

## Minor oral surgery under anticoagulant therapy: A review of the literature

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World Journal of Advanced Research and Reviews, 2023, 18(03), 944–952

Publication history: Received on 07 May 2023; revised on 14 June 2023; accepted on 16 June 2023

Article DOI: <https://doi.org/10.30574/wjarr.2023.18.3.1164>

### Abstract

**Objectives:** This literature review seeks to know the management, as well as the limitations, indications, hemostatic measures and the risk to which compromised patients are exposed either by modifying the treatment or decreasing the dose prior to surgery treatment, as well as to establish the management of patients under therapy; before, during and after surgery.

**Materials and methods:** a literature review was carried out during the period September - December 2022. The sources used were the PubMed, ScienceDirect and Medline databases. The search terms were: (Warfarin) AND (Oral surgery), (Anticoagulation bridge ) AND (Anticoagulant) AND (Dental extraction) AND (dentistry). Results: a total of 6281 articles were identified from the three databases used: pubmed, sciencedirect and medline. After applying the exclusion criteria, 3557 articles were eliminated, leaving a total of 2724 for reading and eligibility, resulting in 56 articles, 11 duplicate articles were excluded, leaving 45 articles for analysis and elaboration of the literature. Conclusions: compromised patients under treatment with direct oral anticoagulants (DOAC) or vitamin K antagonists (VKA) present a risk of intraoperative and postoperative bleeding, where VKA presents a higher risk compared to DOAC; it is recommended not to suspend the administration of anticoagulants either before or after surgery. Hemostasis can be controlled using different hemostatic measures.

**Key words:** Oral Surgery; Anticoagulation Bridge; Warfarin; Dentistry; Dental extraction.

### 1. Introduction

Cardiovascular disease is a pathology that is part of the chronic non-communicable diseases, it is one of the main causes of mortality and morbidity worldwide, the treatment used depends on the important risk factors which are expressed in a unique way in high, intermediate and low risk factors. Treatment can range from lifestyle changes to the administration of antithrombotics, the intensity of which depends on the size of the absolute risk. (1-3)

Due to the increased frequency of cardiovascular diseases, the number of patients on long-term anticoagulant therapy continues to increase worldwide. The therapeutic management of such underlying diseases is an internal medicine problem. However, with the increasing incidence of these diseases, anticoagulation therapy remains a primary problem in both high and low complexity oral surgery. (4,5)

Patients on anticoagulation therapy who require dental treatments or other minor oral surgery interventions often find their management challenging and clinically significant due to the risk of bleeding complications during the dental surgical procedure. (6,7)

Minor surgical procedures are actions of the daily clinical practice of the dentist, therefore a correct management of the patient compromised or not is essential, especially in those of the latter group due to the high risk of bleeding during

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the procedure, among the most performed practices are: Exodontia with alveolar preservation technique, Surgical exodontia of third molars, Labial frenilectomies, Lingual frenilectomies, Dentoalveolar traumas, Apicoectomies, etc.... (8)

The drugs mostly used are vitamin K antagonists (VKA) such as warfarin and acenocoumarol, direct thrombin inhibitors, direct factor Xa inhibitors, known as direct acting oral anticoagulants (DOAC) such as apixaban, edoxaban, rivaroxaban and dabigatran indicated for the prevention of thromboembolism due to its more predictable action. Dabigatran appeared as an option to warfarin for anticoagulation in the treatment of atrial fibrillation (AF). The risk associated with bleeding due to its use has been evidenced in several trials, but no large study has examined in detail the risk of bleeding in the process of tooth extraction and other dental procedures involving bleeding. (9-13)

VKAs inhibit vitamin K-dependent coagulation factors (II, VII, IX, X), these are characterized by a slow onset of action, their effect takes 5 to 7 days, the international normalized ratio (INR) determines the intensity of the anticoagulant effect of VKAs so that the INR in a healthy patient is 0.9 to 1.6, this range depends on each pathology, thus in patients with mechanical valve prostheses and in pulmonary thromboembolism with antiphospholipid syndrome the INR is 2.5 to 3.5; meanwhile, most patients with atrial fibrillation, ischemic stroke, acute myocardial infarction and embologenic valvulopathies the INR is 2. (14, 40)

DOACs are new anticoagulant agents that specifically disrupt a single factor in the coagulation system, either activated factor X or thrombin. (15)

They feature "antithrombotic agents" that give them a more predictable effect in blood compared to (VKAs) (16).

