UNIVERSITÉ DE LILLE

FACULTÉ DE MÉDECINE HENRI WAREMBOURG

Année : 2021

THÈSE POUR LE DIPLÔME D'ÉTAT

DE DOCTEUR EN MÉDECINE

Facteurs biologiques prédictifs de la durée d'hospitalisation dans les cellulites dentaires

Présentée et soutenue publiquement le 24 Septembre à 18 heures
au Pôle Formation

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Avertissement

La faculté n’entend donner aucune approbation aux opinions émises dans les thèses : celles-ci sont propres à leurs auteurs.

SOMMAIRE

Résumé :

Objectif : Le but de cette étude était d'évaluer si des paramètres biologiques de routine étaient corrélés à une durée d'hospitalisation plus longue dans les cellulites dentaires

Matériel et méthodes : Tous les patients présentant une cellulite dentaire, traités de janvier 2019 à décembre 2019 au CHU de Lille, et nécessitant un drainage chirurgical sous anesthésie générale, ont été inclus de manière rétrospective. Les données, telles que la durée d'hospitalisation et les paramètres biologiques, à savoir le taux de protéine C-réactive (CRP), le score LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis), et les résultats des prélèvements bactériologiques ont été recueillis.

Résultats : Une corrélation significativement forte a été mis en évidence entre la durée d'hospitalisation postopératoire et le niveau de CRP préopératoire (rs= 0,579). Cette corrélation était significativement modérée concernant le score LRINEC des patients (rs = 0,556). Il existait une corrélation significativement modérée entre la durée d'hospitalisation post opératoire et le taux de pro-calcitonine préopératoire (rs = 0,451), et une faible corrélation entre la durée d'hospitalisation postopératoire et le nombre de leucocytes préopératoire (rs = 0,282). La régression linéaire a permis de vérifier que la CRP était un paramètre indépendant de la durée d'hospitalisation, montrant une relation linéaire significative entre ces deux données ($p < 0,0001$). Une équation de régression significative a été trouvée ($F(1,65) = 27,089$; $p = 0,0001$), avec un $R2$ de 0,294.

Conclusion : Dans cette étude, la CRP était le principal facteur prédictif biologique de la durée d'hospitalisation post opératoire.

1.Introduction

L’ infection d’origine dentaire est une infection touchant les régions de la tête et du cou. Elle peut être causée par une carie dentaire secondaire à une nécrose pulpaire, causée par l'échec du traitement endodontique, secondaire à une maladie parodontale ou être d'origine iatrogène [1,2]. Il s'agit de l'infection la plus fréquente de la tête et du cou. En effet, dans une revue systématique de la littérature incluant 300 000 dents, 5 % d'entre elles présentaient une ostéolyse apicale d’origine infectieuse [3]. Lorsque l'infection s'étend au tissu cellulo-adipeux des espaces de la tête et du cou, elle prend le nom de cellulite dentaire. Dans la majorité des cas, il s'agit de formes aiguës localisées sans signes de gravité, rapidement résolutives grâce à un traitement médical et chirurgical approprié. Cependant, l'infection peut s'étendre en profondeur le long des fascias, engageant alors le pronostic vital et générant une morbidité importante [2]. Des signes de gravité, tels que le trismus, la dysphagie, la dyspnée, l'érythème extensif du cou ou l'atteinte de plusieurs espaces anatomiques radiologiques doivent alerter le praticien [1,4]. Au niveau du maxillaire, on observe fréquemment une extension de l'infection au sein des espaces canins, buccal et masticateur. Bien que les cellulites dentaires maxillaires entrainent rarement une atteinte des voies respiratoires, elles peuvent provoquer des complications graves mais exceptionnelles, telles qu'un abcès orbitaire, une thrombose du sinus caverneux ou un abcès cérébral. Au niveau de la mandibule, la corticale linguale de la région molaire postérieure étant fine, l'infection peut se propager rapidement en profondeur et entraîner une obstruction des voies aériennes et dans les cas extrêmes provoquer une médiastinite. Aujourd'hui encore, la mortalité et la morbidité est non négligeable, malgré les progrès réalisés dans le diagnostic et le traitement de cette maladie [5,6].

