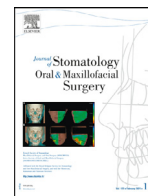




Available online at
ScienceDirect
 www.sciencedirect.com

Elsevier Masson France
EM|consulte
 www.em-consulte.com



Original Article

Surgical difficulty and postoperative course of the third molar extraction under general anesthesia: An intervention trial



Beatríz Sainz de Baranda^a, Francisco Javier Silvestre^{b,c}, Cecilia Fabiana Márquez-Arrico^{b,*},
 Javier Silvestre-Rangil^b

^a Private Dentist, DDS, Dental surgeon, 02001 Albacete, Spain

^b Department of Stomatology, University of Valencia, 46010 Valencia, Spain

^c Department of Stomatology, University Hospital Doctor Peset-FISABIO, 46017 Valencia, Spain

ARTICLE INFO

Article History:

Received 11 September 2023

Accepted 24 October 2023

Available online 27 October 2023

Keywords:

Wisdom tooth extraction

General anesthesia

Pederson scale

Dental extraction postoperative

ABSTRACT

Background: Third molar extractions are one of the most common surgical procedures in the area of stomatology. However, we know that even if they are minor surgeries, they can cause a postoperative period with local and systemic repercussions. Thus, the aim of this intervention trial is to determine the relationship between clinical parameters (pain, inflammation and trismus) and serum parameters (C-reactive protein (CRP), IL-6 and fibrinogen) that are modified in the first postoperative week, and the appearance of complications after extraction with general anesthesia, using the Pederson scale.

Methods: The research question was: Can postoperative discomfort after third molar extraction under general anesthesia be predicted using Pederson scale? An interventional trial was carried out of third molar extractions under general anesthesia in Dr. Peset University Hospital. Patient selection was performed randomized using MS Excel. Then were divided into two groups ($n = 126$): group A (2 complex extractions) and group B (4 extractions: 2 simple and 2 complex). All parameters were collected at the surgery and 7 days after surgery.

Results: The clinical postoperative parameters showed significant differences in relation to surgical difficulty. In summary, the degree of surgical difficulty can be predicted with the Pederson scale before extracting mandibular third molars. CRP and fibrinogen levels increase significantly with the degree of surgical difficulty.

Conclusion: Significant differences ($p < 0.001$) were observed in all the intraoperative parameters according to surgical difficulty as assessed by the Pederson scale. Therefore, this scale was a good indicator to estimate the patient's postoperative period.

© 2023 The Author(s). Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

1. Introduction

Nowadays, dentistry is one of the health specialties that frequently contemplates a high number of minor surgical procedures. Among these surgical procedures, the extraction of retained molars is one of the most frequently performed. The incomplete eruption or impaction generates recurrent infections, pain, inflammation, caries in adjacent molars and periodontal pockets among others [1]. Furthermore, depending on factors such as the age of the patient, the complexity of the impaction within the mandibular ramus and bacterial superinfection, this impaction of the third molars can produce systemic manifestations in the patient such as fever and cellulitis [1–4]. Before surgery, due consideration is required of the characteristics of each individual patient, with the adoption of contingency plans

to adequately resolve any unexpected problems. The need to resort to general anesthesia depends on the patient history, the surgical difficulty of extraction, the number of molars to be removed, the anesthetic preferences, and the economical limitations of the patients [2,3,4].

Although the extraction of third molars is a minor surgical procedure, there may be an uncomfortable postoperative period for the patient with local and systemic repercussions [3,5,6]. The most common immediate response to the tissue damage caused by the surgical removal of a third molar is acute pain, inflammation and trismus [5].

The immune system changes induced as a result of surgical trauma can be assessed by measuring different markers such as pro- and antiinflammatory cytokines, hormones such as cortisol, and acute phase reactants such as C-reactive protein (CRP) [5,6]. The latter is secreted by the liver cells during the inflammatory process in response to proinflammatory cytokine action and other innate immunity or tissue damage endogenous signals [6], and can be

* Corresponding author at: Calle Gascó Oliag nº 1, 46010 Valencia, Spain.

E-mail address: cecilia.marquez@uv.es (C.F. Márquez-Arrico).

measured in blood as high sensitivity CRP (hs-CRP) [7]. It has been seen that the serum CRP levels increase after surgical third molar removal and also in patients who have experienced postoperative complications [8–11].

One of the challenges that we face as surgeons is to contemplate surgical planning that seeks the least discomfort for the patient, including the postoperative period. Correct planning of the surgical procedure can reduce operating time and consequently complications after extraction. To this end, radiographic exploration together with the use of surgical complexity scales can be very useful in said planning [10,11]. Pederson scale [10,11] relates the position of the molar with respect to the mandibular branch, the depth of the inclusion and the angulation that the molar presents with respect to the central axis of the tooth. After evaluating these parameters, it indicates the degree of surgical complexity that the extraction presents [10,11].

