

Risk Factors for Maxillofacial Space Infection Complications: A Retrospective Analysis of 457 Patients

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Abstract: This study was performed to determine the risk factors associated with systemic complications of maxillofacial space infection (MSI), and to propose an objective evaluation index - severity score of MSI. 457 MSI patients from Jan 2010 to Dec 2020 were reviewed retrospectively. The predictor variables included demographic, origin of infection, underlying systemic disease, pre-hospital medication history, laboratory examinations and severity scores of space infection. The severity score of space infection was proposed to evaluate the airway compromise of anatomic spaces. The primary outcome variable was the complication. The impact factors of complications were analyzed using univariate analysis and multivariate logistic regression. 457 patients were included (average age 46.3 y, male to female ratio 1.43:1). Among them, 39 patients developed post-operative complications. In the complication group, there were 18 patients (46.2%) with pulmonary infection, and two patients died. We found that the history of diabetes mellitus (OR = 4.74, 95% confidence interval (CI) = 2.22, 10.12), high temperature ($\geq 39^\circ\text{C}$) (OR = 4.16, 95% CI = 1.43, 12.06), advanced age (≥ 65 y) (OR = 2.88, 95% CI = 1.37, 6.01), and severity score of space infection (OR = 1.14, 95% CI = 1.04, 1.25) were independent risk factors for complications of MSI. All the risk factors needed to be closely monitored. Severity score of MSI was an objective evaluation index to predict complications.

Key Words: complication, oral and maxillofacial, risk factor, severity score, space infection

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Maxillofacial space infection (MSI) refers to infections of potential spaces and fascial planes in the maxillofacial region,¹ whose incidence rate is approximately 9 to 15/100,000.² MSI is mainly caused by odontogenic infection, lymphadenitis, and trauma.³ The treatment of MSI is relatively well-established. However, life-threatening infections and complications, such as necrotizing fasciitis, meningitis, descending necrotizing mediastinitis, and toxic shock, can lead to life-threatening consequences if not detected early and treated promptly.^{4–6} The incidence of complications was 3.5 to 41.6%,^{7–11} and the mortality rate was 0.7% to 11.3%.^{7,10,12} However, the mortality rate of patients with complications can reach 40% to 62%.^{8,13} In addition, patients with complications have higher treatment costs⁵ and prolonged hospital stays.¹⁴ Therefore, it is necessary to timely identify risk factors of complications to improve prognosis of MSI, which is the purpose of this study.

In previous studies, advanced age (≥ 65 y old), history of self-medication, dyspnea, diabetes mellitus (DM), high temperature ($\geq 39.1^\circ\text{C}$), white blood cell (WBC) count at admission, and neutrophil percentage (NEUT%) at admission ($\geq 85\%$) were risk factors for complications.^{7,11,15,16} Dyspnea is identified as one of the risk factors for complications.¹ Respiratory obstruction is the most critical complication, accounting for 6.7% to 76.8% of all complications,^{1,17–19} and is also the most common cause of death. Accurate and efficient identification of airway compromise could reduce the risk of death. However, dyspnea, as a subjective symptom, could not reflect the impact of infection on the respiratory tract objectively and effectively. Hence, this study strives to explore an objective evaluation index to reflect the relationship between airway compromise and complications. In 1999, Flynn et al designed the severity scores (SSs) of fascial space infections,²⁰ which is to score each infection space according to the impact of infection space on the respiratory tract, and is an objective indicator to evaluate the impact of infection on the respiratory tract. This study introduced this indicator to explore its relationship with complications.

The Peking University School and Hospital of Stomatology (Beijing, China) is one of the largest specialized stomatological medical institutions in the world and is also one of the dental medical centers in China. In this study, 457 cases of MSI admitted to our institution in the past 11 years were investigated retrospectively. The clinical characteristics, complications, and related risk factors of patients were analyzed in order to provide an objective basis for early identification of risk factors for complications.