Les cellulites dentaires sévères avec des signes de gravité sont traitées chirurgicalement par un drainage, des soins appropriés en fonction de l'étiologie dentaire (extraction dentaire ou traitement endocanalaire) et une antibiothérapie parentérale probabiliste [1]. Dans sa forme la plus grave, une protection des voies aériennes supérieures ou une oxygénothérapie hyperbare peuvent être nécessaires [7,8], entrainant par conséquent une hospitalisation prolongée. Malgré une baisse de l'incidence des cellulites dentaires ces dernières années, elles n'en restent pas moins un poids économique important pour notre société [5,9,10,11].

Plusieurs études ont analysé des facteurs de risque d'infection grave, comme l'alcoolisme chronique, l'immunodéficience (un diabète de type 2 non équilibré ou le syndrome d'immunodéficience acquise par exemple), l'utilisation d'anti-inflammatoires non stéroïdiens (AINS) ou une antibiothérapie incomplète ou inadaptée. Ils ont ainsi pu mettre en évidence leur impact sur l'augmentation du risque de cellulite dentaire grave et sur l'augmentation de la durée du séjour hospitalier [8,12-14]. Cependant, des paramètres biologiques peuvent également prédire la sévérité d'une cellulite dentaire et la durée d'hospitalisation. Le "Laboratory Risk Indicator for Necrotizing fasciitis" (LRINEC) est un score basé sur six paramètres biologiques usuels, dont la protéine C-réactive (CRP), le nombre de leucocytes, l'hémoglobine, le sodium, la créatinine et la glycémie veineuse. Cet indicateur pronostic permet de détecter les cas les plus graves d'infection [15,16]. Lorsque le score LRINEC est supérieur ou égal à 6, le risque de développer une fasciite nécrosante est plus élevé. Ce score ne tient pas compte de la procalcitonine (PCT), considérée comme le meilleur marqueur diagnostique d'une infection bactérienne grave et du sepsis [17,18].

L'objectif de cette étude était d'évaluer si des facteurs biologiques usuels étaient corrélés à une augmentation de la durée d'hospitalisation des patients. La prédiction de la gravité de l'infection et de la durée de l'hospitalisation a un intérêt pour optimiser la gestion des soins et le flux des patients dans les établissements de santé.

2. Material and methods

2.1 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.

2.2 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.

2.3 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 (/mm3), CRP (mg/L), PCT (ng/mL), blood glucose (g/dL), creatinine (mg/L), and creatine phosphokinase (CPK) (IU/L).
- LRINEC score
- Peroperative bacterial sample

2.4 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.

3. Results

3.1 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/mm3 (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 Fig. 1. Microbiological characteristics of the study population are listed in Table 2.

3.2 Analyses of the post-operative 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 ($rs = 0.556$) and the presurgical CRP level ($rs = 0.579$). There was a significant moderate correlation between postoperative length of stay and the presurgical PCT level ($rs = 0.451$), and a weak correlation

between postoperative length of stay and the presurgical white blood cell count (rs = 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 R2 of 0.360 (Fig. 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 R2 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 (Fig. 3). In other words, when the CRP is equal to 125 mg/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 Fig. 4.

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 h with a peak at 24−48 h, 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 R2 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 (rs = 0.579), we found a weaker linear relationship with an R2 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 R2 value close to our results (respectively, R2 = 0.53 and R2 = 0.60). Similarly, only CRP was a significant predictor of hospital stay when analyzed using multivariate regression with an adjusted R2 of 0.396, which is consistent with our results: R2 = 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 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 LRI- NEC 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].

5. Conclusion

La valeur de la CRP préopératoire est un paramètre biologique simple et peu coûteux, significativement corrélé à la durée d'hospitalisation. Il devrait être réalisé de manière systématique car c'est le facteur biologique prédictif le plus pertinent.