The aim of this study was to evaluate the postoperative evolution of patients undergoing surgical extraction of third molars under general anesthesia, based on clinical and serum (biochemical) markers. Likewise, evaluate the usefulness of the Pederson scale [10,11] as an indicator of the surgical difficulty of third molar extraction under general anesthesia. Finally, determine if there is a correlation between clinical parameters (pain, inflammation and trismus) and serum parameters (CRP, IL-6 and fibrinogen), and the appearance of postoperative complications.

2. Material and methods

2.1. Design

An intervention study was carried out in Dr. Peset University Hospital (Valencia, Spain). The study was made in abidance with the recommendations of the Declaration of Helsinki on medical research, and was approved by the local Clinical Research Ethics Committee (protocol ref.: 48/12). All patients gave written informed consent before their inclusion in the study. The patients were divided into the following two groups, group A: patients who required 2 complex extractions under general anesthesia, involving the raising of a flap with releasing incision, and osteotomy; group B: patients who required 4 extractions under general anesthesia (2 simple extractions without the raising of a flap, osteotomy or tooth sectioning, and 2 complex extractions involving the raising of a flap with releasing incision, and osteotomy). Fig. 1.

2.2. Participants

2.2.1. Inclusion criteria

Adult male and female patients, without any active inflammatory or infectious disease, or periodontal disease, and no third molar clinical symptoms for at least one month before removal. To confirm oral health, the absence of infectious chronic systemic pathologies and inflammatory pathologies, a complete anamnesis and medical evaluation were carried out to rule out any type of pathology.

2.2.2. Exclusion criteria

Patients requiring prophylactic antibiotic treatment, as were those using antiinflammatory drugs or any other medication on a chronic basis or during the month before surgery, patients performing oral rinses before extraction, pregnant or nursing women, patients using oral contraceptives, individuals with third molar symptoms in the month before removal, and individuals with basal CRP concentrations in excess of 1.69 mg/l. Patients with chronic diseases such as diabetes, psoriasis, obesity, digestive or liver diseases, cancer patients or patients with infectious diseases such as HIV, hepatitis or coagulation disorders were also excluded.

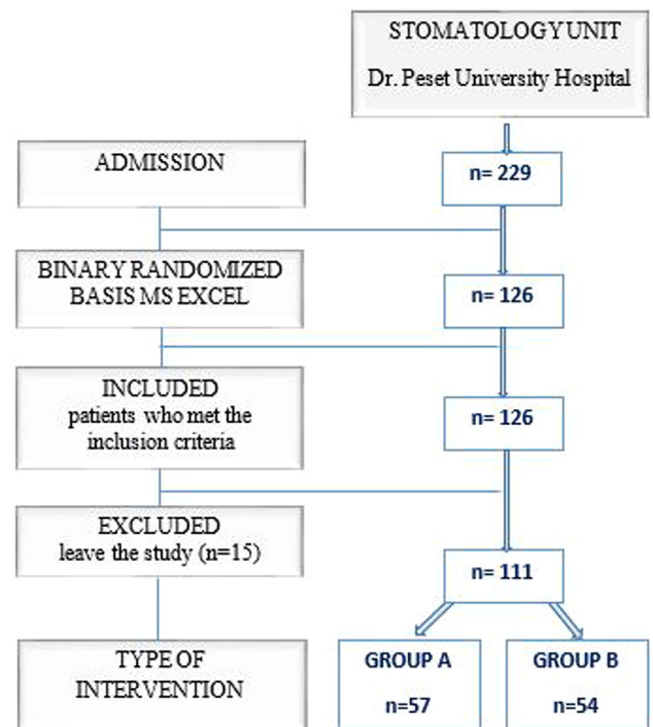


Fig. 1. Flowchart of patients recruited in the intervention study.

Group A: were carried out 2 complex extractions under general anesthesia, involving the raising of a flap with releasing incision, and osteotomy; group B: were carried out 4 extractions under general anesthesia: 2 simple extractions without the raising of a flap, osteotomy or tooth sectioning, and 2 complex extractions involving the raising of a flap with releasing incision, and osteotomy.

2.3. Interventions

2.3.1. Surgical technique and postoperative medication

Simple extractions were made with the usual technique using elevators and/or forceps, while complex extraction involved a supra-crestal incision with a releasing incision mesial to the second molar. Odontosection and osteotomy was carried out in the complex extraction. To avoid the risk of emphysema, both procedures were performed with a handpiece and no. 6 or 8 round tungsten carbide drill under abundant irrigation with sterile saline solution. Luxation and avulsion were carried out with elevators, followed by careful curettage of the surgical field under irrigation using 0.12 % chlorhexidine. In the case of complex extractions, the wound was closed by first intention using sutures. Non-resorbable 3/0 braided silk sutures were used, recording the type of wound closure (primary or secondary). All extractions were performed by the same professional. All patients received intravenous rescue analgesia with 50 mg dexketoprofen, 1 g paracetamol and 125 mg methylprednisolone immediately after surgery. In addition, antibiotic prophylaxis was prescribed in the form of amoxicillin – clavulanic acid 875/125 mg via the oral route every 8 h during the 7 days after surgery, together with oral antiinflammatory medication in the form of dexketoprofen 25 mg/12 h upon demand in the event of pain. The patients were also instructed to perform oral rinses with 0.12 % chlorhexidine after tooth brushing following each meal in order to ensure correct oral hygiene from the day after surgery.

