Journal of Cranio-Maxillo-Facial Surgery 47 (2019) 334–340

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

A mathematical approach improves the predictability of length of hospitalization due to acute odontogenic infection: A retrospective investigation of 303 patients

Nils Heim [a,*], Moritz Berger [b,1], Valentin Wiedemeyer [a,1], Rudolf Reich [a,1], Markus Martini [a]

[a] Department of Oral & Maxillofacial Plastic Surgery, Universitätsklinikum Bonn, Sigmund-Freud-Strasse 25, D- 53127, Bonn, Germany

[b] Institut für Medizinische Biometrie, Informatik und Epdidemiologie (IMBIE), Universitätsklinikum Bonn Sigmund-Freud-Strasse 25, D- 53127, Bonn, Germany

ARTICLE INFO

Article history:
Paper received 3 April 2018
Accepted 4 December 2018
Available online 11 December 2018

Keywords:
Odontogenic infection
Length of hospitalization
Head and neck infection
LOS

ABSTRACT

Purpose: Increasing rates of hospitalization of patients diagnosed with acute odontogenic infection have become a burden for public health care, with significant economic concerns. The aim of this study was to investigate factors that tend to prolong hospital length of stay (LOS) in the treatment of severe infections. We present a statistical model that enables the prediction of LOS by exposing the feasibility of the essential statistical determinants.

Materials and methods: A 5-year retrospective study investigated records of 303 in-hospital patients with abscess of odontogenic origin. Time-to-event models were used to analyse data where the outcome variable is the time to the occurrence of a specific event. Here, the focus is on a statistical model for the prediction of LOS of patients.

Results: The group of all patients ($n = 303$) was analysed by considering seven characteristics of the patients (age, gender, spreading of infection, localization of infection focus, type of administered antibiotics, diagnosed diabetes mellitus, and existence of a remaining infection focus). Age ($p = 0.049$; $rc = -0.007$) and spreading of infection ($p < 0.001$; $rc = -0.965$) showed a significant impact on the LOS. Subjects were divided into two groups. Group A ($n = 185$) consisted of patients who presented with a severe odontogenic infection and not yet removed infection focus; group B were patients having undergone outpatient operative tooth removal ($n = 118$). To group A patients' data, two new risk factors ("**d**ays **b**etween abscess **i**ncision and **r**emoval of infection focus" = **dbir** and "**r**emoval of **i**nfection focus during the **s**ame **s**tay as abscess incision" = **riss**) replaced the risk factors "remaining infection focus." A significant impact on the LOS was detected for **dbir** ($p < 0.001$; $rc = -0.15$) and **riss** ($p < 0.001$; $rc = -1.76$). Our statistical model explicitly describes how the probability for discharge depends on the time and how specific characteristics affect the LOS. We observed a significantly higher LOS in older patients and subjects with infection spreading. In group A patients, **dbir** and **riss** had a highly significant impact on the LOS.

Conclusion: Predicting the LOS may promote transparency to costs and management of patients under inpatient treatment. Our statistical model describes the probability of a discharge at time t compared to a discharge later than t (a LOS longer than t). Furthermore, the model enables a prediction of the LOS of each patient for practitioners in an easy way.

1. Introduction

The acute odontogenic infection remains a major burden for patients' health and public health care systems in western countries (Seppanen et al., 2010; Burnham et al., 2011). Secondary to trauma, failed root treatment and most of all dental caries and acute

* Corresponding author. Fax: +0049 (0) 228 287 22604.
E-mail addresses: nils.heim@web.de, nils.heim@ukb.uni-bonn.de (N. Heim), moritz.berger@imbie.uni-bonn.de (M. Berger), valentin.wiedemeyer@ukbonn.de (V. Wiedemeyer), rudolf.reich@ukb.uni-bonn.de (R. Reich), markus.martini@ukb.uni-bonn.de (M. Martini).
[1] Co-authors.

https://doi.org/10.1016/j.jcms.2018.12.002
1010-5182/

dental abscesses occur, with a diverse compound of aerobic and anaerobic bacteria (Shu et al., 2000; Zirk et al., 2016). Once the bacteria has migrated from the necrotic root canals via the apical foramen into the periapical tissue, these bacteria and their toxic products can induce infection and subsequent formation of pus (Nair, 2004). While suppuration is mainly located in the periapical tissue of the affected tooth in the beginning, the acute infection has the potential to spread into other spaces and cause life-threatening events (Wang et al., 2003). Practically every patient suffers from pain, swelling, erythema and hyperthermia (Robertson and Smith, 2009). If not treated at an early stage odontogenic, infections are likely to spread into deep neck spaces and cause dangerous complications by menacing anatomical structures, such as major blood vessels, the upper airway and even the mediastinum (Biasotto et al., 2004). Beside the risk of a descending infection, bacterial expansion may also invade blood vessels and cause septicemia (DeAngelis et al., 2014) or travel into facial spaces and harm vulnerable tissues such as orbita and brain (Azenha et al., 2012; Tavakoli et al., 2013). Surgical intervention comprising incision and drainage is indisputably inevitable for a sufficient treatment of abscess (Walia et al., 2014). Intravenous antibiotics are often selected as a sustaining therapy option (Islam et al., 2008). Unfortunately, subsiding susceptibility rates of bacteria against commonly administered antibiotics are undoubtedly an increasing issue in odontogenic infection treatment (Heim et al., 2016).