This literature review seeks to know the management as well as limitations, indications, hemostatic measures and the risk to which compromised patients are exposed either by modifying or suspending the dose of treatment prior to surgery as well as to establish the management of patients under therapy before, during and after oral surgery.

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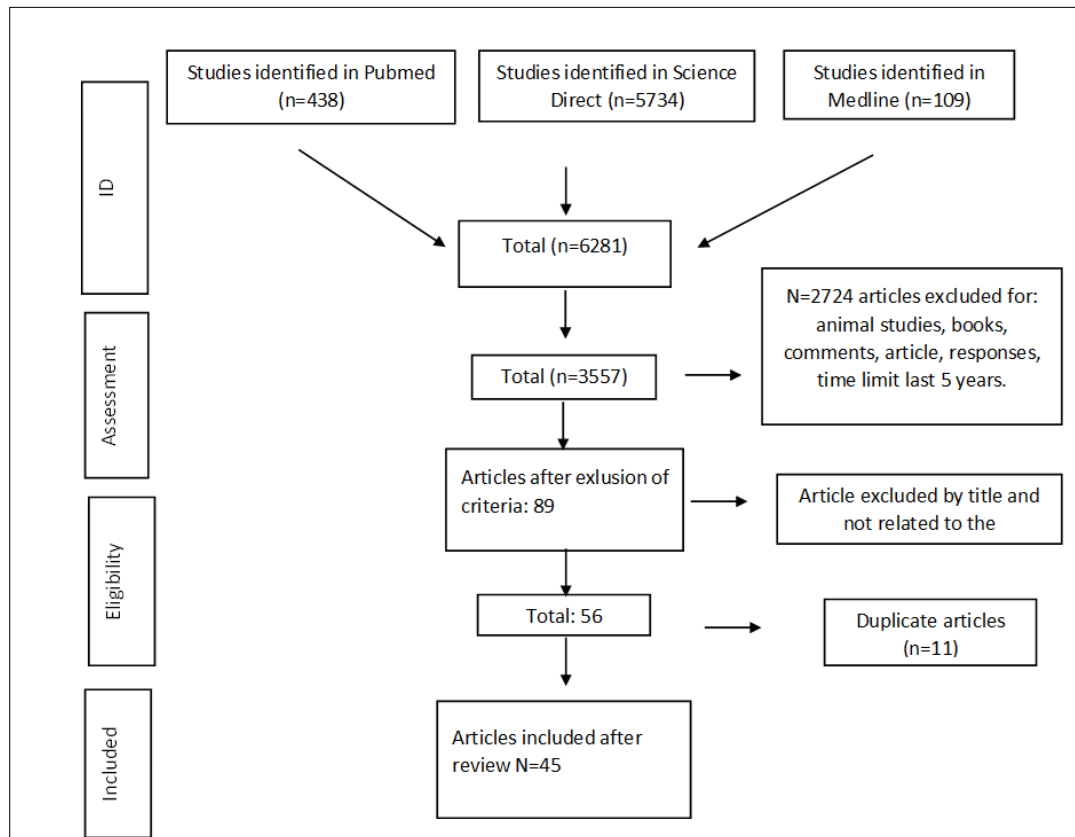
## 2. Materials and Methods

Under the question what is the risk to which patients under anticoagulant therapy are subjected during dental extractions and what is the protocol to follow? A literature review was conducted during the period September - December 2022. The sources used were the PudMed, ScienceDirect and Medline databases. The search terms were: Warfarin) AND (Oral surgery), (Anticoagulation bridge ) AND (Anticoagulant) AND (Dental extraction) AND (dentistry).