2.3.2. Clinical and serum parameters compilation

A full patient medical history was compiled, and surgical difficulty was assessed from the orthopantomography radiographic study (panoramic projection of both jaws) based on the Pederson scale [10,11] (table 1). Patients were classified into three groups according

Table 1
Surgical third molar extraction difficulty according to the Pederson scale [10,11].

VARIABLE	SCORE
SPATIAL RELATIONSHIP	(1–4)
Mesioangular	1
Horizontal/transversal	2
Vertical	3
Distoangular	4
DEPTH	(1–3)
Level A	1
Level B	2
Level C	3
RELATION TO RAMUS/AVAILABLE SPACE	(1–3)
Class I	1
Class II	2
Class III	3
GRADE OF DIFFICULTY	(3–10)
Very difficult (high)	8–10
Moderately difficult (moderated)	5–7
Not difficult (low)	3–4

Class A: The occlusal plane of the impacted tooth is at the same level as the occlusal plane of the second molar. Class B: The occlusal plane of the impacted tooth is between the occlusal plane and the cervical line of the second molar. Class C: The impacted tooth is below the cervical line of the second molar. Class 1: There is sufficient space between the ramus and the distal part of the second molar. Class 2: The space between the distal part of the second molar and the ramus is less than mesiodistal diameter of the third molar. Class 3: All or most of the third molar is in the ramus of the mandible.

to the degree of surgical difficulty following the Pederson scale parameters (table 1); low: not difficult; moderate: moderately difficult or high: very difficult. Clinical parameters: a) Pain: the patients received a follow-up sheet and were instructed to record the variations in pain based on a 10-mm visual analog scale (VAS) [12,13] (0 = no pain, 10 = maximum pain imaginable); b) Inflammation was scored according to García et al. scale (12): 1 = none (no swelling), 2 = mild (intraoral swelling in the extraction zone), 3 = moderate (extraoral swelling in the extraction zone) and 4 = intense (extraoral swelling with spread to tissues adjacent to the extraction zone). The pain and inflammation data were recorded by the patients at 2, 4, 6 and 12 h postsurgery, and again on each of the following 6 consecutive days (between 7 and 9 a.m.) c) Trismus: was assessed by measuring maximum interincisal opening with calipers (in mm), from the mesial margin of the upper incisor to the mesial margin of the lower incisor. The sutures were removed 7 days after surgery, coinciding with the recording of maximum interincisal opening and laboratory tests in the same way as was done before surgery. Serum parameters: Following data collection, and prior to surgery, blood testing was made (basal) to record CRP concentration (mg/l), IL-6 (pg/ml) and fibrinogen (mg/dl). Another blood test was made to collect the same parameters on the day of suture removal 7 days after surgery.

2.4. Sample size

The presence of 30 subjects in each group (60 in total) was established as sufficient to find significant differences in biochemical and clinical parameters. Taking into account a 95 % confidence interval and a $p \leq 0.05$ as significant. However, since the study was part of hospital clinical care, more patients were included, taking into account the number of losses expected as 20 %.

2.5. Randomization

Patient selection was performed on a binary randomized basis using MS Excel among the patients seen in the Stomatology Unit of the hospital for the removal of multiple third molars.

2.6. Statistical analysis

The collected data were processed using the SPSS 27.0 statistical package (SPSS Statistics Inc., Chicago, IL, USA). The measured effect was a CRP value between 3 and 5.5 mg/dL and based on this proportion, calculate the differences between groups, taking into account a loss rate of 20 % of patients, requiring at least 75 patients. We applied the chi-squared test, Student T test, ANOVA and OR tests. In order to present the data of this research in a clear way and to allow critical appraisal by the scientific community, the CONSORT guide [14] has been used for the writing of this manuscript.

3. Results

A total of 226 patients were received at the admission of the Stomatology Unit in the period of conducting the investigation. After randomization 126 patients were initially included, of which 15 abandoned the study and were excluded from the analysis. Thus the final sample size consisted of 111 patients (Fig. 1). There were 65 females (58.6 %) and 46 males (41.4 %), with a mean age of 25.7 ± 6.8 years (range 18–40). The patients were divided into two groups according to the extraction requirements: group A (57 patients) required two surgical extractions under general anesthesia, while group B (54 patients) required four extractions (Fig. 1). The two groups were homogeneous as regards surgical difficulty ($p = 0.195$, χ^2), age ($p = 0.140$, t) and gender distribution ($p = 0.532$, χ^2), smoking habit ($p = 0.691$, χ^2) and reason for extraction ($p = 0.583$, χ^2).

3.1. Prognostic usefulness of the difficulty scale

The two groups were studied under the same conditions and the same parameters were evaluated. With regard to surgical difficulty as evaluated by the Pederson scale [10,11] (table 1), 24.3 % of the operations were classified as not difficult, 61.3 % as moderately difficult, and 14.4 % as very difficult. The mean surgery time in group A was 1244.7 ± 725.2 s, versus 572.4 ± 696.0 s in group B (table 2).