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MATERIALS AND METHODS

Patients

This is a retrospective study of all cases of MSI treated in the Department of Oral and Maxillofacial Surgery at the Hospital of Stomatology of Peking University over a period of 11 years (between January 2010 and December 2020). This study was approved by the Biomedical Ethics Committee of Peking University School and the Hospital of Stomatology (PKUSSIRB-202162012).

Inclusion criteria: (i) cases diagnosed as “cellulitis and abscess of mouth” according to the tenth edition of the International Classification of Disease Tenth Revision (ICD-10); (ii) patients undergoing surgery; (iii) the infection spaces determined by computed tomography (CT).

These patients were admitted to hospital as outpatients or via emergency department. Admission criteria included local swelling that threatened their breathing or swallowing, the need for surgery, and hospitalization to control systemic diseases. Antibiotics were used before operation. All patients underwent local incision and drainage, and dressings were changed regularly. The discharge criteria were that the patients’ systemic diseases and infection symptoms were significantly improved, including (a) improvement or disappearance of symptoms or signs of elevated body temperature, dyspnea, and dysphagia; (b) the WBC count and NEUT% were normal. The patients were followed up for 2 weeks to 1 month until complete resolution of the infection.

Data Collection

The predictor and outcome variables were reviewed:

Demographic Data

Data of the age, sex, and residence of patients were collected.

Origin of Infection

Odontogenic, glandular, trauma, and unclear origins were considered.

Anatomic Spaces of Infection

The anatomic spaces were identified according to computed tomography by two radiologists, and decided by the lead surgeon in case of dispute.

Severity Scores of Fascial Space Infections

The anatomic spaces of the head and neck can be graded in severity by the level to which they threaten the airway. In 1999 Flynn and colleagues devised a SS that assigned a numerical value of 1 to 4 for involvement of each of the low, moderate, severe, or extremely severity anatomic spaces, respectively.²⁰ Low-risk spaces (SS=1) included spaces in the following regions: vestibular, subperiosteal, mandible, infraorbital, and buccal; the moderate-risk spaces (SS=2) included the following areas: submandibular, submental, sublingual, pterygomandibular, submasseteric, superficial temporal, and deep temporal (or infratemporal); severe-risk spaces (SS=3) included the following bodily domains: lateral pharyngeal, retropharyngeal, and pretracheal; and the extremely severe risk spaces (SS=4) included the following conditions and/or regions of the body: Ludwig’ angina, mediastinum, and intracranial infections.

In this study, every anatomic space of infection was scored. And total SS for a given patient was the sum of the SSs for all of