Controlled clinical trials, observational, practice guidelines, risk factor studies, research case reports, meta-analyses, literature reviews, research articles, systematic reviews, comparative, prospective, cross-sectional studies published in the last 5 years, with no language limit, were taken into account. Articles that are animal studies, books, commentaries, article responses, and that are not part of the last 5 years of publication were excluded.

Reviewed articles were collected, stored, and organized using Microsoft Excel 2016.

Flowchart



**Figure 1** Flow diagram of the selection of articles for the literature review: A total of 6281 articles were identified from the three databases used: pubmed, sciencedirect and medline. After applying the exclusion criteria, 3557 articles were eliminated, leaving a total of 2724 for reading and eligibility, resulting in 56 articles, 11 duplicate articles were excluded, leaving 45 articles for analysis and elaboration of the literature.

### 3. Results

Over time, different dental surgery protocols have been generated for patients with anticoagulants, and these are modified in relation to the anticoagulant therapy they receive. There are two families of drugs used: vitamin K antagonists and direct oral anticoagulants. It has now been demonstrated that there is a greater risk for the patient when anticoagulant therapy is interrupted because it can produce thromboembolism and "rebound hypercoagulation", compared to post-extraction bleeding when continuing with anticoagulants.

#### 3.1. Theoretical framework

##### 3.1.1. Risk

The management of ASA II patients under anticoagulant therapy should be treated with caution taking the necessary measures and having adequate safety to provide efficient care to the compromised patient, therefore, it is necessary to know the risks to which patients are subjected.

The risk of slowing healing and increasing hemostasis during third molar extraction, specifically in the extraction of the lower third molar in those patients treated with warfarin tends to be notably higher, however, risk factors significantly influence during the surgical procedure, among them are an increased prothrombin time value (PT-INR), preoperative administration of prophylactic antibiotics, elevated serum creatinine levels and postoperative bleeding after extraction in patients under VKA. (17-19)

Current studies are moving towards the prescription of direct oral anticoagulants, which have fewer interactions and better perioperative management. (20)

Systolic blood pressure control is also important during tooth extraction to avoid complications in patients taking warfarin and in hypertensive patients not taking warfarin. The highest systolic blood pressure (SBP) values were

observed in patients receiving warfarin before administration of local anesthetics (highest SBP = 0.9415 mm Hg) and in hypertensive patients not taking warfarin (highest SBP = 1.0027 mm Hg). (21, 41)

In elderly patients regardless of the type of anticoagulant, the dental extraction procedure may generate postoperative bleeding problems after dental extraction due to the influence of other medical problems, caution is accurate even more when they are being administered with rivaroxaban. (22, 42)

### **3.2. Risk in case of multiple extractions**

If patients on anticoagulants are scheduled to undergo multiple tooth extractions or their HAS-BLED score (scale for calculating the risk of bleeding in patients with atrial fibrillation receiving oral anticoagulation, based on risk factors)<sup>22</sup>. If the scale is above 3 points in the case of warfarin, patients are informed about the risk of bleeding after the extraction, risk-benefit should be considered before the operation and hemostasis should be carefully performed, and patients should be instructed to bite down precisely on the gauze for longer than normal. (23)

### **3.3. Protocols in patients undergoing vitamin K antagonist (VKA) therapy during minor or major oral surgery procedures.**

- continue VKAs with no change in administration
- discontinued days before with heparin
- discontinued days before surgery