The level of difficulty was significantly correlated to all the parameters considered. A total of 12.6 % of the low difficulty cases required osteotomy, versus 76.8 % and 84 % of the moderately difficult and very difficult cases, respectively, thus reflecting a significant association between surgical difficulty and the need for osteotomy ($p < 0.001$). The duration of osteotomy was also dependent upon the degree of difficulty ($p < 0.001$). The frequency of crown sectioning likewise increased significantly with the degree of difficulty ($p < 0.001$), in the same way as root sectioning ($p < 0.001$). In turn, increased surgical difficulty was associated to longer surgery ($p < 0.001$) and wound healing times ($p < 0.001$), and to an increased need for suturing ($p < 0.001$). The bleeding rate was also significantly associated to surgical difficulty ($p < 0.001$). The incidence of complications was 13.8 %, 38.4 % and 40 % in low, moderated and high surgical difficulty, respectively, with statistically significant differences between the three levels of difficulty. The most frequent complications were dry socket (23 %), fever (2.4 %) and bleeding (2.4 %). The incidence of dry socket was 28.1 % in group A and 20.4 % in group B.

3.2. Clinical parameters

3.2.1. Pain

Regarding to the subjective evolution of pain sensation from the immediate postoperative period to one week after surgery, the statistical model detected significant variations in pain intensity over time ($p < 0.001$), though of a similar magnitude in both groups ($p = 0.954$). The patients in both groups experienced maximum pain in the first 12–24 h after extraction, though pain intensity was comparatively greater in group A. The statistical model also evidenced an effect

Table 2

Analysis of the study parameters according to patient group, surgical difficulty as assessed by the Pederson score [10,11] and complications.

VARIABLES	Group (G) Student T test	Time (T) Linear Regression	Difficulty (D) Linear Regression	Complexity (C) Linear Regression	G x D	T x D ANOVA test	T x C	TxGxD
OPENING	0.842	<0.001*	0.432	0.001*	0.650	0.027*	<0.001*	0.365
PAIN	0.039*	<0.001*	0.331	<0.001*	0.960	0.371	0.059	0.646
INFLAMMATION	0.008*	<0.001*	<0.001*	<0.001*	0.188	0.073	0.001*	0.166
IL-6	0.456	<0.001*	0.672	0.001*	0.662	0.173	0.043*	0.873
CRP	0.615	<0.001*	0.167	<0.001*	0.594	0.164	<0.001*	0.506
FIBRINOGEN	0.883	<0.001*	0.723	<0.001*	0.363	0.028*	<0.001*	0.115

CRP: c reactive protein; Group A: 2 complex extractions; Group B: 4 extractions: 2 simple extractions and 2 complex I extractions; IL-6: interleukin 1; PRE: before third molar extraction; POST: after third molar extraction; SD: standard deviation.

* Significant association between variables, $p < 0.05$.

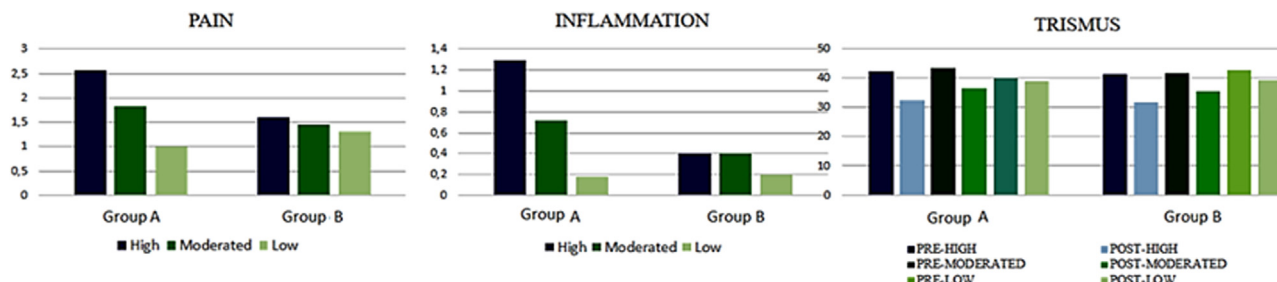


Fig. 2. Evolution of the clinical parameters (pain, inflammation and trismus) according to surgical difficulty.

associated to surgical difficulty ($p = 0.038$), i.e., there were differences in pain according to the degree of surgical difficulty at all timepoints, with low difficulty cases being correlated to significantly lesser pain (table 2 and Fig. 2).

3.2.2. Inflammation

The level of inflammation varied over time ($p < 0.001$), with no differences between the groups ($p = 0.287$) (table 2). The significant differences were associated to the degree of surgical difficulty ($p = 0.023$). Although in global terms inflammation was seen to peak in intensity 24 h after surgery, there were differences according to the level of surgical difficulty – with lesser inflammation being recorded in the low difficulty cases.