Increasing rates of emergency department visits and hospitalization of patients diagnosed with acute dental infection have recently been documented by public health facilities in the United States and Europe (Okunseri et al., 2012; Shah et al., 2013; Ottaviani et al., 2014) and have already become a significant economic concern (Jundt and Gutta, 2014).

Previous reports associated the hospital length of stay (LOS) with the severity of infection and the presence of coexisting systemic diseases and conditions (Seppanen et al., 2008; Staffieri et al., 2014).

The aim of this retrospective study was to investigate new risk factors and evaluate well-known risk factors that tend to prolong the LOS in the treatment of severe odontogenic infections. Based on the data of 303 patients diagnosed with severe odontogenic abscess, we particularly present a statistical model that enables the prediction of LOS by exposing the feasibility of the essential determinants that show an effect the length of inpatient treatment.

2. Materials and methods

2.1. Patients

A 5-year retrospective study investigated patient records of 303 patients with abscess of odontogenic origin and treatment under inpatient conditions in the department of Oral and Maxillofacial Plastic surgery of the university clinic of Bonn, Germany. The patients enrolled in this study were reviewed for clinical characteristics including: gender, age, involved facial spaces, tendency of infection spreading, hospital length of stay (LOS), infection focus remaining, type of administered antibiotics, medical records and comorbidities. All patients included in this study presented with swelling and pain. Most of the patients additionally presented with one or multiple symptoms such as trismus, dysphagia, fever or respiratory restrictions based on compression of the upper airways. Every subject in this study was classified as a severe case of odontogenic infection and underwent surgical treatment in terms of incision and drainage of the abscess under general anesthesia. Furthermore we administered intravenous (IV) antibiotics during the operation and for the length of inpatient treatment.

Exclusion criteria for this study was an inpatient stay of less than 24 h.

The antibiotic therapy for inpatient-managed patients consisted of ampicillin/sulbactam, administered three times a day in a dose according to the patients' body weight (<70 kg = 3x/2 g; >70 kg = 3x/3 g). Renal dysfunction was checked by investigating patients' blood values of creatinine and glomerular filtration rate. The dose was adjusted if necessary. Patients with self-reported or documented history of penicillin allergies or intolerances, such as allergic reactions or abnormal skin sensations, received clindamycin at a dose of 600 mg three times a day. Children received lower doses according to their body weight.

All information was arranged electronically and analyzed (Microsoft Excel; Microsoft Corp., Redmond, WA, USA). Measurements were described by the means and corresponding standard deviations (sd). Wald tests were used for determining the significance of regression-coefficients (rc). P-values ≤ 0.05 were regarded as statistically significant.

Regression analysis was performed by the statistical software R (R Core Team, 2017). The add-on packages mgcv (Wood, 2011) and discSurv (Welchowski and Schmid, 2018) were utilized to fit the statistical model described in the next section.

2.2. Statistical model

Time-to-event models are a popular tool to analyse data where the outcome variable is the time to the occurrence of a specific event. Here, the focus is on a statistical model for the prediction of the LOS of patients. For this purpose, a time-to-event model can be exploited, where the event of interest is the discharge from the hospital, with the hospitalization measured in days (on a discrete scale). A comprehensive introduction into the class of discrete time-to event models was given by Tutz and Schmid (2016) and in the tutorial by Berger and Schmid (2018).

For modeling the LOS, we apply the semiparametric logistic discrete hazard model, specified by the equation.

$$\frac{P(T_i = t|x_i)}{P(T_i > t|x_i)} = e^{(f_0(t)+x_i^T Y)}, i = 1, \ldots, n,$$

where T_i is the time of discharge, x_i are the investigated characteristics of the patients (using an appropriate coding) and n is the number of patients. The right-hand side of the model contains a smooth function $f_0(t)$ of the time $t = 1, \ldots, 18,$ and a linear predictor of the patient's characteristics with regression coefficients Y.

The model describes the probability of a discharge at time t compared to a discharge later than t (a LOS longer than t). It follows that the probability of discharge at (any) time t, compared to the probability of discharge later than t, changes by the value e^{Y_j} if the corresponding characteristic of the patient x_{ij} increases by 1 unit (given that all the other characteristics remain the same).