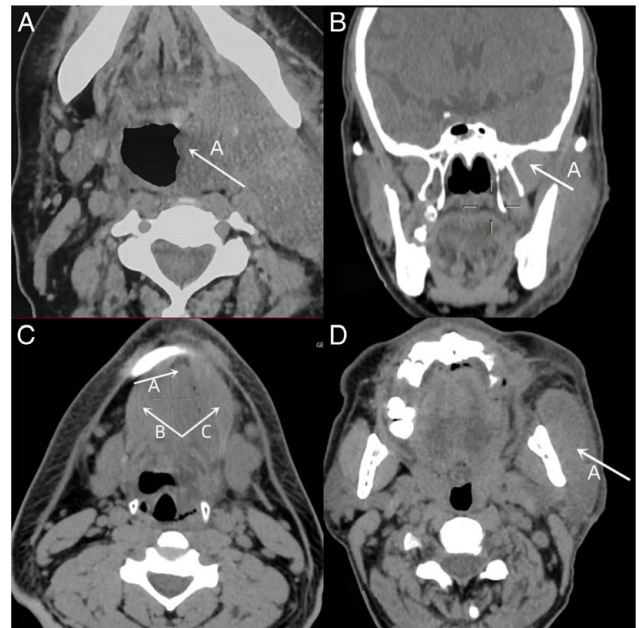


FIGURE 1. Image of the infection spaces and corresponding scoring explanation. A, Arrow A in the image shows the lateral pharyngeal space (SS = 3). The total severity score of this patient is 3. B, Arrow A in the image shows the pterygomandibular space (SS = 2). The total severity score of this patient is 2. C, Arrow A in the image shows the submental space (SS = 2). Arrow B and C, show the bilateral submandibular spaces (SS = 2) respectively. The total severity score of this patient is 6. D, Arrow A in the image shows the submasseteric space (SS = 2). The total severity score of this patient is 2.

the affected anatomic spaces, based on radiographic examination (Fig. 1).

Pre-hospital Time and Medication History

Pre-hospital time referred to the time from the onset of infection symptoms to admission; the medication history before admission included the history of oral and intravenous use of antibiotics.

Underlying Systemic Disease

The diagnosis was based on ICD-10, including DM, hypertension, pregnancy, coronary heart disease, systemic lupus erythematosus, and rheumatoid arthritis.

Body Temperature at Admission

It was body temperature measured at the time of admission.

Laboratory Examinations

Laboratory examinations included admission WBC count and NEUT%, fasting blood glucose, and bacterial culture.

Days of Antibiotics Therapy

Patients were empirically treated with antibiotics according to local and general symptoms of inflammation. The days of antibiotic usage during hospitalization were recorded.

Clinical Outcome Variable

The primary outcome variable was the complication, secondly, there were length of stay and cost. Complications referred to diseases associated with space infection during hospitalization, which were determined in compliance with the ICD-10 guidelines. Pulmonary infection, acute cardio-cerebrovascular acci-

dent, septic shock, intracranial infection, respiratory infarction, sepsis, and mediastinal abscess were recorded.

Statistical Analysis

The database was established by two operators using Microsoft Excel (version 2010; Microsoft Corporation, Redmond, WA, USA) and imported into the SPSS (version 19.0; IBM Corporation, Armonk, NY, USA) for statistical analysis. In general, continuous variables were described by mean ± standard deviation ($\bar{x} \pm s$), whereas categorical variables were summarized by the number and percentage. The impact factors of complications were analyzed using univariate analysis and logistic regression. Univariate analyses were performed using the Chi-square test or Mann-Whitney U test to identify the statistically significant univariate variables affecting the occurrence of complications. Factors with P values <0.05 were included in multivariate logistic regression models to calculate the odds ratio (OR), which ultimately resulted to identify the potential risk factors related to complications of MSI. A P -value of <0.05 was considered to be statistically significant.

RESULTS

Patient Characteristics

Four hundred and eighty-four cases of MSI were collected over the period of 11 years. Twenty-seven patients were excluded due to lack of CT examination or undergoing infusion therapy instead of surgery. Ultimately, a total of 457 patients with MSI were enrolled in this study, including 269 males (58.9%) and 188 females (41.1%), with an age range of 1 to 86 years (median 48 y). The average age was 46.3 years old.

Distribution of the Underlying Systemic Diseases

Of the 457 patients, 154 had underlying systemic diseases, with 106 cases (68.8%) of cardiovascular diseases including hypertension and coronary heart disease, etc., and 86 (55.8%) immune system diseases including DM and rheumatoid arthritis, etc. Besides, 3 cases (1.9%) had hematological diseases including anemia, other 5 had pregnancy and mental illness (Fig. 2).

Clinical Characteristics Severity Scores of the Space Infections

The SS of 457 patients ranged from 2 to 21 points, with an average of 5.2 points and a median of 4 points (Fig. 3).

Origin of Infection

The most common origin of infection was odontogenic infection (352 cases, 77.0%), followed by adenogenic infection (50 cases, 10.9%).

