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Biological factors predicting the length of hospital stay in odontogenic cellulitis

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Biological factors predicting the length of hospital stay in odontogenic cellulitis.

Abstract:

Objective: The purpose of this study was to assess whether common biological factors are correlated with a longer hospital stay.

Study Design: All patients having odontogenic cellulitis, treated from January 2019 to December 2019 at Lille University Hospital, and requiring surgical drainage under general anesthesia, were included, retrospectively. Data, such as length of hospital stay and biological factors, namely, C-reactive protein (CRP) level, Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score, and bacterial samples were collected.

Results: Significant moderate-strong correlations were found between postoperative length of stay and patients' LRINEC score (r_s = 0.556) and presurgical CRP level (r_s = 0.579). There was a significant moderate correlation between postoperative length of stay and presurgical procalcitonin level (r_s = 0.451), and a weak correlation between postoperative length of stay and presurgical white blood cell count (r_s = 0.282). Linear regression verified CRP as an independent predictor of length of hospital stay, showing a significant linear relationship between them ($p < 0.0001$). A significant regression equation was found ($F(1,65) = 27.089$; $p = 0.0001$), with an R^2 of 0.294.

Conclusion: In this study, CRP was the key biological predictor of length of hospital stay.

Keywords: odontogenic infection; odontogenic cellulitis; length of hospital stay; hospitalization duration; C-reactive protein; white blood cell count.

Statement of clinical relevance: The ability to predict length of hospital stay and identify patients requiring intensive care management, using simple and inexpensive biological parameters (such as CRP), will enable more cost-effective care and efficient hospital bed management.

INTRODUCTION:

Odontogenic infection is an infection of the head and neck, originating in a tooth. It may be caused by dental caries with pulp necrosis, failed root canal treatment, periodontal disease, or complications of dental procedures [1,2]. It is the most frequent head and neck infection. Indeed, periapical radiolucency has been found to affect 5% of all the teeth included in a systematic review including 300,000 teeth [3]. When the infection spreads to the cellular-adipose tissue of the head and neck, it becomes odontogenic cellulitis. Most of the cases are acute localized forms without signs of severity, and are rapidly resolved through appropriate medical and surgical treatment. However, the infection can disseminate deeply along the fascial planes, becoming life-threatening and causing extensive morbidity [2]. Pre-existing “red flag” symptoms, such as trismus, dysphagia, dyspnea, extensive erythema of the neck or multispace infection should alert the practitioner [1,4]. In the maxilla, it is common to observe extension into the canine, buccal, and masticator spaces. Although maxillary odontogenic infections rarely pose a threat to the airway, they do have the potential to cause serious but exceptional complications, such as orbital abscess, cavernous sinus thrombosis, and cerebral abscess. In the mandible, the thin lingual cortex in the posterior molar region allows for the rapid spread of the infection in the fascial planes and can lead to airway obstruction and, ultimately, to mediastinitis. Even today, mortality and morbidity are not negligible, despite the progress made in the diagnosis and treatment of the disease [5,6].

Severe odontogenic cellulitis with “red flag” symptoms is treated surgically with extensive drainage, care based on the dental etiology (dental extraction or root canal treatment), and probabilistic parenteral antibiotic therapy [1]. In its most serious form, upper airway protection or hyperbaric oxygen therapy may be necessary [7,8], and the duration of hospital stay is prolonged. Despite a declining incidence of odontogenic cellulitis in recent years, the economic burden of its combined frequency and severity has been significant [5,9,1011].

Several studies have investigated various risk factors for severe infection, such as chronic alcoholism, immunodeficiency (e.g., poorly controlled diabetes mellitus, acquired immunodeficiency syndrome), use of non-steroidal anti-inflammatory drugs (NSAIDs), and incomplete or unsuitable antibiotic therapy, and they have identified the impact of them on the increased risk for severe odontogenic cellulitis and prolonged hospital stay [8,12–14]. However, biological parameters may also predict severe odontogenic cellulitis and prolonged hospital stay. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC), which is based on 6 common biological parameters, including C-reactive protein (CRP), white blood cell count, hemoglobin, sodium, creatinine, and glucose, is a prognostic measure developed to detect the most serious cases of soft-tissue infection [15,16]. When the LRINEC score is greater than or equal to 6, there is a higher risk of developing necrotizing fasciitis. This score does not include procalcitonin (PCT), which is considered the best diagnostic marker for severe bacterial infection and sepsis [17,18].

