Perioperative management of tooth extraction in patients with antiplatelet and anticoagulant treatment

Olariu I.[1], Todor L.[2], Popovici R.A.[3], Fluieras R.[1,3], Todor S.A.[4], Kis A.M.[5], Roi C.[6], Riviş M.[6]

[1]*Department of Denistry, Faculty of Dentistry, Faculty of Medicine, "Vasile Goldis" Western University of Arad*
[2]*Department of Dental Medicine, Faculty of Medicine and Pharmacy, University of Oradea, Romania*
[3]*Department 1, Faculty of Dental Medicine, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania*
[4]*Dentist doctor, private medical office, Oradea, Romania*
[5]*Phd Student University of Medicine and Pharmacy "Victor Babes" Timisoara, Faculty of Medicine*
[6]*Department 2, Faculty of Dental Medicine, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania*

Correspondence to:
Name: Liana Todor
Address: Department of Dental Medicine, Faculty of Medicine and Pharmacy, University of Oradea, Romania, December 1st Square no.10, 410068 Oradea, Bihor County, Romania
Phone: +40 723517100
E-mail address: liana.todor@gmail.com

Abstract

Patients on anticoagulant or antiplatelet treatment require close monitoring during extraction surgery because of the significant risk of postoperative bleeding. There is no consensus regarding the treatment of patients with anticoagulants, recently dentists opt for a conservative approach, in which the intervention takes place without interrupting the medication, and haemostasis is achieved through local measures.

Discontinuation of anticoagulant treatment during oral surgery increases the risk of thromboembolic events through various mechanisms, such as INR (international normalized ratio), compensatory hypercoagulability and the post-thrombotic effect. Thus, patients are prone to the risk of pre- and postoperative arterial thromboembolism and postoperative venous thromboembolism if the INR value returns to normal shortly after discontinuation of treatment.

This study aims to evaluate the haemorrhagic complications associated with dental extractions in patients under chronic anticoagulant treatment, with the modification of drug therapy and following a standard perioperative management protocol

Keywords: Tooth extraction, anticoagulant, antiplatelet, haemorrhagic complications

INTRODUCTION

Under the name of antithrombotic medication, this group includes drugs useful in the treatment and prophylaxis of thromboembolic conditions. They are indicated both in the treatment of arterial and venous thrombosis, acute or chronic [1].

The category of antithrombotic drugs includes: antiplatelet agents, anticoagulants and fibrinolytics, which play an important role in the phenomenon of atherothrombosis, thus preventing the formation of intravascular thrombi or disintegrating already formed thrombi.

Antiplatelet agents are medicinal substances that inhibit platelet functions in the process of haemostasis (manifested by prolonging bleeding time) and reduce the aggregation capacity of blood platelets, preventing the formation of thrombi. The most common antiplatelet agent is acetylsalicylic acid (Aspirin), it has an antiaggregant effect on platelets.

Oral anticoagulants are coumarin derivatives that act as vitamin K antagonists by inhibiting the synthesis of coagulation factors II (prothrombin), VII, IX and X, preventing the blood coagulation process.

Most practice guidelines consider tooth extractions as minor interventions associated with a low risk of bleeding and self-limited blood loss that can be managed with local hemostatic agents [2]. However, certain surgical interventions in the oral cavity may require temporary discontinuation of antithrombotic therapy [3].

There are both an increasing number of patients prescribed anticoagulation or antiplatelet therapy and drugs for this purpose. There is strong evidence for older drugs (e.g. warfarin, antiplatelet agents), as well as limited evidence for newer direct-acting oral anticoagulant drugs, that for most patients no change in anticoagulant or antiplatelet therapy is necessary before tooth extraction [4].

Planning dental extractions for patients on antithrombotic therapy remains controversial [5].

Aim and objectives

The present work aims to evaluate the haemorrhagic complications associated with dental extractions in patients under chronic anticoagulant treatment, with the modification of drug therapy and following a standard perioperative management protocol.

We analysed the therapeutic management used in the extraction treatment for this category of patients and tried to fit the clinical aspects into the therapeutic protocol. Another objective was to draw the attention of the dentist and the dentoalveolar surgeon to some useful aspects and particularities in the management of these cases, which present a high haemorrhagic risk and require special attention.

MATERIAL AND METHODS

The first stage of the prospective study was to establish the clinical characteristics necessary for patient selection. Patients under antiplatelet or anticoagulant therapy who required extraction treatment and presented themselves at the Timișoara Oral and Maxillofacial Surgery Clinic between January 2019 and December 2019 were included in the study.