6. Bibliographies

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7. Annexes

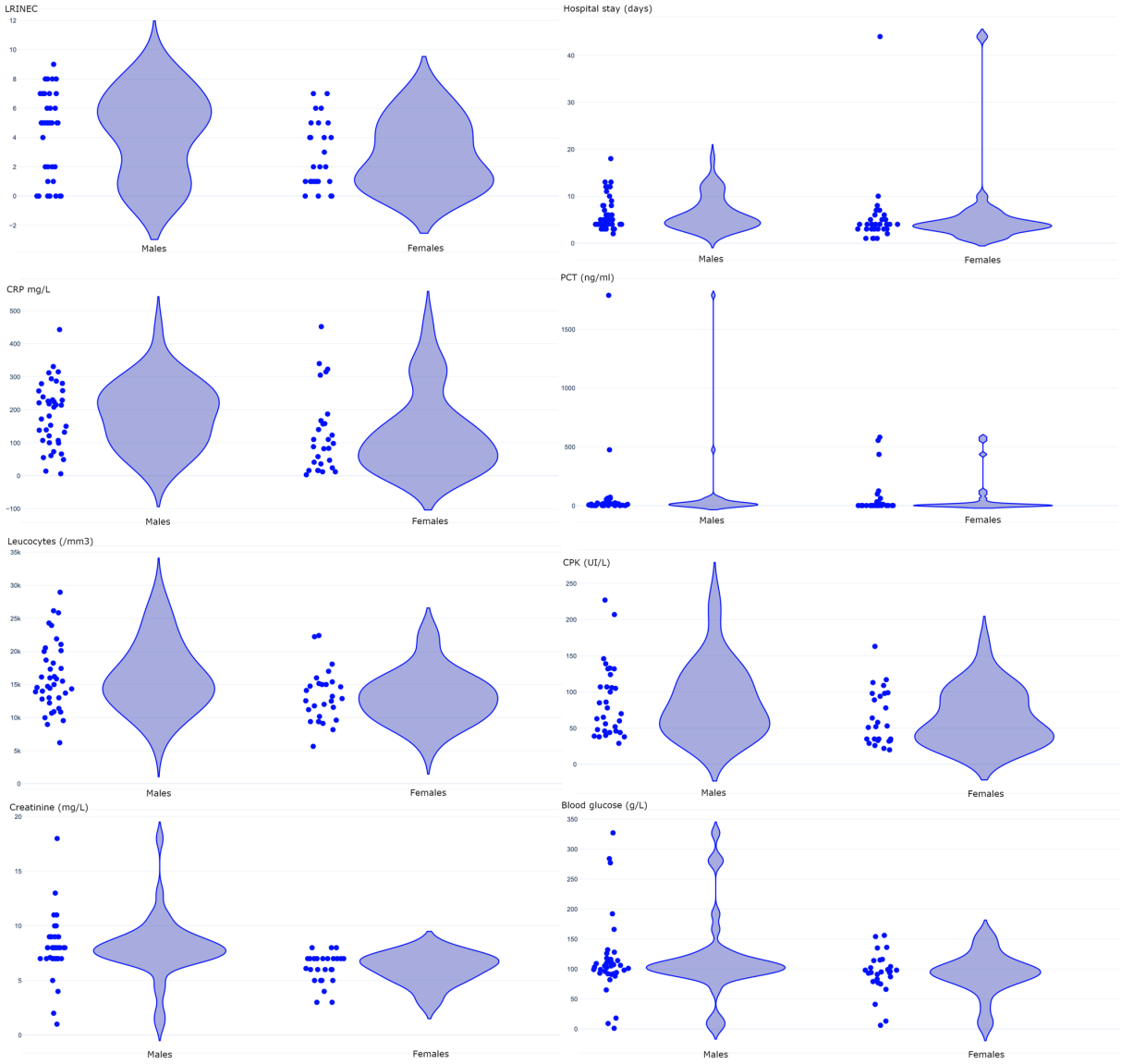

Figure 1. Violin plots representing biological values and length of hospital stay distributions across sex. CRP value on admission to the hospital was higher in males than in females.