3. Results

Of 303 patients enrolled, 157 (51.8%) were males and 146 (48.2%) were females. The mean age was 48.6 ± 20.2 years, ranging from 6 to 92 years. The records of all hospitalized patients were reviewed based on the criteria for inclusion. The affected facial spaces were investigated in every subject. Perimandibular/buccal spaces (n = 187, 61.7%) and submandibular spaces (n = 84, 27.7%) were mainly affected, followed by the canine fossa (n = 18, 5.9%). The frequencies of all affected spaces are given in Fig. 1. In 35 cases (11.5%), a spreading into other spaces could be detected. The mean duration of hospitalization was 5.9 ± 2.9 days, ranging from 1 to 18 days. In all, 263 (86.8%) of the subjects were treated with

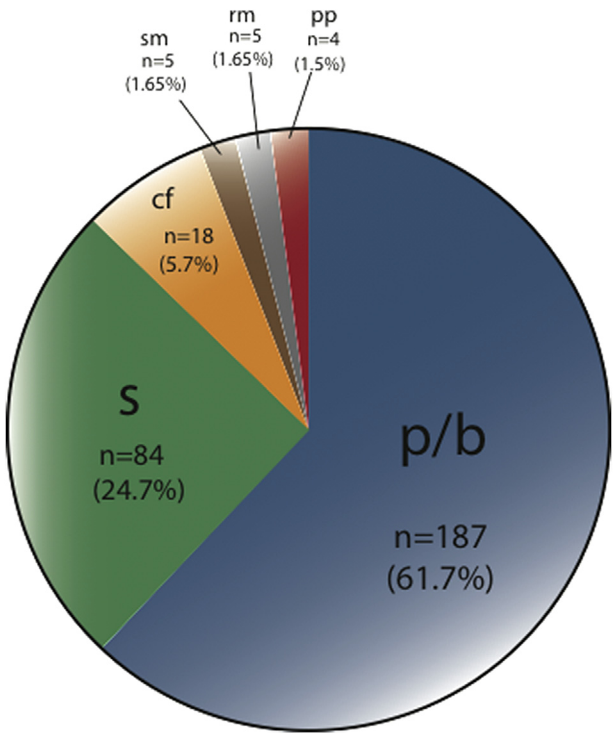

Fig. 1. Frequencies of affected spaces involved. p/b = Perimandibular/buccal space; s = submandibular space; cf = canine fossa; sm = submental space; rm = retromaxillary space; pp = parapharyngeal space.

intravenous ampicillin/sulbactam, while 40 (13.2%) reported a history of penicillin allergy; hence clindamycin was administered in these cases. A total of 23 patients (7.6%) had diabetes mellitus in their medical records. Infected teeth located in the mandible constituted by far the majority of abscess foci (n = 263, 86.8%).

Subjects were further divided into two groups. Group A (n = 185) consisted of patients who presented with a severe odontogenic infection. The tooth/teeth as the cause of infection was/were not yet removed in this group. Group A was characterized by higher age (53.5 ± 19.5), a greater number of men (n = 101, 54.6%), a slightly lower tendency of infection spreading into other facial spaces (n = 20, 10.8%), a greater LOS (6.08 ± 3.05 days) and a higher rate of diabetes mellitus (n = 17, 9.2%). Clindamycin was administered in 14.2% of the cases. Additionally, we investigated the time between surgical incision and removal of infection focus (mean 7.4 ± 6.5 days) and the number of patients who received surgical incision and tooth removal at the same stay (n = 132, 71.25%).

Group B patients presented with severe odontogenic infection after outpatient tooth removal (n = 118). Subjects showed younger age (40.95 ± 18.8 years), more men (n = 62, 52.5%), lower rates of maxillary infection focus (1.7%), a slightly higher rate of infection spreading (12.7%) and fewer cases of diabetes mellitus (6.8%). The mean LOS in this group was 5.6 ± 2.6 days.

Table 1 exhibits all investigated risk factors and numbers for the all patients in group A and group B.

Regression analyses were conducted for entire group patients (n = 303) and additionally for group A patients.

The entire group of patients was analysed by considering seven major characteristics: age (for the analysis, age was centered on 48 years), gender, spreading of infection, location of infection focus (maxilla vs. mandible), administered antibiotics, presence of diabetes mellitus and remaining infection focus. Age ($p = 0.049$; rc = −0.007) and spreading of infection into contiguous spaces ($p < 0.001$; rc = −0.965) showed a significant impact on the LOS (Table 2).

Group A patients' data were similarly investigated. Six of the seven characteristics mentioned above were analysed applying the regression model. Furthermore, the two new risk factors ("**d**ays **b**etween abscess **i**ncision and **r**emoval of infection focus" = **dbir** and "**r**emoval of **i**nfection focus during the **s**ame **s**tay as abscess incision"" = **riss**) replaced the characteristics "remaining infection focus." The risk factor "dbir" demonstrates a relation between a greater period of time between abscess incision and removal of infection focus and the effect of this period on an increased LOS. The risk factor "dbir" assesses the correlation between the event whether the infection focus is removed during the same hospital stay as incision is performed or not and its effect on the LOS.