3.2.3. Trismus

A statistically significant reduction of oral opening was found after surgical intervention ($p < 0.001$), though with no significant differences between the two groups ($p = 0.328$) (table 2). Although the tendency for pain, inflammation and trismus is to increase according to surgical difficulty in both groups, no significant differences were found with the number of teeth extracted. It was shown that the complexity of the procedure has greater importance on the

postoperative discomfort of the patient than the number of extractions performed (table 2 and Fig. 2).

3.3. Serum parameters

The CRP levels experienced a significant increase after molar extraction ($p < 0.001$), with no differences between the two groups ($p = 0.227$). However, CRP elevation was seen to increase with the surgical difficulty of extraction ($p = 0.022$) (Table 3 and Fig. 2). The results referred to IL-6 were similar to those corresponding to CRP in the operating room, since the former increased significantly after surgery ($p < 0.001$), without differences between the groups ($p = 0.476$). No significant correlation to surgical difficulty was found ($p = 0.082$) (Fig. 3). Fibrinogen in turn increased significantly with surgery ($p < 0.001$), with no significant correlation to either the patient group ($p = 0.155$) or surgical difficulty ($p = 0.074$) (Fig. 3).

3.4. Postoperative complications

At least 44 patients (39.6 %) experienced some type of complication. Binary logistic regression analysis or principal effects and interactions, adjusted for surgical difficulty, found the probability of

Table 3

Analysis of biochemical parameters according to patient group assessed by Pederson scale [10,11].

VARIABLES	GROUP A			GROUP B		
	Mean	SD	T- Test pared	Mean	SD	T- Test pared
PRE- IL-6	0,86	1599	<0.01*	1,02	1479	<0.001*
POST- IL-6	1,64	2340		2,14	2928	
PRE- CRP	0,71	0,614	<0.001*	0,650	0,518	<0.001*
POST- CRP	3,54	5339		3,5648	3916	
PRE- FIBRINOGEN	322,84	66,595	<0.001*	346,24	50,333	<0.001*
POST- FIBRINOGEN	400,46	82,215		427,76	68,036	

CRP: c reactive protein; Group A: 2 complex extractions; Group B: 4 extractions: 2 simple extractions and 2 complex I extractions; IL-6: interleukin 1; PRE: before third molar extraction; POST: after third molar extraction; SD: standard deviation.

* Significant association between variables, $p < 0.05$.

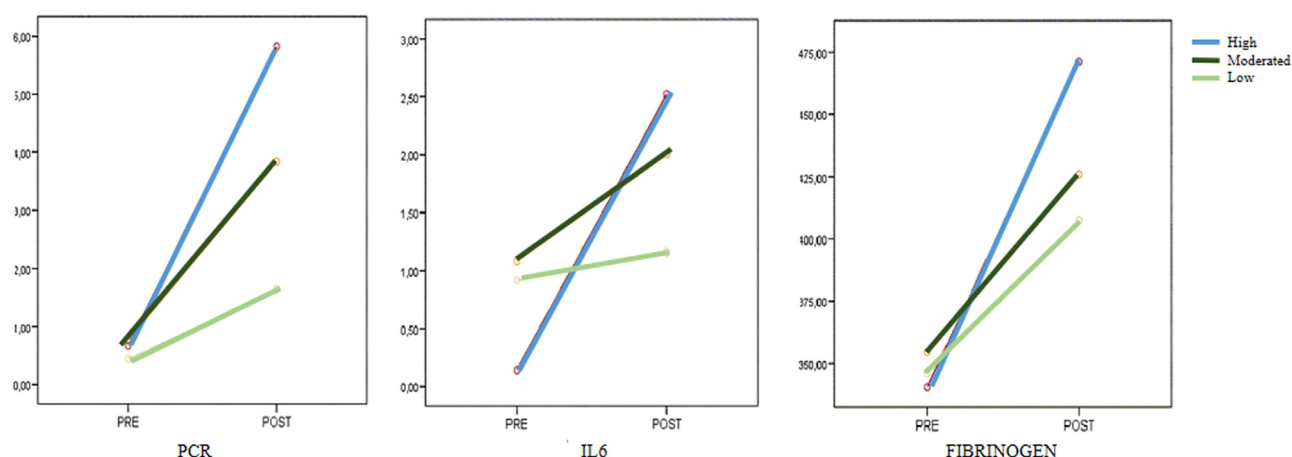


Fig. 3. Evolution of the biochemical (serum) parameters (CRP, IL-6 and fibrinogen) according to surgical difficulty.

complications to be similar in both patient groups, under conditions of similar surgical difficulty ($p = 0.136$). However, surgery classified as not difficult was associated to an 81.4 % lesser risk of complications than surgery classified as high difficulty cases ($OR=0.186$; $p = 0.036$).

Analysis of variance (ANOVA) with the F test was used to assess the influence of the appearance of complications upon the clinical and serum parameter outcomes. On adjusting the model for the presence of complications, pain was seen to be influenced ($p = 0.039$), in the same way as trismus ($p < 0.001$) and the development of inflammation ($p = 0.008$). The appearance of complications was also seen to have a significant impact upon the variations in CRP ($p < 0.001$). Patients with complications were seen to have higher values during the postoperative period. Both IL-6 ($p = 0.043$) and fibrinogen yielded similar results ($p < 0.001$) (table 2).