The patients were informed about the medical research we are carrying out and expressed their consent in writing, according to Ministry of Health Order 1411 of 12.12.2016, annex no. 1 to the methodological norms - Form for expression of consent of the informed patient.

The selection of patients for inclusion in the study was based on the clinical examination, radiological investigations (orthopantomography) and laboratory examinations (complete blood count, coagulogram, ESR).

Patient selection and inclusion criteria:

1. Adult patients (over 18 years);
2. Both gender;
3. Anticoagulant treatment supervised by the attending physician;
4. Indication of extraction of one or more dental units;
5. INR values between 1 and 3;
6. Admission to the Oro-Maxillo-Facial Surgery Clinic Timişoara for the possibility of monitoring the patient.

Exclusion criteria:

1. Minor patients (under 18);
2. Patients with acute infectious processes, malignant tumors;
3. Administration of an antiplatelet or anticoagulant treatment not supervised by the attending physician;
4. The existence of associated conditions that contraindicate tooth extraction;
5. Too low or too high INR values;
6. Lack of patient compliance and cooperation.

The patients were hospitalized in the Timişoara Oral and Maxillo-Facial Surgery Clinic, where they underwent clinical evaluation and blood sample collection for laboratory examinations: complete blood count, coagulogram (prothrombin time, INR, TTPa), ESR, C-reactive protein, creatinine, urea, blood sugar, followed by referring patients to the specialist consultation, to the cardiologist.

The orthopantomography radiological examination was performed, accompanied by retroalveolar radiography where necessary. All data collected were recorded in the patient record.

Bleeding risk was assessed based on information gathered from the history, clinical examination, and laboratory test results. We attributed an increased risk of bleeding to patients who presented associated comorbidities (which can influence both haemostasis and the patient's predisposition to infections, e.g. diabetes) and those who required multiple extractions, teeth with periodontal problems or ankylosed teeth.

The therapeutic protocol included the modification of the pre-operative treatment scheme, according to the cardiologist's indication, recorded in the patient's observation sheet in the interdisciplinary consultation section, as follows: stop the chronic anticoagulant treatment administered orally and replace it with Clexane 0.6 or 0, 8 depending on the patient's weight up to INR values <1.2. The INR value is checked and when it is <1.2, and the patient has not been administered Clexane at least 6 hours before the intervention, the tooth extraction is performed.

The surgical intervention began with asepsis of the perioral skin using Betadine solution and asepsis of the oral mucosa with Chlorhexidine, followed by local anaesthesia with Articaine anaesthetic with adrenaline 1:200.000. Atraumatic extraction of irretrievable dental units was performed, with minimal detachment of the muco-periosteum and avoidance of extensive denudations of the maxillary bones. Extraction accidents such as dental root fractures, alveolar bone fractures and oral soft tissue wounds should also be avoided due to the intense vascularity at this level. In the cases where it was necessary to make a flap, its expansion was minimal (Figure 1), avoiding its tension or tearing.

In those cases where osteotomy was necessary (ankylosed teeth or root remnants located in the depth of the alveolar bone-Figure 2), an attempt was made to remove as little

bone tissue as possible, in order to keep the alveolar walls intact and facilitate the subsequent stabilization of the blood clot.