The purpose of this study was to assess whether common biological factors are correlated with an increase in patients' hospital stay. Predicting the severity of infection and the length of hospital stay are very important to optimize care management and patient flow in the healthcare facility.

MATERIAL AND METHODS:

Patients:

All patients diagnosed with odontogenic cellulitis, treated from January 2019 to December 2019 at Lille University Hospital, and requiring surgical drainage under general anesthesia, were included retrospectively. Patients who could be managed with local anesthesia or did not have hospital follow-up were not included in the study. All procedures performed in the study were in accordance with the ethical standards of the Helsinki declaration. No institutional review board assessment was required because of the retrospective nature of the study in accordance with French law.

Variable to be explained: Length of the hospital stay

Length of the hospital stay was measured in days. It started on the day of the patient's admission to the emergency unit. Patients were discharged from the hospital with antibiotics when they were afebrile and clinically improved and after switching from intravenous to oral antibiotics. The main clinical criteria for improvement were body temperature < 38°C decreased edema or erythema, and cessation of trismus.

Explanatory variables

- Age, sex, and consumption of NSAIDs before admission.

- Clinical presentation on admission to the hospital: fever (> 38°C), pain (visual analog scale), swelling, trismus (mild, moderate, or severe), signs of obstruction (dyspnea, dysphagia), and severe sepsis (systemic infection with organ failure or peripheral hypoperfusion or arterial hypotension before volume expansion).

- Laboratory analysis on admission to the hospital: white blood cell count ($/mm^3$), CRP (mg/L), PCT (ng/mL), blood glucose (g/dL), creatinine (mg/L), and creatine phosphokinase (CPK) (IU/L).

- LRINEC score

- Peroperative bacterial sample

Statistical analysis

Quantitative variables are expressed as mean (standard deviation, SD) in the case of normally distributed data or median (interquartile range Q1–Q3) otherwise. Categorical variables are expressed as number (%). The normality of the distributions was assessed using histograms and the Shapiro-Wilk test. The Mann–Whitney U test was applied to compare non-normally distributed means. Spearman's correlation was used to calculate the correlations between pairs of non-normally distributed variables, and a p-value less than 0.05 was considered statistically significant. The strength of the correlations for the absolute values of the ratios of the compared variables were: very weak (0–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (0.80–1.0). An adjusted hypothesis of linearity across length of hospital stay and the selected biological variables was estimated using analysis of covariance (ANCOVA). The model included sex, age, CRP, PCT, white blood cell count, and LRINEC score as covariates. Single linear regression models were also used for a better explanation of the relationship between postoperative length of hospital stay and the significance of the selected biological variables. Analyses were performed using R statistical software.

RESULTS:

Characteristics of the study population

Seventy-one patients who underwent surgical management and hospital follow-up for their odontogenic cellulitis were included in the final analysis. Characteristics of the study population are listed in Table 1.

Our analysis of the study population included 41 males (57.75%) and 30 females (42.25%). Their mean age was 40.78 years (18.97). The median levels of the biological variables were: 14440 white blood cells/mm^3 (11465–17160); the CRP was 140 mg/L (69.5–229.5); the PCT was 0.110 ng/mL (0.100–0.325); blood glucose was 1.160 g/dL (1.015–1.140); creatinine was 7 mg/L (6–8), and the CPK was 63.50 IU/L (39.25–105.75). The median hospital stay was 4 days (3.5–6.5). Violin plots representing the distributions of the biological variables and length of hospital stay across sex are presented in Figure 1. Microbiological characteristics of the study population are listed in Table 2.