4. Discussion

In the field of oral surgery, correct surgical planning will help us minimize risks and achieve predictable results. The success is largely attributed to the planning and experience of the surgeon. The adequate evaluation of surgical difficulty before third molar extraction is very useful to have enough information to carried out the surgical planning. However, individual factors of variability among patients (such as behavior, bone density, anatomical differences, among others) sometimes makes the planning evaluation difficult. In our study, the Pederson scale [10,11] was seen to be a good indicator of surgical difficulty in the extraction of third molars under general anesthesia. A number of authors have underscored the importance of radiographic parameters in estimating surgical difficulty, such as the relation to the second molar, the number of roots, or bone density [10,11,15–17]. Some researchers recommend measuring surgical difficulty before surgery and intraoperatively during the process to obtain a more realistic assessment. [18,19].

We observed a statistically significant association between the Pederson scale [10,11] and the need for osteotomy and its duration, sectioning of the crown and root, bleeding, surgery time, the type of closure and number of sutures, and the appearance of complications. In a previous study [9] on simple tooth extraction under local anesthesia performed on an outpatient basis, we likewise found the surgery time to be strongly correlated to the Pederson scale. Other authors such as Osunde et al. [20] report similar data. This reinforces the Pederson scale [10,11] as a good predictor of surgical difficulty, and suggests that surgery time can be used as a tool for assessing the difficulty of surgical third molar extraction.

Pain, inflammation and trismus are typically observed in the postoperative period after third molar extraction. The pain threshold can

be influenced by a number of factors, including patient age and gender, and surgical difficulty [16–18]. Even though pain is a subjective variable it has been shown in several investigations that the VAS scale is a good tool for measuring pain in a way that allows its measurement to be compared between patients [12]. In our study, pain intensity was seen to peak between the first 12–24 h after surgery, and then tended to subside until the day of suture removal. However, the first severe inflammation episode in both groups occurred after 24–48 h, which is later than in other studies where only a single tooth was removed. Apart from the fact that we performed more extractions per patient, this could be explained by the circumstance that extraction was performed under general anesthesia with the administration of 125 mg of methylprednisolone, in concordance with the observations of other authors [21].

We found no significant association between the number of extracted teeth and postoperative pain, inflammation or trismus – though surgical difficulty was seen to be the factor that most clearly influenced the postoperative clinical parameters. This could be due to the fact that the processes with high difficulty present a longer operative time, a variable that has been related to greater postoperative discomfort for the patient, while performing a greater number of extractions of less complexity may result in a short operative time [17,22–25]. With regard to pain, other investigators have also reported a significant association between pain sensation and preoperative difficulty [17,22]. The inflammation was similar in both moderated and in high difficulty surgeries, though after 12 h swelling was seen to be greater in the most difficult cases. Thus, and in coincidence with other authors, we can suggest that there is a direct relationship between preoperative surgical difficulty and the degree of inflammation [23–26].

We recorded CRP elevation one week after surgical extraction; however, the increase was not conditioned by the number of teeth removed but by the degree of surgical difficulty involved, as assessed using a validated scale [9,10,11]. In contrast, other investigators have reported no direct relationship between CRP elevation and surgical complexity; instead, increased concentrations of this protein were associated to the appearance of postoperative complications [27–29]. Our own results evidence an association between CRP elevation and both surgical difficulty and the appearance of complications.

The fibrin levels clearly increased with surgical difficulty, in the same way as CRP. Similar results in relation to surgical difficulty have been reported by other authors [27–31], though they found the increase to be greater in patients who developed postoperative infection. In the case of the other two biochemical parameters, elevations in IL-6 have been reported in the literature, though in our study the data were less conclusive. On the other hand, this study has the

advantage of bringing together the previous evaluation of the difficulty and the real assessment of the complexity of the case in addition to determining biochemical variables correlated to the clinics, giving a global vision of the patient.

Our study has limitations, such as the fact that blood testing was only performed one week after surgery. However, we feel that additional tests (e.g., 24 and 48 h after surgery) are not justified in routine clinical practice, and our study moreover aimed to assess the late postoperative course, taking advantage of the patient visit for control and suture removal. Furthermore, biochemical changes must be maintained for some days in order to reflect them in serum analysis.

To summarize, the degree of surgical difficulty can be largely predicted with the Pederson scale before extracting mandibular third molars. CRP and fibrinogen levels increase significantly with the degree of surgical difficulty. Number of extractions is not a good predictor of postoperative complications. Future research would be necessary to determine surgical protocols focused on preventing systemic inflammation and reducing postoperative complications and also to expand the findings found in this research and to clarify details that remain unclear.

5. Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Beatriz Saiz de Baranda, Francisco Javier Silvestre, Cecilia Fabiana Márquez-Arrico and Javier Silvestre-Rangil. The first draft of the manuscript was written by Beatriz Sainz de Baranda, Francisco Javier Silvestre and Cecilia Fabiana Márquez-Arrico and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declaration of Competing Interest

All authors declare that they have no conflict of interest.