A significant impact on the LOS was detected for "spreading of infection into contiguous spaces" ($p < 0.001$; rc = −1,18), "dbir" ($p < 0.001$; rc = −0.15) and "riss" ($p < 0.001$; rc = −1.76) (Table 3).

3.1. Sample calculations

1a. Sample calculation for the item of "spreading of infection into contiguous spaces" in Group A:

The calculation is based on the assumption that infection spreading is the only different item between two identical patients:

The calculated regression coefficient for this feature was *−1.180*. Accordingly, the probability for discharging the patient from inpatient treatment at time t compared to a discharge after time t is

Table 2
Patient characteristics and regression analyses with corresponding p-values for all patients (n = 303).

Characteristics	regression coefficient	p value
age	−0.007	0.049*
gender (male) = yes	−0.212	0.120
spreading = yes	−0.965	<0.001*
infection focus = maxilla	0.085	0.680
antibiosis = clindamycin	−0.074	0.683
diabetes mellitus = yes	−0.421	0.090
remaining infection focus	−0.198	0.176

Table 1
Patient characteristics.

Characteristics	All patients (n = 303)	Group A (n = 185)	Group B (n = 118)
age(y)	48.6 ± 20.2	53.5 ± 19.5	40.95 ± 18.8
gender	m:51.8% f:48.2%	m:54.6% f:45.4%	m:52.5% f:47.5%
LOS(d)	5.9 ± 2.9	6.1 ± 3.05	5.6 ± 2.6
antibiosis = clindamycin	13.2%	14.2%	16.8%
diabetes mellitus	7.6%	9.2%	6.8%
dbir		7.4 ± 6.5	
riss		71.25%	

(y) = years; (d) = days; dbir = days between abscess incision and removal of infection focus; riss = removal of infection focus during the same stay as abscess incision.

Table 3
Patient characteristics and regression analyses with corresponding p-values for of group A patients (n = 185).

Characteristics	regression coefficient	p value
age	−0.003	0.441
gender (male) = yes	−0.298	0.114
spreading = yes	−0.180	<0.001*
infection focus = maxilla	0.253	0.357
dbir	−0.149	<0.001*
riss	−0.759	<0.001*
antibiosis = clindamycin	−0.419	0.087
diabetes mellitus = yes	−0.149	0.627

exp(−1.180) = 0.31 lower. Inversely, the probability for discharging a patient with infection spreading after a certain day is 3.22 times lower (*1/0.31 = 3.22*) than a discharge on that certain day.

1b. Assuming that three example patients exhibit the same particular characteristics except for 1 salient risk factor, it is applicable:

Equal characteristics: age = 48 years; gender = female; location of infection focus = mandible; days between incision and removal of the odontogenic focus = 6; diabetes mellitus = no.

Calculation for: riss: **no**/spreading: **no** (first pair of graphs); riss: **no**/spreading: **yes** (second pair); riss: **yes**/spreading: **no** (third pair) (Fig. 2).

2a. Sample calculation for the item of "spreading of infection into contiguous spaces" in the group of all patients (n = 303):

The calculated regression coefficient for this feature was *−0.965*. Accordingly, the probability of discharging the patient from in-patient treatment at time t compared to a discharge after time t is *exp(−0.965) = 0.38* lower. Inversely the probability for discharging a patient with infection spreading after a certain day is 3.22 times lower (*1/0.31 = 2.63*) than a discharge on that certain day.

2b. Calculation for age: **48y**/spreading: **no** (first pair); age: **88y**/spreading: **no** (second pair); age: **48y**/spreading: **yes** (third pair) (Fig. 3).

4. Discussion

The present findings show that patients with acute odontogenic infections are nearly gender balanced. This is similar to findings in other studies (Sato et al., 2009; Opitz et al., 2015). The mean age of 48 years is higher than reported in the literature (Sanchez et al., 2011), and distribution of affected spaces and the predominance of mandibular involvement (86.8%) is likewise reasonably similar to previous data (Zirk et al., 2016). Our standard IV antibiotic treatment consisted of ampicillin/sulbactam. In cases of self-reported or documented penicillin allergy in patients' medical history, we administered clindamycin as an effective substitute (Warnke et al., 2008; Opitz et al., 2015). The LOS in our study averaged 5.9 ± 2.9 days and was therefore slightly higher than in numerous other studies. The range of mean hospital LOS in the literature is admittedly large (Boffano et al., 2012; Kim et al., 2012).

Initially focusing on the group of all patients (n = 303), seven risk factors were evaluated of which two showed a significant impact on the overall LOS.