Analyses of the postoperative length of stay and presurgical biological parameters

There was a significantly higher postoperative length of stay in the male population ($p = 0.01$). The mean postoperative length of stay was 6.43 days (3.62) in the male population and 5.40 days (7.59) in the female population. There was a significant moderate-strong correlation between postoperative length of stay and the LRINEC score ($r_s = 0.556$) and the presurgical CRP level ($r_s = 0.579$). There was a significant moderate correlation between postoperative length of stay and the presurgical PCT level ($r_s = 0.451$), and a weak correlation between postoperative length of stay and the presurgical white blood cell count ($r_s = 0.282$).

The ANCOVA model showed a marginal effect of CRP on the length of hospital stay and a significant regression equation ($F(6,52) = 4.879$; $p = 0.001$), with an R^2 of 0.360 (Figure 2). A further linear regression verified the independent effect of CRP on length of hospital stay, showing a significant linear relationship between the two variables ($p < 0.0001$). A significant regression equation was found ($F(1,65) = 27.089$; $p = 0.0001$), with an R^2 of 0.294. Participants' predicted length of hospital stay was equal to 1,502+0,028*CRP, with CRP measured as mg/L. This model indicates that each time the CRP increased by 1 mg/L, the hospital stay increased by 0.03 days (Figure 3). In other words, when the CRP is equal to 125mg/L, the predicted hospital stay is 5 days.

The entire results suggest that CRP was the key biological parameter of length of hospitalization. A 3D scatter plot representing the CRP level across sex and length of hospital stay is illustrated in Figure 4.

DISCUSSION:

We showed that preoperative CRP was strongly correlated with length of hospital stay. CRP is an inflammation protein mainly produced by the liver, which is usually present in very small amounts in healthy persons (< 10 mg/L). In severe infections or inflammatory reactions, a rise in the CRP serum concentration can reach 1000-fold within a few hours of the development of clinical symptoms. It increases significantly in the first 6 hours with a peak at 24-48 hours, and it decreases rapidly after resolution of the infectious episode, making it a sensitive marker of systemic inflammation [19–21]. In addition, CRP level is not influenced by usual anti-inflammatory drugs [22].

Some studies have investigated the link between the initial CRP concentration and acute odontogenic cellulitis severity or hospital length of stay [19–21,23–26]. Most of these studies have found that CRP was an effective parameter for predicting hospital length of stay [19–21,23,24]. Similarly, Sharma et al. [23] showed that CRP level was a significant marker of length of hospital stay using a quantitative approach. The higher the CRP concentration was, the longer the patient's hospital stay. They found a linear relationship with an R^2 value of 0.401, implying that 40.1% of the variation in hospital stay was explained by the CRP level. Despite a fairly strong correlation between these two variables in our analysis ($r_s = 0.579$), we found a weaker linear relationship with an R^2 value of 0.294. Stathopoulos et al. [21] and Christensen et al. [27] also found a significant positive correlation between duration of stay and CRP, with an R^2 value close to our results (respectively, $R^2 = 0.53$ and $R^2 = 0.60$). Similarly, only CRP was a significant predictor of hospital stay when analyzed using multivariate regression with an adjusted R^2 of 0.396, which is consistent with our results: $R^2 = 0.360$. In their retrospective study using a qualitative approach, Heim et al. [19] found that patients hospitalized 10 days or more showed a significantly higher CRP level and white blood cell count on their admission day than patients with a shorter length of stay. In contrast to these findings, Mirochnik et al. [25] did not find any significant correlations between CRP level and length of hospital stay. However, they showed a clear correlation between the clinical severity score and duration of stay ($p = 0.00016$). On the other hand, an undisclosed number of patients included in their study had a surgical procedure before presenting to the emergency department, leading to interpretation bias. It is well known that surgical interventions, even minor surgeries, can be responsible for a rise in the CRP level [19,25]. Other articles have highlighted the role of the CRP level for predicting the severity of odontogenic cellulitis [4,19,27] Heim et al. [19] showed that the CRP level and the white blood cell count were significantly higher in patients with multiple-space infections. In addition, Christensen et al. [27] found a higher CRP level in a reoperation group, suggesting that this biological parameter was a severity marker. Fu et al. [4] pointed out that CRP levels exceeding 150 mg/L are associated with intensive care management. Patients admitted to intensive care units were approximately 5 times more likely to present with CRP levels greater than 150 mg/L.