#### *3.3.1. Continue VKAs with no change in their administration.*

VKA treatment should be continued for all surgical procedures if the INR is in the therapeutic range (warfarin INR<4.0) the American College of Chest Physicians recommends an INR of 2.0-3.0 for most cardiac conditions therefore discontinuation of antiplatelet therapy prior to dental extractions is not necessary, hemostasis can be achieved by applying local measures. (24)

#### *3.3.2. Stopped before with heparin, stopped before surgery.*

Anticoagulation therapy with warfarin, whether continued, suspended or joined a few days before surgery with heparin therapy, is not indicated due to the complexity of managing vitamin K antagonists, their interaction with various medications and foods, and their persistent need for monitoring of effectiveness and their blood concentration, in other words may increase the risk of other complications, such as thromboembolic diseases (25, 43)

#### *3.3.3. Reducing the dose days before surgery.*

Factors such as diet, concomitant use of other medications and other comorbidities may alter the activity of anticoagulants for such reason reducing the dose before surgery presents risks of thromboembolic complications that outweigh the risks of bleeding events. (26)

### **3.4. Protocols in patients undergoing DOAC during minor or major oral surgery procedures**

Maintain unchanged direct oral anticoagulant therapy and apply local hemostatic measures.

Following minor oral surgery such as tooth extractions, the risk of postoperative bleeding is slightly lower in patients receiving DOAC without interruption of DOAC administration both preoperatively and postoperatively compared to patients receiving VKA, therefore, it is NOT necessary to adjust the dose of DOAC prior to tooth extractions.(27,28)

Discontinue DOACs one day before or one day after surgical treatment.

Compared to VKAs, DOACs have different pharmacokinetics, their plasma concentrations vary from 3-4 hours and their half-lives vary from 10-17h, allowing an immediate onset and loss of their anticoagulant effects, which has led to consider the suspension of their administration prior to surgery compared to warfarin, which has a prolonged half-life and a subtherapeutic dose that could leave the patient in a prothrombotic state. (29, 44)

### **3.5. Protocol for dental extractions in anticoagulated patients.**

The management of the compromised patient should be widely known due to the number of patients that require dental extractions and this being a daily practice of the dentist, their knowledge and management should be sufficiently clear to eradicate any type of complication during the intervention.

**Table 1** Protocol for dental extraction in anticoagulated patients. (45)

DOAC		AVK	
Extraction of 1 to 3 pieces and minor procedures	Extraction of ≥ 4	Extraction of 1 to 3 pieces and minor procedures	Extraction of ≥ 4
normal vital signs Laboratory exams normal blood count INR < 4.0	Request advice from the oral and maxillofacial surgery department and/or contact the patient's doctor to determine risk factors	normal vital signs Laboratory exams normal blood count INR < 4.0 normal pt normal PTT	Request advice from the oral and maxillofacial surgery department and/or contact the patient's doctor to determine risk factors
Anticoagulant therapy is maintained- extraction in 1-3 pieces		Anticoagulant therapy is maintained at intervals of 4 to 6 h- extraction in 1-3 pieces	
Antibiotic coverage if necessary, surgical approach extractions in 1st 3 pieces DOAC/ AVK			
light bleeding	moderate bleeding	severe bleeding	
Gauze compression 30 min Chew the gauze soaked with a fibrinolytic agent	Application of a topical hemostatic with a gelatin sponge ( gelfoam or oxidized cellulose tape, along with single suture)	Systemic therapy or hospitalization	
postoperative medication		postoperative medication	
4.8% mouth rinse use 4 times a day for 2 minutes - follow-up			

### 3.6. Hemostatic measures

Among the hemostatic agents used to control bleeding, the literature has highlighted oxidized cellulose, resorbable gelatin sponges, collagen sponges, fibrin glue, cyanoacrylate glue, platelet-rich plasma gel, calcium alginate and topical thrombin. Local interventions, such as sutures, sealants, adhesives, ligature clips, vasoconstrictor agents, or combination of these measures have also been used to control bleeding. (30, 31)