Coexisting systemic conditions have been identified as factors with a great impact on the severity of odontogenic infections and LOS (Flynn et al., 2006). Among numerous comorbidities, diabetes stands out as a well-investigated cause of an increased LOS (Rao et al., 2010). However, our results revealed no significant increase of the LOS in patients with diabetes (p = 0.09; rc = −0.422). Advanced age is a known risk factor for the severity and LOS in odontogenic infections (Wang et al., 2003). Likewise, we investigated a significantly higher LOS in older patients (p = 0.049; rc = −0.007). Due to bone-related and anatomical differences of

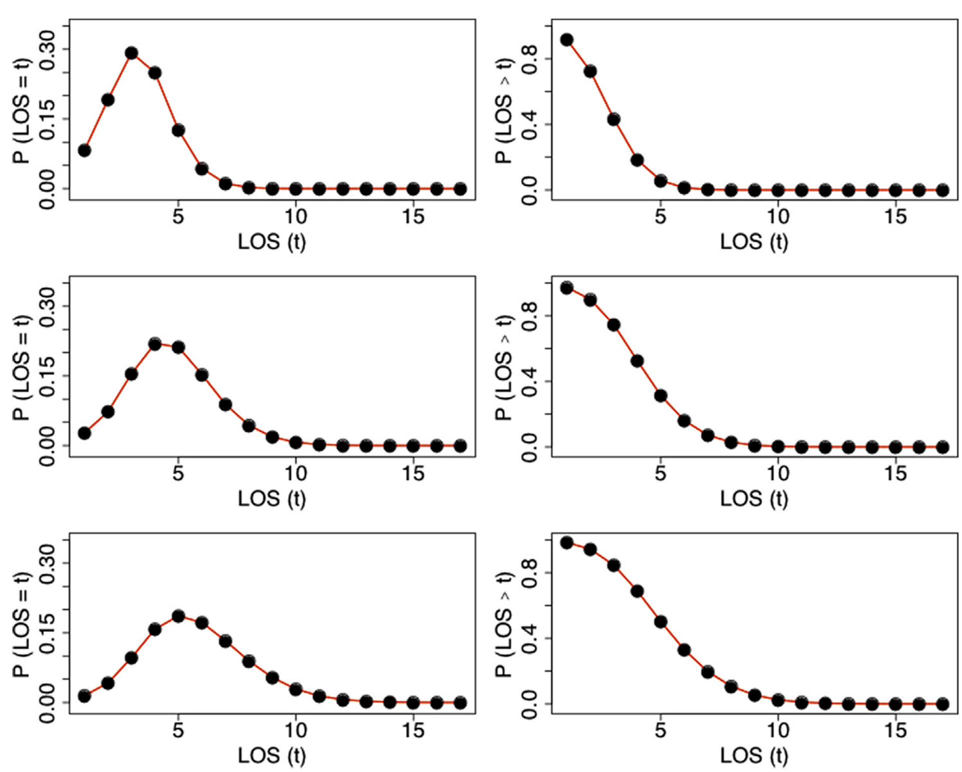

Fig. 2. Probability (P) of patients' discharge on a certain day (LOS = t) and probability (P) of patients' discharge after a certain day (LOS > t).