The median leukocyte count was 14440/mm3. An elevated white blood cell count may be considered a normal finding in patients with odontogenic cellulitis. However, we found a significant though weak correlation between postoperative length of hospital stay and presurgical white blood cell count, and this correlation was weaker than the correlation between postoperative length of hospital stay and presurgical CRP level. Gholami et al. [28] and Stathopoulos et al. [21] have also shown a significant relationship between white blood cell count and length of hospital stay. Heim et al. [19] showed that the white blood cell count on the day of admission was higher when abscesses centered on the mandible or when patients presented with multiple space infections, suggesting that this parameter could be, in addition to the CRP level, a severity marker. Moreover, Gallagher et al. [29] reported the usefulness of the neutrophil to lymphocyte ratio (NLR) in the assessment of length of hospital stay. The cut-off value for the NLR of 4.65 predicted a length of hospital stay ≥ 2 days with 61.4% sensitivity and 61.5% specificity. According to their study, the NLR can be used to identify patients requiring admission to a hospital ≥ 2 days and those with a purulent collection requiring surgical drainage, suggesting a potential advantage over CRP, as well as a cost savings per patient.

An earlier and more specific marker than CRP, PCT is considered the best diagnostic marker for severe bacterial infection and sepsis [17,18]. Bertolus et al. [30] did not find the the PCT measurement to be useful in the usual management of head and neck odontogenic cellulitis because the serum PCT concentrations remained in the low range. We found similar results with a significant moderate correlation between the presurgical PCT level and the postoperative length of hospital stay. PCT is a biomarker of systemic bacterial infection; therefore, it might not rise in a strictly localized infectious process [17]. In our analyses, very few signs of severe sepsis were noted, which supports the localized evolution of odontogenic cellulitis. In addition, several patients took anti-inflammatory drugs prior to hospital care, which could have affected their PCT levels [31].

We found a significant strong correlation between patients' LRINEC score and length of hospital stay. The LRINEC score was proposed by Wong et al. [15] to determine the risk of necrotizing soft tissue infections. The numerical score, ranging from 0 to 13, is computed using six laboratory indices: CRP, white blood cell count, hemoglobin, sodium, creatinine, and blood glucose. A higher score indicates a higher risk of necrotizing fasciitis. According to Zemplenyi et al. [32], the LRINEC score indicating necrotizing soft tissue infection had a sensitivity of 60% (95% CI 15-95%) and a specificity of 68.4% (95% CI 51-82%). Nevertheless, while they found a significant relationship between the LRINEC score and its ability to detect necrotizing fasciitis in some patients, the score failed to predict the stage of necrotizing fasciitis. Indeed, out of a cohort of 479 patients, only 5 patients had necrotizing fasciitis, which the LRINEC score failed to predict in two cases. None of the patients in our study had cervical or mediastinal necrotizing fasciitis. Nevertheless, the LRINEC seemed to be a useful tool for screening severe odontogenic cellulitis and for estimating the length of hospital stay [33].

In our study, there was a significantly higher postoperative length of stay in males. This gender difference in length of stay could be influenced by hormonal factors. Ciarambino et al. [34] have shown an immune stimulatory role for estrogen as opposed to testosterone which is more immunosuppressive. In addition, Orooji et al. showed that male gender (RR: 0,92) was statistically a reducing factor for length of stay among elderly patients (> 65 years), which would be consistent with the hypothesis of a better female immune system defense before the menopause [35]. On the other hand, diabetes has been shown to be the systemic disease the most associated with odontogenic infection and has a higher male prevalence [5,32]. In our study, all the 6 cases of diabetes were reported in men.