Funding

Ministry of Science, Innovation and Universities with a FPU grant to the doctoral student MSc. M-A CF.

Ethical Approval

Hospital University Dr Psetet Ethics Committee approved this investigation (protocol ref.: 48/12).

Informed Consent

All patients gave written informed consent before their inclusion in the study.

Acknowledgement

We thanks to the Ministry of Science, Innovation and Universities for the support with a FPU grant to the doctoral student MSc. M-A CF.

References

- [1] Low SH, Lu SL, Lu HK. Evidence-based clinical decision making for the management of patients with periodontal osseous defect after impacted third molar extraction: a systematic review and meta-analysis. *J Dent Sci* 2021 Jan;16(1):71–84. doi: [10.1016/j.jds.2020.06.018](#).
- [2] Ryu DS, Lee DW, Choi SC, Oh IH. Sedation protocol using dexmedetomidine for third molar extraction. *J Oral Maxillofac Surg* 2016;74:1–7. doi: [10.1016/j.joms.2015.12.021](#).
- [3] Chung PK, Dhanrajani P. Comparative randomized study of Propofol target-controlled infusion versus sevoflurane anesthesia for third molar extraction. *J Dent Anesth Pain Med* 2018;18:169–75. doi: [10.17245/jdpm.2018.18.3.169](#).
- [4] Inverso G, Dodson TB, Gonzalez ML, Chuang SK. Complications of moderate sedation versus deep sedation/general anesthesia for adolescent patients undergoing third molar extraction. *J Oral Maxillofac Surg* 2016;74:474–9. doi: [10.1016/j.joms.2015.10.009](#).
- [5] Osunde OD, Saheeb BD. Effect of age, sex and level of surgical difficulty on inflammatory complications after third molar surgery. *J Maxillofac Oral Surg* 2015;14:7–12. doi: [10.1007/s12663-013-0586-4](#).
- [6] Del Giudice M, Gangestad SW. Rethinking IL-6 and CRP: why they are more than inflammatory biomarkers, and why it matters. *Brain Behav Immun* 2018;70:61–75. doi: [10.1016/j.bbi.2018.02.013](#).
- [7] Pathak A, Agrawal A. Evolution of C-reactive protein. *Front Immunol* 2019;10:943. doi: [10.3389/fimmu.2019.00943](#).
- [8] Ghaemini H, Nienhuijs ME, Toedting V, Perry J, Tummers M, Hoppenreijts TJ, Van der Sanden WJ, Mettes TG. Surgical removal versus retention for the management of asymptomatic disease-free impacted wisdom teeth. *Cochrane Database Syst Rev* 2020 May 4;5(5):CD003879. doi: [10.1002/14651858](#).
- [9] Sainz de Baranda B, Silvestre FJ, Silvestre-Rangil J. Relationship between surgical difficulty of third molar extraction under local anesthesia and the postoperative evolution of clinical and blood parameters. *J Oral Maxillofac Surg* 2019;77:1337–45. doi: [10.1016/j.joms.2019.02.020](#).
- [10] Diniz-Freitas M, Lago-Méndez L, Gude-Sampedro F, Somoza-Martin JM, Gándara-Rey JM, García-García A. Pederson scale fails to predict how difficult it will be to extract lower third molars. *Br J Oral Maxillofac Surg* 2007;45(1):23–6. doi: [10.1016/j.bjoms.2005.12.004](#).
- [11] de Carvalho RWF, Vasconcelos BC. Pernambuco index: predictability of the complexity of surgery for impacted lower third molars. *Int J Oral Maxillofac Surg* 2018;47(2):234–40. doi: [10.1016/j.ijom.2017.07.013](#).
- [12] Thong ISK, Jensen MP, Miró J, Tan G. The validity of pain intensity measures: what do the NRS, VAS, VRS, and FPS-R measure? *Scand J Pain* 2018;18(1):99–107. doi: [10.1515/sjpain-2018-0012](#).
- [13] García B, Penarrocha M, Martí E, Gay-Escoda C, Von Arx T. Pain and swelling after periapical surgery related to oral hygiene and smoking. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;104:271–6. doi: [10.1016/j.tripleo.2007.01.025](#).
- [14] Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *J Clin Epidemiol* 2010;63(8):834–40. doi: [10.1016/j.jclinepi.2010.02.005](#).
- [15] Sánchez-Torres A, Soler-Capdevilla J, Ustrell-Barral M, Gay-Escoda C. Patient, radiological, and operative factors associated with surgical difficulty in the extraction of third molars: a systematic review. *Int J Oral Maxillofac Surg* 2019;49:655–65. doi: [10.1016/j.ijom.2019.10.009](#).