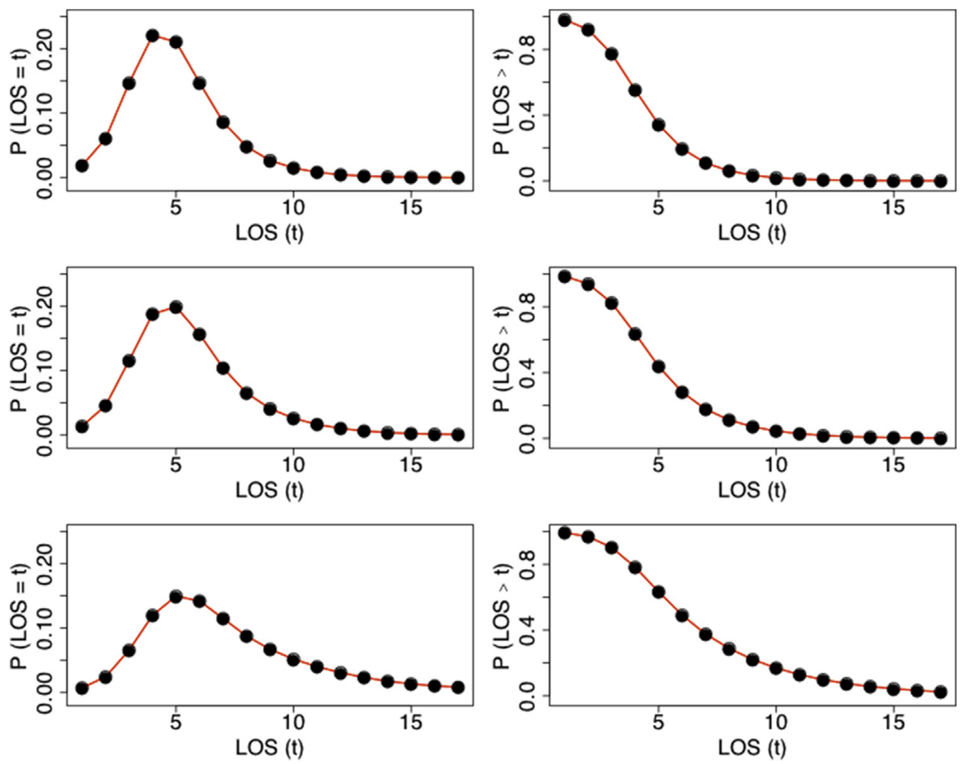

Fig. 3. Probability (P) of patients' discharge on a certain day (LOS = t) and probability (P) of patients' discharge after a certain day (LOS > t).

upper and lower jaw, as well as higher bone density in the mandible and better blood supply in the maxilla, mandibular involvement is prone to have an effect on greater LOS (Dvori et al., 2006; Hwang et al., 2011; Pourdanesh et al., 2013). However we found no significant difference between the groups with maxillary or mandibular involvement ($p = 0.68$; $rc = 0.085$). A detected male-to-female ratio of almost 1:1 is in alignment with previous studies (Flynn et al., 2006), but gender showed no differences in the LOS of hospitalized patients (for males: $p = 0.12$; $rc = -0.215$). Ampicillin/sulbactam was used in 263 patients (86.8%) as clinical standard antibiotic treatment. In cases of documented or reported penicillin allergy, clindamycin was used as the substitute of choice, comparable to what is used in other oral and maxillofacial departments (Zirk et al., 2016). Despite recent reports correlating increased LOS in patients with documented penicillin allergies (Li et al., 2014; Macy and Contreras, 2014), the administration of either clindamycin or ampicillin/sulbactam did not significantly change the LOS (clindamycin: $P = 0.683$; $rc = -0.075$).

There is no question that delay of surgical intervention in head and neck infection of odontogenic focus is associated with a high chance of life-threatening complications, although there is no concordance regarding the right time for tooth extraction (Herrera et al., 2000). Recommendations for tooth removal range from extraction during the surgical intervention of abscess incision and drainage to postponing tooth extraction from the acute phase to a later time in a subacute or chronic phase of the infection (Costich et al., 1969; Martis and Karakasis, 1975). Patients enrolled in our study either presented with acute odontogenic infection after operative removal of a tooth in outpatient management ($n = 118$) or the infection focus was still present and the tooth not yet extracted ($n = 185$). A significant impact on the overall LOS in patients with a present triggering focus was not verifiable (focus = yes; $p = 0.176$; $rc = -0.198$).

Furthermore, it is well understood that infection spreading purulent liquid through communicating spaces in the head and neck regions may endanger sensitive anatomical landmarks such as brain and orbita and have the potential to cause life-threatening conditions (Azenha et al., 2012; Tavakoli et al., 2013). Against this backdrop, we expected to find a higher LOS on subjects with spread infections. The presumptions were endorsed by the verification of highly significant greater LOS in patients with infection spreading ($p < 0.001$; $rc = -0.965$).

With the object of highlighting the role of the infection focus in a temporal context to abscess incision on the time of discharge, we emphasized two novel risk factors **dbir** and **riss** and replaced the item “remaining infection focus” in group A ($n = 185$). Both of the risk factors had a highly significant impact on the LOS (dbir: $p < 0.001$; $rc = -0.149$; riss: $p < 0.001$; $rc = -0.759$). Hence, interpreting the calculated data illustrates that the longer it took to remove the focus of infection after initial incision and drainage, the greater the LOS. Additionally, we must state that removal of the infection focus the same stay that the incision and drainage procedure is performed tends to lower the probability of discharge significantly. Although prima facie the results appear diverting, the assertion may have a simple explanation. The findings of dbir suggest to aim for a short period between abscess incision and focus removal to lower the LOS. At the same time, the findings of **riss** show that the focus removal during the same stay as abscess incision leads to a lengthening of LOS. The easiest explanation for this might be a faster recovery of subjects with early removal of drainage and therefore an early hospital discharge, and thus prompt healing in the home environment with normal dietary and expeditious habitual mouth opening leading to possible focus removal.

The proposed statistical model explicitly describes (1) how the probability of discharge depends on the time (the length of stay in days by now), and (2) how specific characteristics of the patient affect the LOS. It can be derived from the model equation that the function $f_0(t)$ determines the probability of discharge that is always present for any x_i (the basic risk of discharge for any patient). The basic probabilities for each t are then modified by the individual patient's characteristics as illustrated in Figs. 2 and 3.