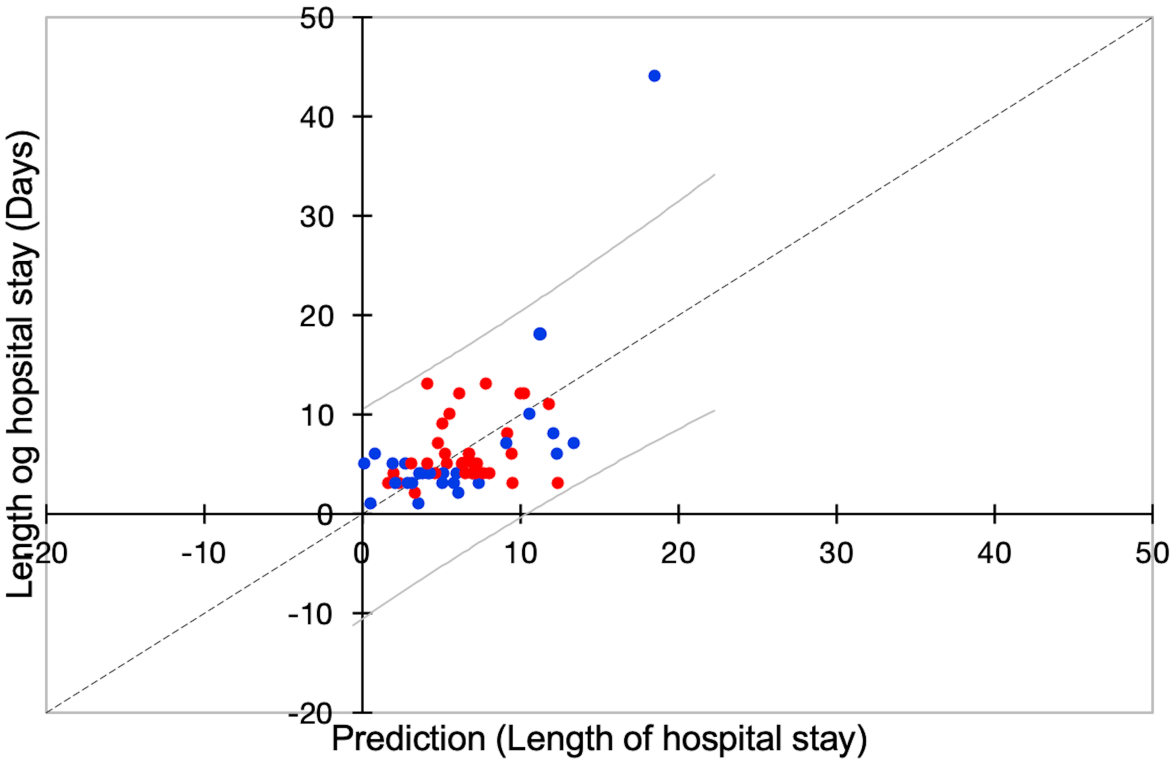

Figure 2: Analysis of covariance estimating the adjusted hypothesis of linearity across length of hospital stay and biological values. Model included sex, age, CRP, PCT, white blood count and LRINEC score as covariates. The ANCOVA model showed a marginal effect of CRP on the length of hospital stay and a significant regression equation (F (6,52) = 4.879; p = 0.001), with an R2 of 0.360.