- [16] Yamada SI, Hasegawa T, Yoshimura N, Hakoyama Y, Nitta T, Hirahara N, Miyamoto H, Yoshimura H, Ueda N, Yamamura Y, Okuyama H, Takizawa A, Nakanishi Y, Iwata E, Akita D, Itoh R, Kubo K, Kondo S, Hata H, Koyama Y, Miyamoto Y, Nakahara H, Akashi M, Kirita T, Shibuya Y, Umeda M, Kurita H. Prevalence of and risk factors for postoperative complications after lower third molar extraction: a multicenter prospective observational study in Japan. *Medicine (Baltimore)* 2022;101(32):e29989. doi: [10.1097/MD.00000000000029989](#).
- [17] Alvira-González J, Figueiredo R, Valmaseda-Castellón E, Quesada-Gómez C, Gay-Escoda C. Predictive factors of difficulty in lower third molar extraction: a prospective cohort study. *Med Oral Patol Oral Cir Bucal* 2017;22(1):e108–14. doi: [10.4317/medoral.21348](#).
- [18] Sainz de Baranda B, Silvestre FJ, Silvestre-Rangil J. Relationship between surgical difficulty of third molar extraction under local anesthesia and the postoperative evolution of clinical and blood parameters. *J Oral Maxillofac Surg* 2019;77(7):1337–45. doi: [10.1016/j.joms.2019.02.020](#).
- [19] De Santana-Santos T, de Souza-Santos JA, Martins-Filho PR, da Silva LC, de Oliveira e Silva ED, Gomes AC. Prediction of postoperative facial swelling, pain and trismus following third molar surgery based on preoperative variables. *Med Oral Patol Oral Cir Bucal* 2013;18:65–70. doi: [10.4317/medoral.18039](#).
- [20] Osunde OD, Adebola RA, Saheeb BD. A comparative study of the effect of sutureless and multiple suture techniques on inflammatory complications following third molar surgery. *Int J Oral Maxillofac Surg* 2012;41:1275–9. doi: [10.1016/j.ijom.2012.04.009](#).
- [21] Falci SGM, Lima TC, Martins CC, Santos CRRD, Pinheiro MLP. Preemptive effect of dexamethasone in third-molar surgery: a meta-analysis. *Anesth Prog* 2017;64(3):136–43 Fall. doi: [10.2344/anpr-64-05-08](#).
- [22] Santana-Santos T, aA Souza-Santos, Martins-Filho PR, da Silva LC, de Oliveira E Silva ED, Gomes AC. Prediction of postoperative facial swelling, pain and trismus following third molar surgery based on preoperative variables. *Med Oral Patol Oral Cir Bucal* 2013 Jan 1;18(1):e65–70. doi: [10.4317/medoral.18039](#).
- [23] Penarrocha M, Sanchis JM, Sáez U, Gay Escoda C, Bagán JV. Escala numérica de valoración de la dificultad quirúrgica en la extracción de 190 terceros molares mandibulares incluidos. *Arch Odontostomatol* 2000;16:96–100.
- [24] Sayed N, Bakathir A, Pasha M, Al-Sudairy S. Complications of third molar extraction: a retrospective study from a tertiary healthcare centre in Oman. *Sultan Qaboos Univ Med J* 2019;19(3):e230–5. doi: [10.18295/squmj.2019.19.03.009](#).
- [25] Freudlsperger C, Deiss T, Bodem J, Engel M, Hoffmann J. Influence of lower third molar anatomic position on postoperative inflammatory complications. *J Oral Maxillofac Surg* 2012;70:1280–5. doi: [10.1016/j.joms.2011.12.014](#).
- [26] Tenglikar P, Munnangi A, Mangalgi A, Uddin SF, Mathpathi S, Shah K. An assessment of factors influencing the difficulty in third molar surgery. *Ann Maxillofac Surg* 2017;7:45–50. doi: [10.4103/ams.ams.194.15](#).
- [27] Milic T, Raidoo P, Gebauer D. Antibiotic prophylaxis in oral and maxillofacial surgery: a systematic review. *Br J Oral Maxillofac Surg* 2021;59(6):633–42. doi: [10.1016/j.bjoms.2020.09.020](#).

- [28] Salgia G, Kulkarni DG, Shetty L. C-reactive protein estimation: a quantitative analysis for three nonsteroidal anti-inflammatory drugs: a randomized control trial. *Indian J Dent Res* 2015;26:43–7. doi: [10.4103/0970-9290.156797](https://doi.org/10.4103/0970-9290.156797).
- [29] Bazurro S, Ball L, Pelosi P. Perioperative management of obese patient. *Curr Opin Crit Care* 2018;24(6):560–7. doi: [10.1097/MCC.0000000000000555](https://doi.org/10.1097/MCC.0000000000000555).
- [30] Bagul R, Chandan S, Sane VD, Patil S, Yadav D. Comparative evaluation of C-reactive protein and WBC count in fascial space infections of odontogenic origin. *J Maxillofac Oral Surg* 2017 Jun;16(2):238–42. doi: [10.1007/s12663-016-0953-z](https://doi.org/10.1007/s12663-016-0953-z).
- [31] Kuśnierek W, Brzezińska K, Nijakowski K, Surdacka A. Smoking as a risk factor for dry socket: a systematic review. *Dent J (Basel)* 2022;10(7):121. doi: [10.3390/dj10070121](https://doi.org/10.3390/dj10070121).