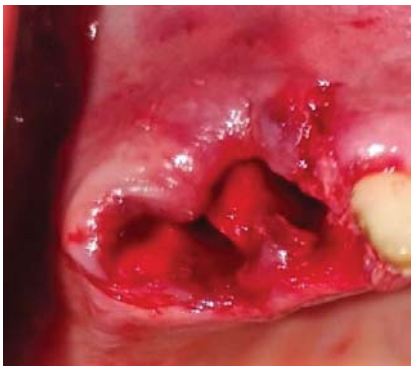

Figure 1. Minimal flap extension

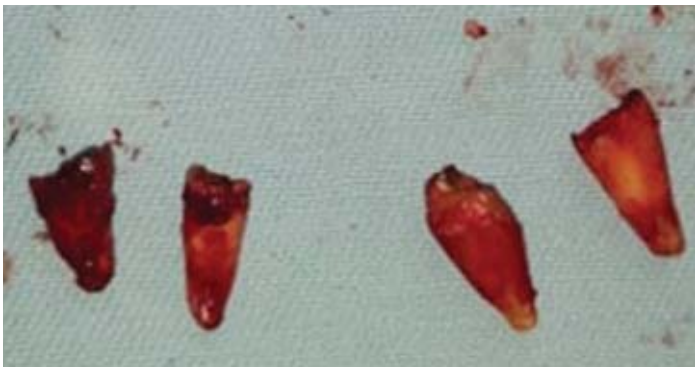

Figure 2. Ankylosed teeth

Regularization of bony margins was performed where necessary to avoid bleeding from mucosal and periosteum injury by sharp bony projections. It was followed by gentle but thorough curettage of the post-extraction alveolus, with careful removal of the remaining infected tissue (to avoid local post-extraction bleeding) and application of the intra-alveolar haemostatic sponge (Figure 3). In all cases, post-extraction wound suture was performed with non-resorbable 4/0 silk thread, triangular needle, made tightly, with the edges flared, followed by the application of a supra-alveolar compressive tamponade for 15-20 minutes post-extraction. Where adhesion of the wound edges was not possible, an "X" suture was performed and a supra-alveolar surgical dressing was applied (Figure 4). It was suppressed 24 hours postoperatively.

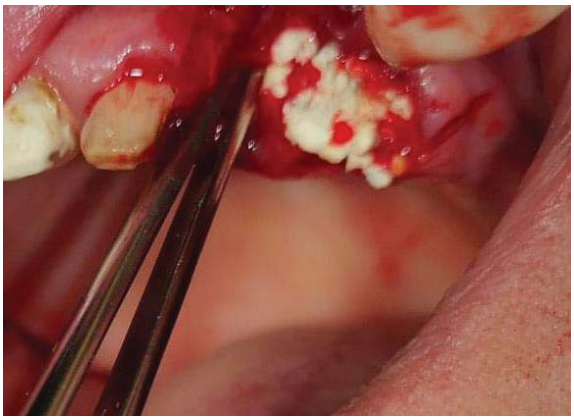

Figure 3. Application of haemostatic sponge

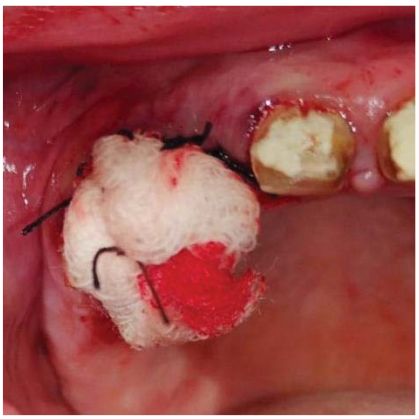

Figure 4. Supra-alveolar dressing

The patients were instructed to follow the post-operative indications to exclude haemorrhagic complications of local origin: maintain supra-alveolar compressive tamponade for 30 minutes; the post-extraction wound will not be explored; vigorous rinsing of the oral cavity is contraindicated to prevent blood clot mobilization; a liquid or semi-liquid and cold diet is recommended for 24 hours; sucking or pushing with the tongue in the wound area is contraindicated; the consumption of hot or thick foods is contraindicated; oral hygiene can be resumed after 24 hours, avoiding touching the wound.

Clexane dose is administered at least 6 hours post-extraction. Any episode of post-extraction haemorrhage is observed and noted on the observation sheet.

The decision to resume anticoagulant treatment is made only after the absence of bleeding from the post-extraction wound. Oral treatment with Sintrom is resumed, overlapping with injectable treatment with Clexane for 3 days. If on the 3rd day the INR is within the target values recommended by the cardiologist, the patient is discharged.

Suture removal was done 7 days after the extraction intervention.

During the intervention, we followed its duration and complexity, the occurrence of haemorrhagic accidents or complications, the cause and duration of the haemorrhage along with the therapeutic behaviour applied in those cases. Intra-alveolar clot formation was assessed at 30 minutes postoperatively, followed by reassessment at 24 and 48 hours.

In cases where post-extraction bleeding was found, the therapeutic approach included (Table 1): haemostasis achieved by renewing the supra-alveolar compressive dressing, held in occlusion for 30 minutes by the patient, in the event of low or medium intensity bleeding; haemostasis achieved by the application of a compressive dressing soaked in haemostatic substances, in the event of the occurrence of a haemorrhage of medium intensity or in the event that haemostasis cannot be obtained by means of a compressive dressing; if the bleeding continued even after maintaining the compression dressing, a new cardiological consultation was performed, with the adjustment of the anticoagulant dose, followed by the surgical revision of the post-extraction wounds. The wound was explored to identify and eliminate the source of bleeding through local haemostasis measures: identification of the source of bleeding (at the level of the soft parts or at the level of the bone), anaesthesia, curettage of the alveolus, washing the wound, ligation/electrocautery of the blood vessel (if applicable), applying haemostatic materials, suturing the wound and applying the supra-alveolar compressive dressing.