With the definition of the hazard function $\lambda(t|x_i)$ and the corresponding survival function $S(t|x_i)$ that are the main tools to describe the stochastic behavior in time-to-event models, it can be derived that the probability of a discharge at time t is given by $P(T_i{=}t|x_i) = \lambda(t|x_i)S(t\text{-}1|x_i)$ (Tutz and Schmid, 2016). In order to perform the sample calculations presented in Fig. 1, this expression was implemented in R and allows for predicting the LOS of each patient for practitioners in an easy way.

The present study attempts to provide a mathematical approach to the hospital LOS of inpatients treated for severe odontogenic infection and is conceived as a pilot study. A future aim should be the testing of the mathematical formula on cohorts of other departments, for an examination of its usefulness in a wider context.

5. Conclusion

Increased LOS in patients with acute odontogenic infection remains a major burden for patients' health and for public health care systems. Predicting the LOS may promote transparency regarding costs and management of patients under inpatient treatment. Our statistical model describes the probability of a discharge at time t compared to a discharge later than t (a hospital LOS longer than t). Furthermore, the model enables a prediction of the LOS of each patient for practitioners in an easy way.

Ethical approval

Due to the fact that explicitly anonymous data were retrospectively analyzed, approval is not necessary.

Financial disclosure

There are no financial disclosures or commercial interests from any authors.

Conflicts of interest

There were no conflicts of interest.

Acknowledgements

We state that the analyzed patients are an extension to a cohort that was already published in part in another publication, but in another context.