Odontogenic cellulitis is a very common disease [4,36,37]. Predicting the severity of infection and length of hospital stay are, therefore, very important to optimize care management and patient flow in the healthcare facility. Based on the literature review and the results of this study, it seems certain that simple and inexpensive biological parameters, such as the CRP, are effective tools for estimating the length of hospital stay. Hospitalization costs are mainly related to the length of stay and the use of the operating room [10]. This bill is significantly higher for patients requiring intensive care management with or without mechanical ventilation or tracheotomy [9]. The ability to predict the length of hospital stay and to identify patients requiring intensive care management, using simple and inexpensive biological parameters, will enable more cost-effective and efficient hospital bed management [21,38].

CONCLUSION:

Preoperative CRP level is simple and inexpensive biological parameter significantly correlated with hospital length of stay. It is the most useful predictive biological factor; it should be performed systematically.

Declarations of interest: None.

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TABLES AND FIGURES:

Table 1: Characteristics of the population at admission

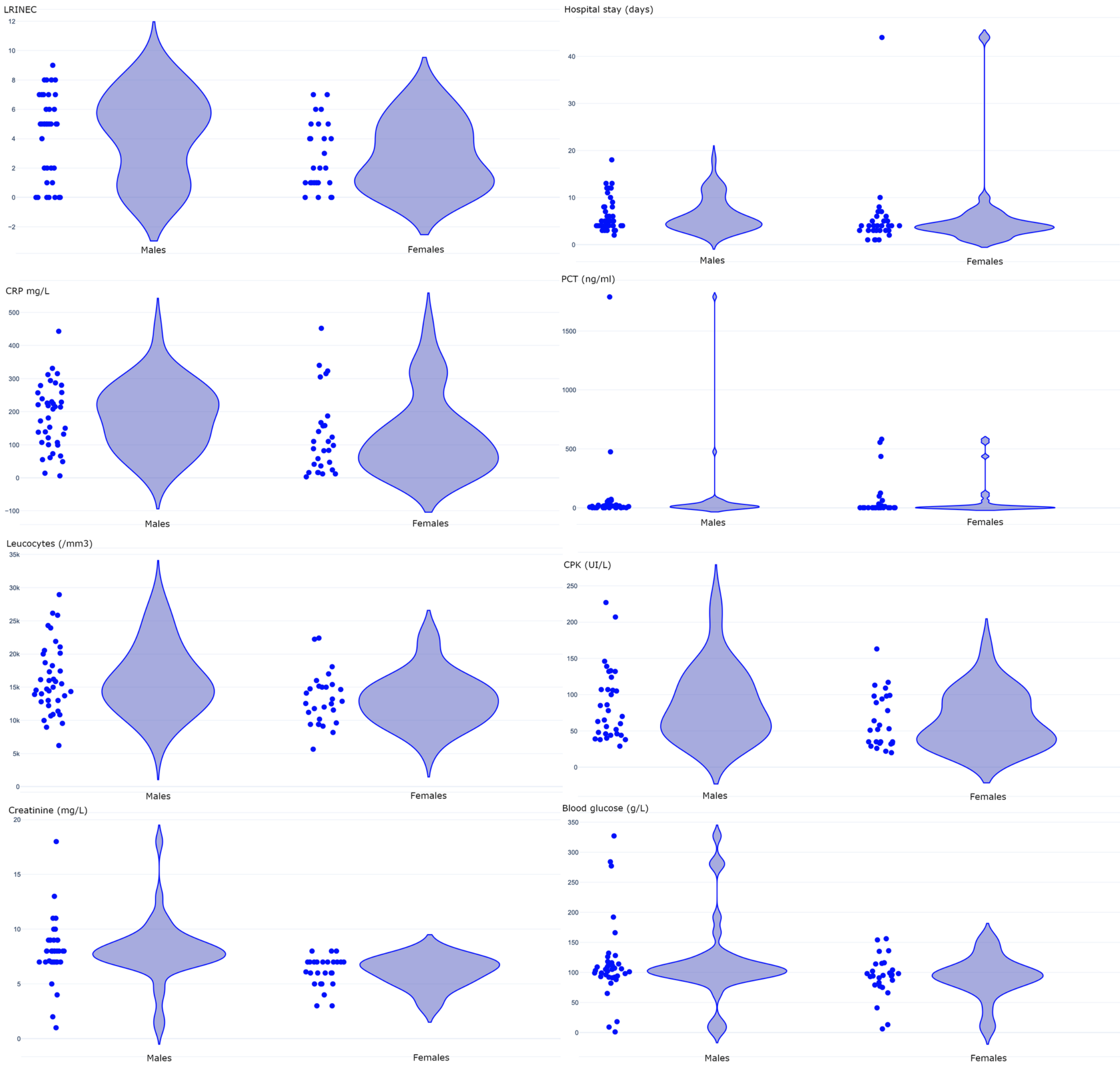
Table 2: Isolated pathogens in surgical samples