Measures of general haemostasis included treatment modification as follows: lowering the dose of Clexane by 2 units; skipping a dose.

Table 1. Measures of local haemostasis

Post-extraction bleeding	Haemostatic technique
Haemorrhage of low or medium intensity	hemostasis achieved by renewing the supra-alveolar compressive dressing, kept in occlusion by the patient for 30 minutes
Moderate bleeding or failure of hemostasis by compression dressing	hemostasis achieved by applying a compressive dressing soaked in hemostatic substances
Severe bleeding	carrying out a new cardiological consultation, with the adjustment of the anticoagulant dose, followed by the surgical revision of post-extraction wounds

RESULTS

The study included 78 patients who presented themselves in the Oral-Maxillo-Facial Surgery Clinic. Of them, 42 were men (54%) and 36 were women (46%). 11 (14.11%) were up to 60 years old, 59 patients (75.64%) were between 60 and 80 years old, and 8 patients (10.25%) were over 80 years old. Patients are evenly distributed according to gender. Regarding the age group, the share of people between 60 and 80 years old is the majority.

Table 2 shows the distribution of patients by age group, depending on gender. The share of male patients is the majority in almost all age groups.

Table 2. Distribution of patients according to gender and age group

Age group	Female patients	Male patients	Total
< 60 years	3	8	11
60-80 years	29	30	59
> 80 years	4	4	8

Regarding the chronic oral anticoagulant treatment followed by the patient on an outpatient basis, in 50 cases (64.1%) it was represented by SINTROM, and in 28 cases (35.89%) by TROMBOSTOP.

Regarding the associated pathology, for which chronic anticoagulant treatment is administered, a number of 42 patients (53.84%) were diagnosed with atrial fibrillation, 8 cases (10.25%) had a history of myocardial infarction and 28 cases (35.89%) have cardiac valvular pathology.

Regarding the associated comorbidities, a number of 39 patients (50%) presented hypertension in their medical history, 11 patients (14.11%) presented strokes in the antecedents, and 28 cases (35.89%) presented type 2 diabetes.

The patients presented chronic osteitis predominantly at the level of the maxillary arch, as follows: 45 patients (57.69%) were diagnosed with chronic odontogenic osteitis in the maxilla and 33 (42.3%) with chronic odontogenic osteitis in the mandible.

From the group of patients, 33 patients (42.3%) required a single extraction, 28 patients (35.89%) between two and four extractions, and 17 patients (21.79%) more than 4 extractions.

Of all the extractions performed, 48 extractions (61.53%) were simple extractions, and 30 extractions (38.46%) required the application of surgical extraction techniques.

Regarding the postoperative evolution of the cases, post-extraction haemorrhage was found in 22 cases (28.2%).

We analysed the dental and therapeutic peculiarities that influenced the occurrence of haemorrhagic accidents. The frequency of bleeding has been increased in the following cases: dental extractions that required the creation of a flap; extractions that required alveolotomy; extraction of large teeth with curved or divergent roots; extraction of ankylosed teeth; extraction of periodontal teeth; the anaesthetic technique did not influence the occurrence of bleeding.

Depending on the moment of the haemorrhage, there were three situations: prolonged haemorrhage: 4 cases; early secondary haemorrhage: 7 cases; late secondary haemorrhage: 11 cases.

The treatment applied in these cases was as follows: in 16 cases out of the 22 haemostasis was achieved with the help of the compressive dressing kept in occlusion by the patient for 30 minutes; in 6 cases, a consistent haemorrhage was found with the formation of massive alveolar clots, which plunged into the oral cavity. These cases required a new cardiological consultation with the adjustment of the dose of anticoagulant treatment and the revision of the post-extraction wounds by alveolar curettage, the introduction of haemostatic material (Gelaspon or Tachosyl sponge) and wound suture. The emergency treatment involved: applying a compressive dressing soaked in Etamsilate 250 mg and rinsing the mouth with tranexamic acid (500 mg tablets dissolved in water).