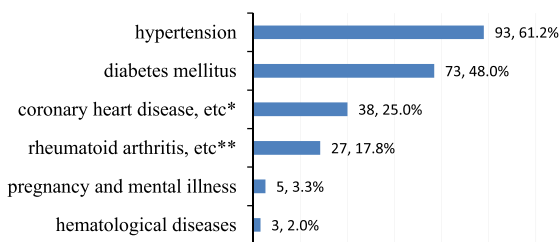


FIGURE 2. Distribution of comorbidities. *means coronary heart disease, arrhythmia, and/or myocardial ischemia; **means rheumatoid arthritis, systemic lupus erythematosus, Schoenlein-Henoch purpura, and/or asthma.

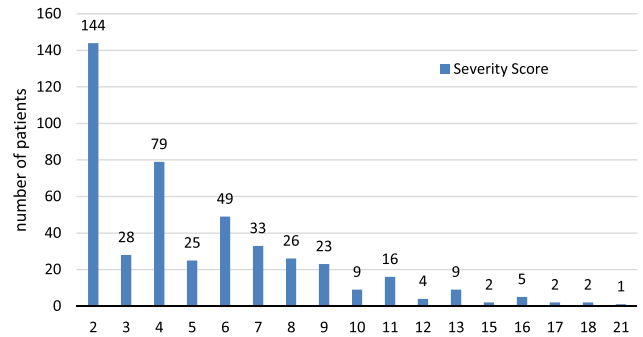


FIGURE 3. Severity score of space infections.

Distribution of the Complications

Thirty-nine patients (8.5%) developed complications during the period of treatment. Pulmonary infection was the most common complication, followed by acute cardiovascular and cerebrovascular accidents (30.8%), and sepsis (15.4%). Two patients died of septic shock or multiple organ dysfunction syndrome. The distribution of the complications is displayed in Fig. 4.

Significant differences were observed in the length of stay (10.3 ± 5.3 d vs. 7.8 ± 4.1 d, $P=0.001$) and the total cost of hospitalization (2120.6 ± 1624.6 dollars vs. 1037.1 ± 959.3 dollars, $P<0.001$). (Note: according to the annual average exchange rate of RMB in 2020: US \$1: RMB 6.8974.)

Univariate Analysis Between the two Groups

The results of univariate analysis are shown in Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/SCS/F32>, six individual factors might affect risk of developing complications ($P<0.05$), including advanced age (≥ 65 y), SSs of space infections, DM, admission temperature, admission NEUT%, and fasting blood glucose.

Logistic Regression Analysis of the Complications

The six factors with statistically significant differences, determined by univariate analysis, were further included in logistic regression analysis as independent variables. The complication was taken as the dependent variable, and multivariate logistic regression by method (Forward: LR) was used to analyze the selected independent variables. The variance analysis of this model showed that $F=44.334$ ($P<0.001$), which indicated that the fitting equation was statistically significant. Hosmer and Lemeshow equation showed that $\chi^2=7.191$ ($P=0.304$, $P>0.20$), which indicated a well-fitting effect.

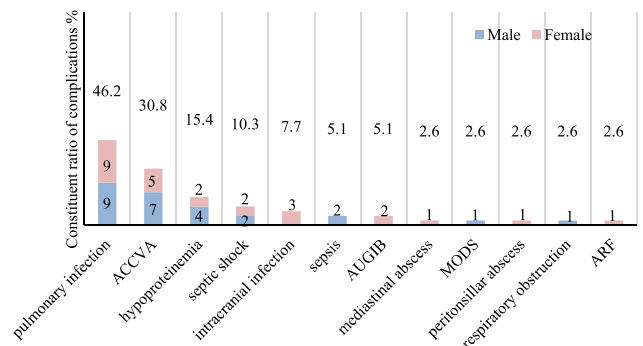


FIGURE 4. Distribution of complications. ACCVA indicates acute cardiovascular and cerebrovascular accidents; AUGIB, acute upper gastrointestinal bleeding; ARF, acute renal failure; MODS, multiple organ dysfunction syndrome.