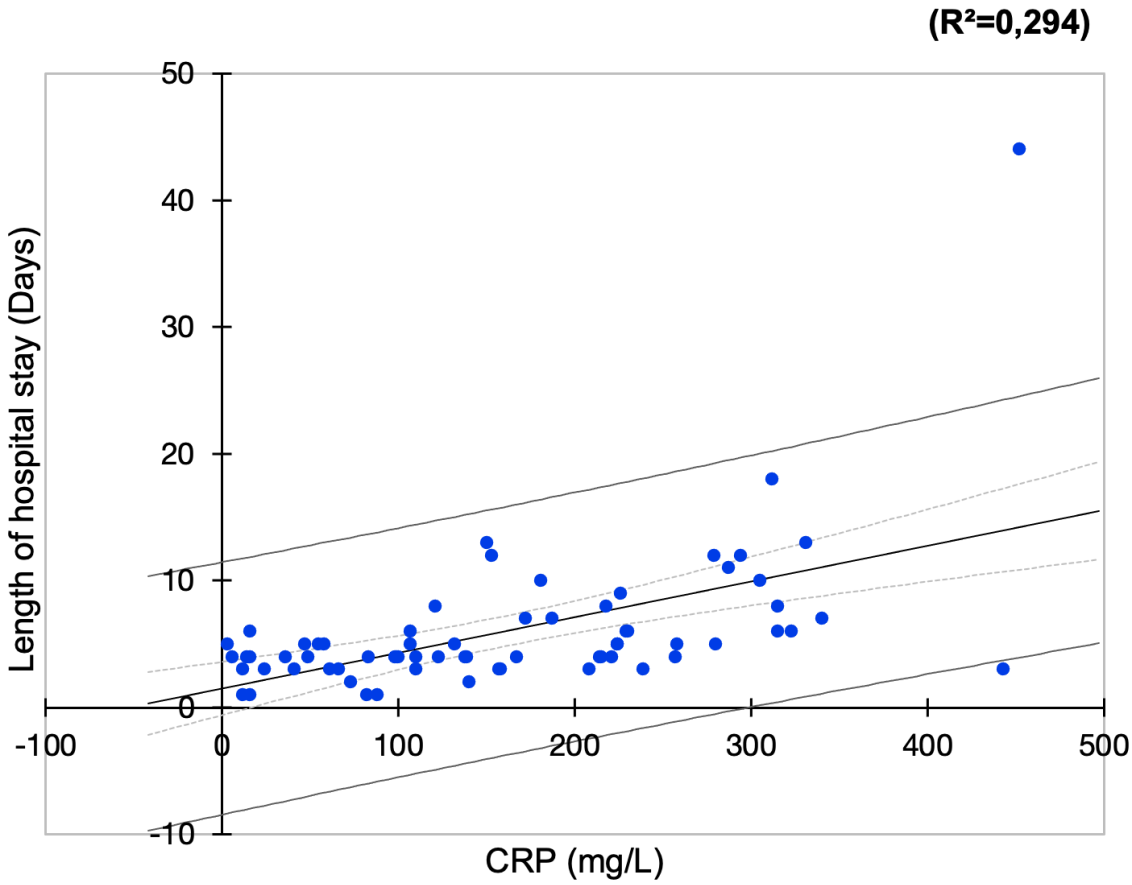

Figure 3: Simple linear regression between CRP and length of hospital stay, showing a significant linear relationship between the two variables ($p < 0.0001$).