Hemostatic interventions also include antifibrinolytic agents, such as tranexamic acid (TXA) which helps promote safe hemostasis at the surgical site to improve intraoperative visibility and postoperative hemostasis. The importance of antifibrinolytic mouth rinses in the prevention of post-extraction bleeding has been observed in several studies. They are used to mitigate bleeding in surgical procedures because they stabilize and inhibit the breakdown of blood clots. (32,33)

In all studies reviewed by Ockerman et al (2019) : mentions that during minor oral surgery, employing the technique of gauze pressure as a primary hemostatic measure, in combination or not with sutures in conjunction with other hemostatic measures allows greater control of bleeding in patients under dual and single antiplatelet therapy, hemostatic measures included: absorbable collagen sponges, gelatin or gelfoam gauze impregnated with Tranexamic Acid as a primary hemostatic method and gauze pressure and re(suturing) as a secondary hemostatic measure in case bleeding occurred. All studies confirmed that local hemostatic measures were adequate to stop bleeding however the risk of perioperative bleeding in minor oral surgery is higher in patients receiving dual antiplatelet therapy than in those receiving single antiplatelet therapy. (34, 35,36)

### 3.7. Platelet-rich fibrin (PRF)

It is made up of three key parameters that distinguish it from platelet-rich plasma.

Activated platelets and growth factors: they are introduced into the fibrin matrix in the natural polymerization process

Leukocytes and their cytokines: provide anti-infective action and assist in immune regulation in the healing process . Natural density and organization without anticoagulants and gelling agents.

The fibrin matrix promotes angiogenesis, facilitating access to the injured site, playing an important role in residual healing.

However, according to the study by Edson et al. (2021) From a total of 130 patients to whom platelet-rich fibrin was applied after tooth extraction it was shown that the use of FRP in extraction wounds did not reduce the risk of bleeding after extraction in anti-coagulated patients ( $P = 0.330$ ;  $I2 = 99\%$ ). did not reduce pain ( $P = 0.470$ ;  $I2 = 96\%$ ) or the risk of postoperative alveolitis ( $P = 0.4300$ ;  $I2 = 38\%$ ). (37)

Local hemostatic agents such as TXA and feracrylum stop bleeding without having systemic action and without the need to alter the anticoagulant regimen. Feracrylum has the added advantage of a single application, formation of a mechanical barrier and an additional antimicrobial effect. These agents should be incorporated into the protocol for managing patients on oral anticoagulants. (38, 39)

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#### 4. Conclusions

Patients who are under treatment with DOAC or VKA and who undergo minor surgical interventions are at risk of intraoperative and postoperative bleeding regardless of the range in which they are, however in this literature review it was corroborated that patients under VKA have a slightly higher level of risk compared to patients under DOAC regardless of whether the surgical procedure is of lesser or greater complexity.

Almost all the articles reviewed recommend not to suspend the administration of anticoagulants either before or during the surgical procedure, and that hemostasis can be controlled according to the level of bleeding by means of hemostatic measures, including topical hemostatic application, especially TXA zhaguicon, a gelatin sponge, gelfoam or oxidized cellulose tape, together with individual suture, compression with gauze for 30 min soaked with an antifibrinolytic agent and in case of severe bleeding use systemic therapy or hospitalization, however the latter must be previously communicated to the oral surgery department.

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#### Compliance with ethical standards

##### *Acknowledgments*

We would like to express our most sincere gratitude to Dr. Mario Calderón for his professional help and patience in the preparation of this work.

Likewise, I, Wendy Marca, want to thank my siblings Wilmer, Marina, Carolina and my parents Manuel and Pilar, especially my mother Pilar for always supporting me in spite of everything and my grandmother Lucinda who is in heaven for being my guardian angel throughout this journey, this goal has been achieved by the support of my entire family.

##### *Disclosure of conflict of interest*

The authors did not declare any potential conflict of interest with respect to the research, authorship and/or publication of this article.

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