Resumption of oral anticoagulant treatment was possible in 40 cases (51.28%) after 24 hours postoperatively, in 25 cases (32.05%) anticoagulant treatment was resumed after 48 hours postoperatively, and in 13 cases (16.6 %) resumed more than 48 hours post-operatively.

DISCUSSIONS

The main pathologies involved in the prescription of antithrombotic drugs are atrial fibrillation, followed by deep vein thrombosis, coronary stenting, percutaneous coronary intervention, atherosclerotic cardiovascular disease and prevention of multiple cardiovascular events [6]. This aspect can also be observed in the present study, with 42 patients (53.84%) being diagnosed with atrial fibrillation, and 28 cases (35.89%) showing valvular cardiac pathology.

The management of these patients represents a challenge for dentists as they should carefully balance the risk of bleeding with the risk of thromboembolic complications resulting from the temporary interruption of antithrombotic therapy. Dental procedures are generally associated with a low risk of bleeding. Studies have demonstrated that in the case of dental procedures, the risk of thrombotic events due to altering or discontinuing antithrombotic therapy far outweighs the low risk of potential perioperative bleeding complications among patients treated with single or dual antiplatelet therapy or vitamin K antagonists [7-12].

The management of patients on anticoagulant therapy has changed considerably over time, and there are still differences in approach between dentists, oral and maxillofacial surgeons. Several protocols have been proposed, such as: temporary discontinuation of medication or reduction of administered doses to achieve a subtherapeutic INR, replacement of oral anticoagulants with heparin or low molecular weight heparin, or no change in therapy. None of these approaches is without risks for the patient, and the attending physician must make a clinical assessment of the ratio of risks and benefits, between operative management strategies and the complications that may arise [13]. The balance between drug dose reduction on the one hand and excessive bleeding during surgery on the other are the major issues, especially in outpatient procedures [14].

The patients included in the study follow chronic oral anticoagulant treatment with acenocoumarol (in 50 cases it was represented by Sintrom, and in 28 cases by Thrombostop), benefiting from the advantage of a broad spectrum of action, being a good alternative for long-term anticoagulation due to the rapid onset, long duration of action and stable anticoagulant effect. Acenocoumarol is effective and safe for all age groups and offers an advantage over warfarin in terms of better stability of the anticoagulant effect. After oral administration, a maximal prothrombin time-increasing effect is observed between 24-30 hours [15,16].

INR values should be obtained 24 hours before the extraction procedure. Depending on the reason for anticoagulant therapy, the therapeutic INR target is different [17]. For invasive oral surgical procedures, patients with an INR at the upper limit or greater than 3.5 should be referred for a new consultation with the attending physician for dose adjustment or therapy modification before these [18].

Regarding the pre-operative management of patients, the therapeutic approach was to discontinue medication and administer a short-acting anticoagulant for a few days before surgery, known as "bridging therapy", performed mostly with low molecular weight heparin [19]. In our study the modification of the pre-operative treatment scheme was carried out according to the indication of the cardiologist, by stopping the oral chronic anticoagulant treatment and replacing it with Clexane 0.6 or 0.8 ml (depending on the patient's weight) until the INR value dropped below 1,2. If this value was reached, the extraction intervention was carried out at least 6 hours after the administration of the last dose of Clexane.

Bleeding that may occur in patients on antiplatelet or anticoagulant therapy during dental extractions can be controlled by using local hemostatic measures [20-24] which is why it is recommended not to stop antithrombotic treatment in these patients [21,22,24-27].

In patients under anticoagulant treatment with an INR > 3.5, or who require a major oral surgery, the option of interrupting drug treatment for a period between 0-48h before the intervention can be considered, always consulting the cardiologist [28,29]. International societies and organizations such as the American Dental Association (ADA), American College of Cardiology (ACC), the European Council of Dentists (CED), the Spanish Society of Oral and Maxillofacial Surgery (SECOM), support these recommendations and criteria for the management of these patients [30].

Kwak et al. recommend at least one day interruption of the anticoagulant in cases of multiple dental extractions, implant surgery or deep root scaling, considering the half-life of

the drug and renal clearance, although no significant relationship was reported between the duration of anticoagulant discontinuation and the bleeding tendency [24]. This is not in agreement with other authors, because although there is a low thromboembolic risk when antiplatelet and anticoagulant drugs are discontinued, discontinuation leads to significantly higher morbidity and mortality compared to bleeding events [20,23,25].

