito veiksniai palyginti su kontrolinės pacientų grupės (100 pacientų), kuriems apatinio žandikaulio lūžiai sugijo be komplikacijų, duomenimis. Įvertinti kliniki-niai, radiologiniai, mikrobiologiniai ir imunologiniai duomenys. Statistinė veiksnių, lemiančių trauminio apatinio žandikaulio išsivystymą, analizė atlikta naudojant logistinės regresijos modelį.

Rezultatai. 6,5 proc. pacientų apatinio žandikaulio lūžiai komplikavosi trauminiu osteomielitu. 88,5 proc. šių pacientų buvo vyrai, daugiau kaip 80 proc. pacientų jaunesni nei 50 metų. 86,8 proc. atvejo iš infekuoto kaulo išskirti stafilokokai, tarp kurių 69,1 proc. atvejo nustatyti *Staphylococcus aureus*. Veiksnių, lemiančių trauminio apatinio žandikaulio išsivystymą, pasiskirstymas pagal svarbą: imuniteto disfunkcija, dantų ėduonis lūžio linijoje, lūžgalių paslankumas, lūžgalių fiksacija daugiau nei po septynių dienų po traumos, sveiki dantys lūžio linijoje, nepakankama lūžgalių repozicija ir lūžgalių fiksacija po 3–7 dienų po traumos.

Išvados. Lyginamoji veiksnių, lemiančių trauminio apatinio žandikaulio osteomielito išsivystymą, analizė atskleidė imuninės sistemos, dantų būklės ir vyraujančios mikrofloros svarbą gydant apatinio žandikaulio lūžius. Nepakankama bei vėlyva lūžgalių repozicija ir fiksacija turi daug reikšmės komplikacijoms atsirasti.

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