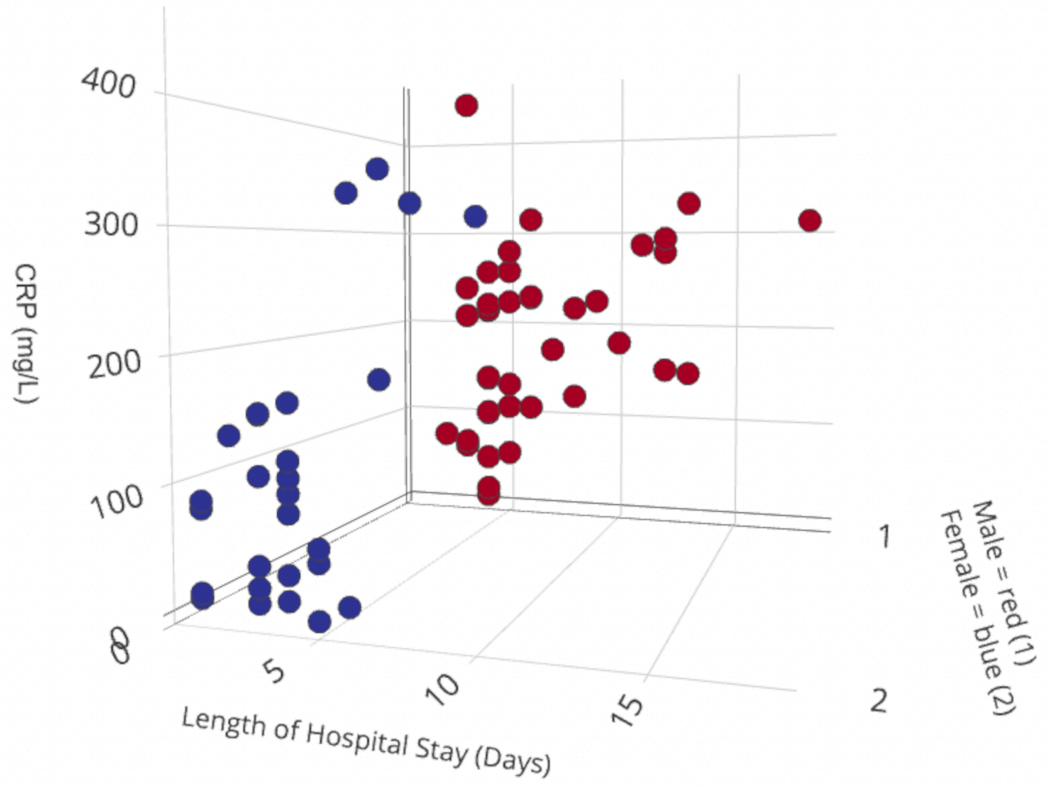

Figure 4: 3D scatter plot representing CRP value across sex and length of hospital stay. Males (red) had a higher CRP value on the admission to hospital and presented a higher length of hospital stay.

Table 1: Characteristics of the population at admission.

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)

Table 2: Isolated pathogens in surgical samples

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

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Date de soutenance : 24 Septembre 2021
Titre de la thèse : Facteurs biologiques prédictifs de la durée d'hospitalisation dans les cellulites dentaires.

Thèse - Médecine - Lille 2021

Cadre de classement : Chirurgie Maxillo-Faciale et Stomatologie

DES : Chirurgie Maxillo-Faciale

Mots-clés : Infection odontogène, Cellulite dentaire, Durée du séjour hospitalier, Durée d'hospitalisation, protéine-C-réactive (CRP), Nombre de leucocytes

Résumé :

Objectif : Le but de cette étude était d'évaluer si des paramètres biologiques de routine étaient corrélés à une durée d'hospitalisation plus longue dans les cellulites dentaires

Matériel et méthodes : Tous les patients présentant une cellulite dentaire, traités de janvier 2019 à décembre 2019 au CHU de Lille, et nécessitant un drainage chirurgical sous anesthésie générale, ont été inclus de manière rétrospective. Les données, telles que la durée d'hospitalisation et les paramètres biologiques, à savoir le taux de protéine C-réactive (CRP), le score LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis), et les résultats des prélèvements bactériologiques ont été recueillis.

Résultats : Une corrélation significativement forte a été mis en évidence entre la durée d'hospitalisation postopératoire et le niveau de CRP préopératoire (rs= 0,579). Cette corrélation était significativement modérée concernant le score LRINEC des patients (rs = 0,556). Il existait une corrélation significativement modérée entre la durée d'hospitalisation post opératoire et le taux de pro-calcitonine préopératoire (rs = 0,451), et une faible corrélation entre la durée d'hospitalisation postopératoire et le nombre de leucocytes préopératoire (rs = 0,282). La régression linéaire a permis de vérifier que la CRP était un paramètre indépendant de la durée d'hospitalisation, montrant une relation linéaire significative entre ces deux données ($p < 0,0001$). Une équation de régression significative a été trouvée ($F(1,65) = 27,089$; $p = 0,0001$), avec un $R2$ de 0,294.

Conclusion : Dans cette étude, la CRP était le principal facteur prédictif biologique de la durée d'hospitalisation post opératoire.

Composition du Jury :

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