CONCLUSIONS

Peri- and postoperative bleeding during dental extractions in patients on antiplatelet or anticoagulant therapy can be easily managed using local hemostatic measures. If any antiplatelet or anticoagulant treatment needs to be changed, this should always be done under the supervision of the responsible hematologist or specialist. In the case of patients with thrombogenic risk, in order to perform dental extractions under appropriate conditions, discontinuation of anticoagulant medication requires hospitalization conditions.

For patients undergoing dental procedures at high risk of bleeding, it is recommended to schedule dental treatment for the morning to allow for monitoring and management of potential bleeding complications, limit the surgical site by performing a single extraction or limit subgingival periodontal scaling to three teeth, and assess bleeding prior to continue and use hemostatic measures to achieve hemostasis as soon as possible.

Based on the type of dental procedure and medical risk assessment, several general treatment approaches can be considered: continuing anticoagulant treatment, scheduling dental treatment as late as possible after the last dose of anticoagulant, stopping treatment for 24 hours or 48 hours. Based on the current reported dental literature, limited dental surgery may benefit from the first two conservative options. However, this needs to be proven in comparative clinical trials.

REFERENCES

1. Mega JL, Simon T. Pharmacology of antithrombotic drugs: an assessment of oral antiplatelet and anticoagulant treatments. Lancet. 2015 Jul 18;386(9990):281-91.
2. Costa-Tort J, Schiavo-Di Flaviano V, González-Navarro B, Jané-Salas E, Estrugo-Devesa A, López-López J. Update on the management of anticoagulated and antiaggregated patients in dental ractice: Literature review. J Clin Exp Dent. 2021;13(9):e948-56.
3. Dézsi CA, Dézsi BB, Dézsi AD. Management of dental patients receiving antiplatelet therapy or chronic oral anticoagulation: A review of the latest evidence. Eur J Gen Pract. 2017;23(1):196-201.
4. Vivas D, Roldán I, Ferrandis R, Marín F, Roldán V, Tello-Montoliu A, et al. Perioperative and Periprocedural Management of Antithrombotic Therapy: Consensus Document of SEC, SEDAR, SEACV, SECTCV, AEC, SECPRE, SEPD, SEGO, SEHH, SETH, SEMERGEN, SEMFYC, SEMG, SEMICYUC, SEMI, SEMES, SEPAR, SENEC, SEO, SEPA, SERVEI, SECOT and AEU. Rev Esp Cardiol. 2018;71:553-64.
5. Lu SY, Lin LH, Hsue SS. Management of dental extractions in patients on warfarin and antiplatelet therapy. J Formos Med Assoc. 2018;117(11):979-986.
6. Cocero N, Basso M, Grosso S, Carossa S. Direct Oral Anticoagulants (DOACs) and Medical Comorbidities in Patients Needing Dental Extractions: Management of the Risk of Bleeding. J Oral Maxillofac Surg. 2019;77:463–470.
7. Morimoto Y, Niwa H, Minematsu K. Hemostatic management of tooth extractions in patients on oral antithrombotic therapy. J Oral Maxillofac Surg. 2008;66:51–57.
8. Napeñas JJ, Oost FCD, DeGroot A, Brennan MT, Lockhart PB, van Diermen DE. Review of postoperative bleeding risk in dental patients on antiplatelet therapy. Oral Medicine. 2013;115(4):491-499.