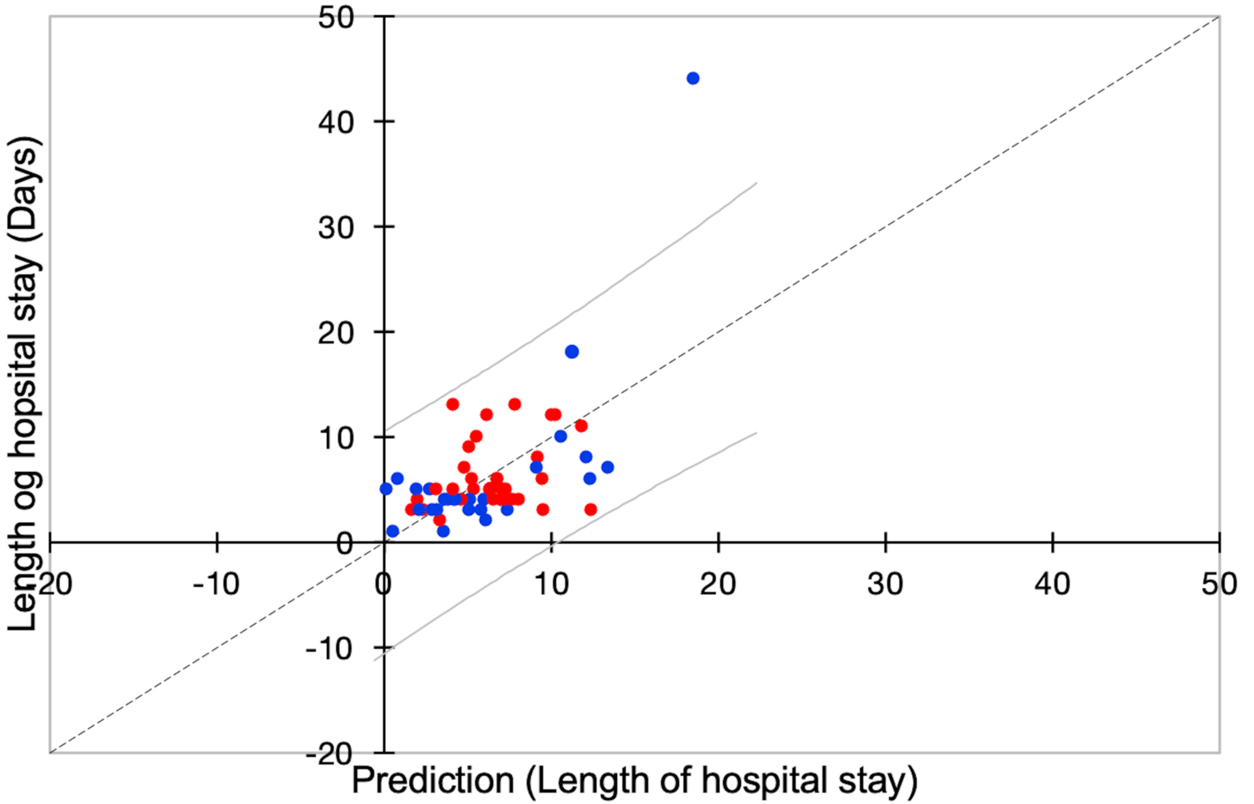
Figure 1: Violin plots representing biological values and length of hospital stay distributions across sex. CRP value on admission to the hospital was higher in males than in females.