References

Azenha MR, Homsi G, Garcia Jr IR: Multiple brain abscess from dental origin: case report and literature review. Oral Maxillofac Surg 16(4): 393–397, 2012
Berger M, Schmid M: Semiparametric regression for discrete time-to-event data. Stat Model 18: 1–24, 2018
Biasotto M, Pellis T, Cadenaro M, Bevilacqua L, Berlot G, Di Lenarda R: Odontogenic infections and descending necrotising mediastinitis: case report and review of the literature. Int Dent J 54(2): 97–102, 2004
Boffano P, Roccia F, Pittoni D, et al: Management of 112 hospitalized patients with spreading odontogenic infections: correlation with DMFT and oral health impact profile 14 indexes. Oral Surg Oral Med Oral Pathol Oral Radiol 113: 207–213, 2012
Burnham R, Bhandari R, Bridle C: Changes in admission rates for spreading odontogenic infection resulting from changes in government policy about the dental schedule and remunterations. Br J Oral Maxillofac Surg 49(1): 26–28, 2011
Costich ER, Cramer JR, White RP: Criteria for tooth removal: dental infection. Dent Clin North Am 13: 913, 1969
DeAngelis AF, Barrowman RA, Harrod R, Nastri AL: Maxillofacial emergencies: oral pain and odontogenic infections. Emerg Med Australas 26(4): 336–342, 2014
Dvori S, Laviv A, Rahima H, Taicher S: [Clinical parameters in evaluating hospitalized patients with orofacial odontogenic infection–a preliminary retrospective study. Refuat Hapeh Vehashinayim 24: 46–49, 2006 93, [in Hebrew]
Flynn TR, Shanti RM, Hayes C: Severe odontogenic infections, part 2: prospective outcomes study. J Oral Maxillofac Surg 64: 1104–1113, 2006
Heim N, Faron A, Wiedemeyer V, Reich RH, Martini M: Microbiology and antibiotic sensitivity of head and neck space infections of odontogenic origin. Differences in inpatient and outpatient management. J Craniomaxillofac Surg 45(10): 1731–1735, 2016
Herrera D, Roldan S, Gonzales I, Sanz M: The periodontal abscess (I). Clinical and microbiological findings. J Clin Periodontol 27: 387–394, 2000
Hwang T, Antoun JS, Lee KH: Features of odontogenic infections in hospitalised and non-hospitalised settings. Emerg Med J 28: 766–769, 2011
Islam S, Loewenthal MR, Hoffman GR: Use of peripherally inserted central catheters in the management of recalcitrant maxillofacial infection. J Oral Maxillofac Surg 66(2), 2008 330e335
Jundt JS, Gutta R: Characteristics and cost impact of severe odontogenic infections. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 114: 558–566, 2014
Kim MK, Nalliah RP, Lee MK, et al: Factors associated with length of stay and hospital charges for patients hospitalized with mouth cellulitis. Oral Surg Oral Med Oral Pathol Oral Radiol 113: 21–28, 2012
Li M, Krishna MT, Razaq S, Pillay D: A real-time prospective evaluation of clinical pharmaco-economic impact of diagnostic label of 'penicillin allergy' in a UK teaching hospital. J Clin Pathol 67(12): 1088–1092, 2014
Macy E, Contreras R: Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. J Allergy Clin Immunol 133(3): 790–796, 2014
Martis CS, Karakasis DT: Extractions in the presence of acute infections. J Dent Res 54: 59–61, 1975
Nair PN: Pathogenesis of apical periodontitis and the causes of endodontic failures. Crit Rev Oral Biol Med 15: 348–381, 2004
Okunseri C, Okunseri E, Thorpe JM, Xiang Q, Szabo A: Patient characteristics and trends in nontraumatic dental condition visits to emergency departments in the United States. Clin Cosmet Investig Dent 4: 1–4, 2012
Opitz D, Camerer C, Camerer DM, Raguse JD, Menneking H, Hoffmeister B, et al: Incidence and management of severe odontogenic infections: a retrospective analysis from 2004 to 2011. J Craniomaxillofac Surg 43(2): 285–289, 2015
Ottaviani G, Costantinidis F, Perinetti G, Luzzati R, Contardo L, Visintini E, et al: Epidemiology and variables involved in dental abscess: survey of dental emergency unit in Trieste. Oral Dis 20(5): 499–504, 2014
Pourdanesh F, Dehghani N, Azarsina M, et al: Pattern of odontogenic infections at a tertiary hospital in Tehran, Iran: a 10-year retrospective study of 310 patients. J Dent (Tehran) 10: 319–328, 2013
Rao DD, Desai A, Kulkarni RD, et al: Comparison of maxillofacial space infection in diabetic and nondiabeteic patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 110: e7–e12, 2010
Robertson D, Smith AJ: The microbiology of the acute dental abscess. J Med Microbiol 58: 155–162, 2009
R Core Team: R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. Available at: https://www.R-project.org/; 2017
Sanchez R, Mirada E, Arias J, Pano JR, Burgueno M: Severe odontogenic infections: epidemiological, microbiological and therapeutic factors. Med Oral Patol Oral Cir Bucal 16(5), 2011 e670-676
Sato FR, Hajala FA, Freire Filho FW, Moreira RW, de Moraes M: Eight-year retrospective study of odontogenic origin infections in a postgraduation program on oral and maxillofacial surgery. J Oral Maxillofac Surg 67(5): 1092–1097, 2009
Seppanen L, Lauhio A, Lindqvist C, Suuronen R, Rautemaa R: Analysis of systemic and local odontogenic infection complications requiring hospital care. J Infect 57: 116–122, 2008
Seppanen L, Rautemaa R, Linqvist C, Lauhio A: Changing clinical features of odontogenic maxillofacial infections. Clin Oral Investig 14(4): 459–465, 2010
Shah AC, Leong KK, Lee MK, Allareddy V: Outcomes of hospitalizations attributed to periapical abscess from 2000 to 2008: a longitudinal trend analysis. J Endod 39(3): 1104–1110, 2013
Shu M, Wong L, Miller JH, Sissons CH: Development of multi-species consortia biofilms of oral bacteria as an enamel and root caries model system. Arch Oral Biol 45: 27–40, 2000
Staffieri C, Fasanaro E, Favaretto N, et al: Multivariate approach to investigating prognostic factors in deep neck infections. Eur Arch Otorhinolaryngol 271: 2061–2067, 2014
Tavakoli M, Bagheri A, Faraz M, Salehirad S, Roghaee S: Orbital cellulitis as a complication of mandibular odontogenic infection. Ophthal Plast Reconstr Surg 29(1): e5–e7, 2013
Tutz G, Schmid M: Modeling discrete time-to-event data. New York, NY: Springer, 2016
Walia IS, Borle RM, Mehendiratta D, Yadav AO: Microbiology and antibiotic sensitivity of head and neck space infections of odontogenic origin. J Maxillofac Oral Surg 13(1): 16–21, 2014
Wang LF, Kuo WR, Tsai SM, Huang KJ: Characterizations of life-threatening deep cervical space infections: a review of one hundred ninety-six cases. Am J Otolaryngol 24(2): 111–117, 2003

Warnke PH, Becker ST, Springer IN, Haerle F, Ullmann U, Russo PA, et al: Penicillin compared with other advanced broad spectrum antibiotics regarding antibacterial activity against oral pathogens isolated from odontogenic abscesses. J Craniomaxillofac Surg 36(8): 462–467, 2008
Welchowski T, Schmid M: discSurv: discrete time survival analysis. R package version 1.3.0; 2018
Wood SN: Fast stable restricted maximum likelihood and marginal likelihood estimation of semiparametric generalized linear models. J R Stat Soc B 73(1): 3–36, 2011
Zirk M, Buller J, Goeddertz P, Rothamel D, Dreiseidler T, Zoller JE, et al: Empiric systemic antibiotics for hospitalized patients with severe odontogenic infections. J Craniomaxillofac Surg 44(8): 1081–1088, 2016