9. Lillis T, Ziakas A, Koskinas K, Tsirlis A, Giannoglou G. Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. Am J Cardiol. 2011;108:964–967.
10. Evans IL, Sayers MS, Gibbons AJ, Price G, Snooks H, Sugar AW. Can warfarin be continued during dental extraction? Results of a randomized controlled trial. Br J Oral Maxillofac Surg. 2002;40:248–252.
11. Bajkin BV, Popovic SL, Selakovic SD. Randomized, prospective trial comparing bridging therapy using low-molecular-weight heparin with maintenance of oral anticoagulation during extraction of teeth. J Oral Maxillofac Surg. 2009;67:990–995.
12. Cannon PD, Dharmar VT. Minor oral surgical procedures in patients on oral anticoagulants-a controlled study. Aust Dent J. 2003;48:115–118.
13. Dinkova A, Kirova DG, Delev D. Management of patients on anticoagulant therapy undergoing dental surgical procedures. Review Article J of IMAB. 2013;19(4):321-326.
14. Franchini M, Liumbruno GM, Bonfanti C, Lippi G. The evolution of anticoagulant therapy. Blood Transfus. 2016;14(2):175-84.
15. Azim A, Baronia AK, Rao PB, et al. Safety and cost-effectiveness of Acitrom for DVT prophylaxis in critically ill patients requiring prolonged mechanical ventilation - A preliminary experience. J Anaesth Clin Pharmacol 2010;26(3): 360-362.
16. Dalmau Llorca MR, Aguilar Martín C, Carrasco-Querol N, Hernández Rojas Z, Forcadell Drago E, Rodríguez Cumplido D, Castro Blanco E, Gonçalves AQ, Fernández-Sáez J. Anticoagulation Control with Acenocoumarol or Warfarin in Non-Valvular Atrial Fibrillation in Primary Care (Fantas-TIC Study). Int J Environ Res Public Health. 2021;18(11):5700.
17. Sanz M. Screening for international normalized ratio in the dental office may provide useful information to prevent both hemorrhagic and thromboembolic events. J Evid Based Dent Pract. 2012;12(3):164-166.
18. Hong C, Napenas JJ, Brennan M, Furney S, Lockhart P. Risk of postoperative bleeding after dental procedures in patients on warfarin: a retrospective study.Oral Surg Oral Med Oral Pathol Oral Radiol. 2012;114(4):464-468.
19. Pettinger TK, Owens CT. Use of low-molecular-weight heparin during dental extractions in a medicaid population. J Manag Care Pharm. 2007;13(1):53-58.
20. Lu S, Lin L, Hsue S. Management of dental extractions in patients on warfarin and antiplatelet therapy. J Formos Med Assoc. 2018;117:979–986.
21. Doganay O, Atalay B, Karadag E, Aga U, Tugrul M. Bleeding frequency of patients taking ticagrelor, aspirin, clopidogrel, and dual antiplatelet therapy after tooth extraction and minor oral surgery. JADA. 2018;149:132–8.
22. Rubino RT, Dawson D, Al-Sabbagh M, Kryscio R, Miller C. Postoperative bleeding associated with antiplatelet and anticoagulant drugs: A retrospective study. Oral Surg Oral Med Oral Pathol Oral Radiol. 2019;128:243–249.
23. Rocha AL, Oliveira SR, Souza AF, Travassos DV, Abreu LG, Dias Ribeiro D. Bleeding assessment in oral surgery: A cohort study comparing individuals on anticoagulant therapy and a non-anticoagulated group. J Craniomaxillofac Surg. 2019;47:798–804.
24. Kwak EJ, Nam S, Park K, Kim S, Huh J, Park W. Bleeding related to dental treatment in patients taking novel oral anticoagulants (NOACs): a retrospective study. Clin Oral Investig. 2019;23:477–484.
25. Lababidi E, Breik O, Savage J, Engelbrecht H, Kumar R, Crossley C. Assessing an oral surgery specific protocol for patients on direct oral anticoagulants: a retrospective controlled cohort study. Int J Oral Maxillofac Surg. 2018;47:940–846.
26. Yoshikawa H, Yoshida M, Yasaka M, Yoshida H, Murasato Y, Fukunaga D. Safety of tooth extraction in Patients receiving direct oral anticoagulant treatment versus warfarin: a prospective observation study. Int J Oral Maxillofac Surg. 2019;48:1102–1108.
27. Berton F, Maglione M, Constantinides F, Visintini E, Rizzo R, Stacchi C. Should we fear direct oral anticoagulants more than vitamin K antagonists in simple single tooth extraction? A prospective comparative study. Clin Oral Investig. 2019;23:3183–3192.
28. Miller SG, Miller CS. Direct oral anticoagulants: A retrospective study of bleeding, behavior, and documentation. Oral Dis. 2018;24:243–248.

29. Rocha AL, Souza A, Martins M, Fraga M, Travassos D, Oliveira A. Oral surgery in patients under antithrombotic therapy: perioperative bleeding as a significant risk factor for postoperative hemorrhage. Blood Coagul Fibrinolysis. 2018;29:97–103.
30. Grines C, Bonow R, Casey D, Gardner T, Lockhart P, Moliterno DJ. Prevention of Premature Discontinuation of Dual Antiplatelet Therapy in Patients With Coronary Artery Stents: A Science Advisory From the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, With Representation From the American College of Physicians. Circulation. 2007;115:813–8.