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The results of multivariate logistic regression confirmed that the history of DM, elevated body temperature ($\geq 39^\circ\text{C}$), advanced age (≥ 65 y), and the SS of space infection were independent risk factors of complications ($P < 0.05$; Supplemental Table 2, Supplemental Digital Content 1, <http://links.lww.com/SCS/F32>).

DISCUSSION

Clinical Characteristics

Our results showed that odontogenic infection was the main origin of MSI. In other studies, odontogenic infections contribute to MSI in the range of 57.5% to 70.6%,^{6,8,15,21} lower than 77.0% reported in the present study. The reasons were as follows: (1) Untimely and improper treatment of pericoronitis of wisdom teeth and periapical periodontitis is considered as the main cause of odontogenic infection;^{22,23} (2) The use of antibiotics in the treatment of odontogenic infection is only an auxiliary treatment due to the anatomical structure of the teeth and the influence of local microorganisms. Nevertheless, 48.1% of the patients had self-medicated before admission to save medical expenses, including analgesics, antibiotics, and Chinese herbal medicine.¹⁹

Self-medication has significant disadvantages because of residents' poor knowledge of safe medication and low medical awareness,²⁴ which could also delay the best time for treatment. This is the main reason why local odontogenic infection develops into MSI, which can affect the detection rate of pathogens and hinder the proper treatment and disease control.²⁵ In our study, the self-medication rate was 87.6%, which was higher than that reported in previous studies. The higher rate of self-medication may be the reason for the higher proportion of odontogenic infection in our survey.

In previous studies, self-medication patients took a long time from onset of symptoms to medical treatment, with an average of 11.9 days;¹⁵ the delay time of 40.9% of them was 5 to 6 days.¹⁰ The average time before hospitalization in our study was 16.4 days, which was longer than that reported in earlier studies; Moreover, it was also significantly longer than the average progression time (8.5 d) of deep cervical space infection (a more serious space infection),⁷ which may delay the treatment. One of the reasons is that patients' personal medication knowledge was deficient²⁴ and medical-seeking behavior was poor.²⁶ Usually, self-medication was started once the onset of symptoms. Patients would seek for professional medical help only when the symptoms had further aggravated. On the other hand, delay treatment may be related to the difficulty in medical assistance in China (complicated procedures and high cost).²⁶ The limited diagnostic and therapeutic potential of primary hospitals, poor treatment methods of general clinics, and the inability to identify the severity of infection would further delay relevant medical treatment.²⁵ Therefore, oral health education should be popularized with the public via traditional media platforms (such as television, radio, newspapers) and social media channels. Popularization of science would also be helpful to improve the awareness of early treatment of wisdom teeth and dental caries and promote awareness of the public and dental practitioners regarding infection. It is imperative to call for public health measures to control infections.

Analysis of the Risk Factors for Complications

Literature evidence indicates a consensus has been reached that airway obstruction is one of the most serious complications with a high incidence rate. Airway evaluation and management

are critically important for the prompt and effective diagnosis of oral and MSIs. However, previous studies regarded dyspnea as a subjective symptom instead of an objective indicator, which overlooked the impact of infection on the respiratory tract objectively and effectively. In our study, a SS of space infection was used as an objective indicator to explore its relationship with complications. Our results showed that the risk factors for complications included DM, high body temperature at admission, advanced age, and SS of space infection. These risk factors for complications have been analyzed in detail below.