Figure 2: Analysis of covariance estimating the adjusted hypothesis of linearity across length of hospital stay and biological values. Model included sex, age, CRP, PCT, white blood count and LRINEC score as covariates. The ANCOVA model showed a marginal effect of CRP on the length of hospital stay and a significant regression equation ($F(6,52) = 4.879$; $p = 0.001$), with an R^2 of 0.360.

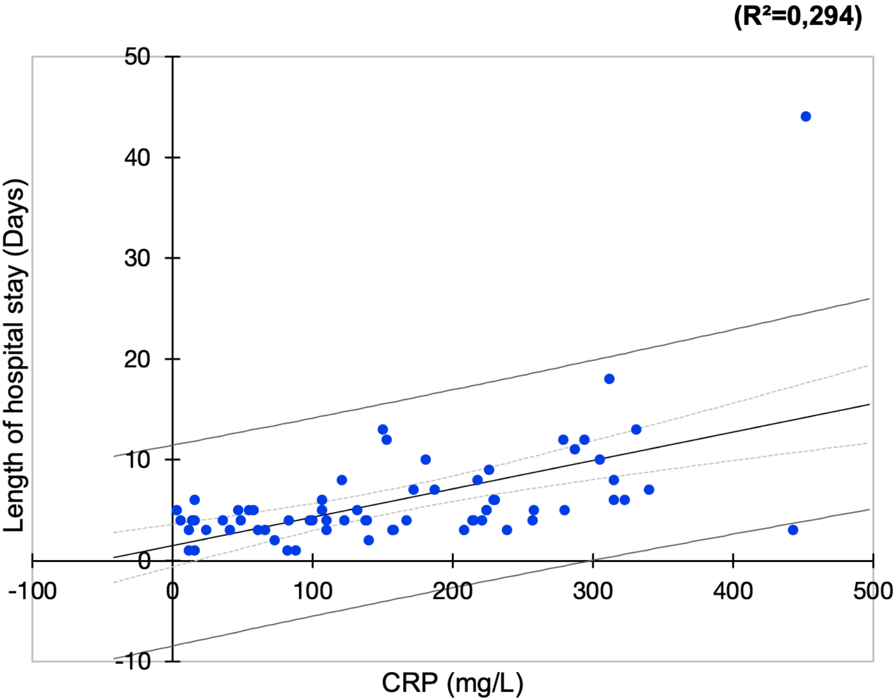
Figure 3: Simple linear regression between CRP and length of hospital stay, showing a significant linear relationship between the two variables ($p < 0.0001$).

Figure 4: 3D scatter plot representing CRP value across sex and length of hospital stay. Males (red) had a higher CRP value on the admission to hospital and presented a higher length of hospital stay.

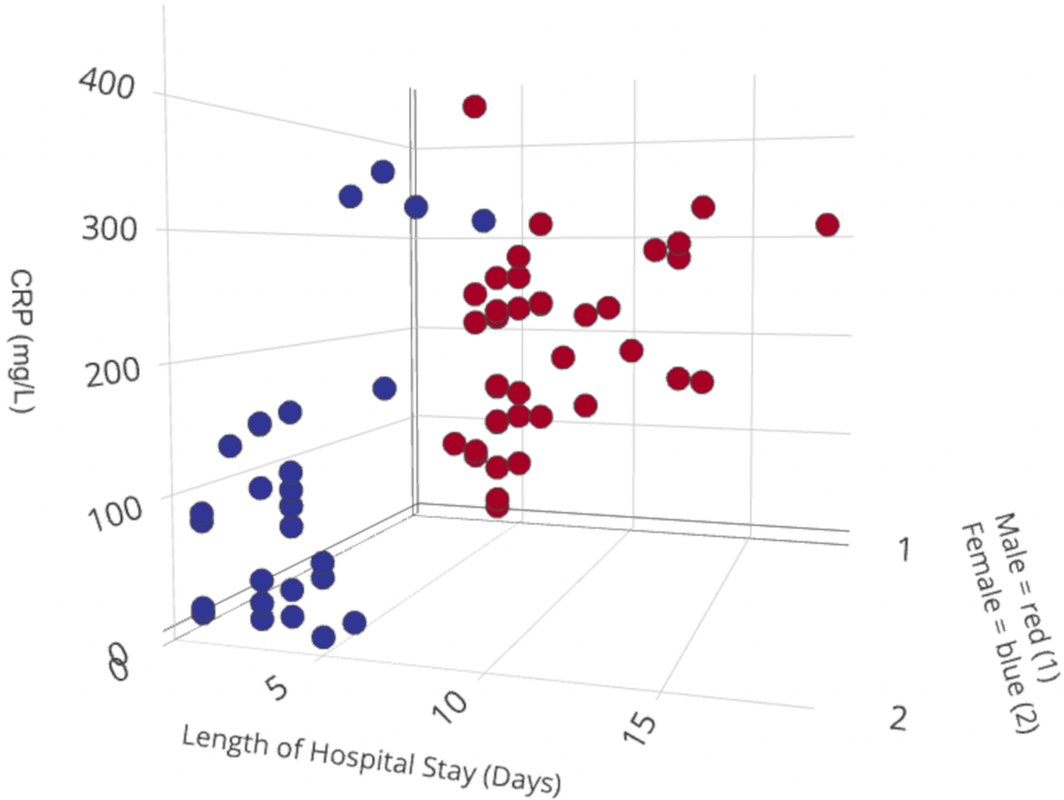

LRINEC
Males
Females
Hospital stay (days)
CRP mg/L
PCT (ng/ml)
Leucocytes (/mm3)
CPK (UI/L)
Creatinine (mg/L)
Blood glucose (g/L)



50
40
30
20
10
0
-10
-20
-20
-10
0
10
20
30
40
50
Length og hopsital stay (Days)
Prediction (Length of hospital stay)



(R²=0,294)
Length of hospital stay (Days)
50
40
30
20
10
0
-10
-100
0
100
200
300
400
500
CRP (mg/L)


400
300
200
100
0
CRP (mg/L)
5
10
15
Length of Hospital Stay (Days)
1
2
Male = red (1)
Female = blue (2)

Characteristics of the population at admission	N=71
Age *means (SD)*	40.78 (18.97)
Females *n (%)*	30 (42.25)
NSAID consumption before admission	18 (25.35)
Clinical characteristics:	
Fever (≥ 38°C)	27 (38.03)
Pain (VAS)	7 (5;8)
Swelling	70 (98.59)
Trismus	
Absence of trismus	2 (2.86)
Mild trismus	12 (17.14)
Moderate trismus	30 (42.86)
Severe trismus	26 (37.14)
Obstructive signs	42 (59.16)
Severe sepsis	3 (4.25)
Biological values:	
White blood count (/mm^3) *median (Q1;Q3)*	14440 (11465;17160)
CRP (mg/L) *median (Q1;Q3)*	140 (69.5;229.5)
PCT (ng/mL) *median (Q1;Q3)*	0.110 (0.100;0.325)
Blood glucose (g/dL) *median (Q1;Q3)*	1.160 (1.015;1.140)
Creatinine (mg/L) *median (Q1;Q3)*	7 (6;8)
CPK (IU/L) *median (Q1;Q3)*	63.50 (39.25;105.75)
LRINEC score *median (Q1;Q3)*	4 (1;6)
Length of hospital stay (days) *median (Q1;Q3)*	4 (3.5;6.5)

Isolated pathogens in surgical samples (N=45)	
Streptoccocus constellatus	22,5
Streptoccocus anginosus	19,7
Streptoccocus intermedius	2,8
Klebsiella pneumoniae	4,2
Klebsiella oxytoca	1,4
Fusobacterium	2,8
Hemophilus influenza B	1,4
Enterobacter aerogenes	1,4
Escherichia Coli	1,4
Eikenella corodens	1,4
Proteus vulgaris	1,4
Morganella morgani	1,4
Yeast	1,4