Severity Score of Space Infection

The investigation showed that the SS of space infection is an independent risk factor for complications. One-point rise in the score increased the probability of complications by 14.1%. The severity of the anatomic spaces of the head and neck region can be graded by the level to which they threaten the airway.²⁷ The buccal, infraorbital vestibular, and subperiosteal spaces can be classified as low severity because infections in these spaces do not directly threaten the airway or other proximal vital structures. Infections of anatomic spaces that can obstruct access to the airway due to swelling or trismus can be classified as moderate severity. Infections with high severity are those relating to anatomic space where swelling can directly obstruct or deviate the airway, or threaten vital structures. The SS devised by Flynn et al was assigned a numerical value for the involvement of each of the respective spaces. Therefore, SS could objectively reflect the impact of space infection on the respiratory tract. In previous studies, the OR values of dyspnea were as high as 17.94 and 211.06, respectively,^{1,28} which was quite different from the OR value of SS (1.141) established in our study. We believe that the following reasons lead to this difference: (1) The types of the two independent variables are different, whereas dyspnea is a categorical variable, and SS is a continuous variable; (2) Dyspnea is the main complaint of patients, and subjective feeling is difficult to precisely define; (3) The sample size of the complication group was small.

Two of 39 patients with complications died over 60 years old. Their infection spaces at admission in both was 6, with an airway risk score of 15 and 16, respectively. The most common cause of death was severe complications caused by underlying systemic diseases.^{18,21} Conversely, there is no underlying systemic disease in both cases. Therefore, SS is closely related to the complications. For patients with higher SS of space infection, more attention should be paid to the disease progression.

History of Diabetes Mellitus

Previous studies have shown that 66.7% of the patients with complications had underlying systemic diseases, with 55.3% DM, and DM was a risk factor for complications.¹ In this investigation, DM (48%) was the most common underlying systemic disease in patients with complications and was also one of the risk factors for complications in MSI patients. An earlier analysis showed that hyperglycemia could lead to immune system disorders, including the destruction of neutrophils, cellular immunity, and complement function.²⁹ Therefore, the autoimmune function of diabetic patients was impaired, and the control of their infection was difficult due to the lack of response to treatment. Moreover, patients with DM are susceptible to airway obstruction, and infection is easily spread to multiple spaces, including more than three spaces,^{14,30} which aggravates their condition even more severely.

Body Temperature at Admission

Body temperature at admission of up to 39°C^{1,15} was evidenced to be a risk factor for complications, and a temperature of up to 39.1°C could independently predict the occurrence of complications.¹ Our present findings also confirmed that an admission temperature of up to 39°C was a risk factor for complications, and their risk was 4.2-fold higher than that of other patients. The reasons for these results are as follows. Temperatures higher than 39°C significantly weaken or even inhibit myocardial contractility, which increases myocardial burden and leads to compensatory dysfunction of the cardiovascular system, eventually resulting in circulatory failure and other cardiovascular-related complications. Hyperthermia is also known to damage the vasomotor center, leading to shock and peripheral vasoconstriction³¹ and causing related complications.

Advanced Age

Patients older than 60 years who suffer from space infection could easily develop multi-space infection, and advanced age was found to be a risk factor for complications.^{1,14} Of aged patients, the ability of resisting acute inflammation decreased, the immunity was impaired and the incidence of underlying systemic diseases increased. Our study confirmed the above findings. Infections occurring in the elderly are characterized by a higher speed of development, larger scope, and more significant disease severity.³² Therefore, particular attention is to be paid to older patients because multi-space infection could easily and rapidly develop and spread.

There are limitations in our research. This study was a single-center retrospective study with limited hospitalization time and a relatively small sample size of patients with complications. We will continue to collect cases and expand the sample size in our follow-up study to provide more favorable evidence for a more representative assessment of the risk factors for MSI complications.

CONCLUSION

In this study, the SS of space infection as an objective indicator was used to evaluate the relationship between the airway compromise caused by infection and complications. We utilized the history of DM, temperature > 39°C, and age to evaluate the aforementioned relationship. Meanwhile, we suggest that oral health care knowledge should be popularized the public through social media, networking, or community activities. Popularization of science would also be helpful to further improve the ability and awareness of early identification of oral diseases, reduce self-medication, and avoid treatment delays.

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