Universidad Europea

GRADUATION PROJECT

Degree in Dentistry

PREVALENCE AND TYPE OF ANTICOAGULATION BEFORE DENTAL PROCEDURES

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ABSTRACT

Introduction: This study examines the use of anticoagulant medication in patients undergoing dental procedures. Dental treatment for patients on anticoagulation therapy can result in bleeding complications, making it essential to understand the prevalence and type of anticoagulants used before dental procedures and how dentists manage these patients during invasive dental procedures to ensure patient safety and optimal treatment outcomes. **Objectives:** The study aims to investigate the prevalence and types of anticoagulant therapy used and the management strategies employed by dentists. **Methodology:** For this study, we analyzed 6 different research studies. We studied the prevalence of patients using anticoagulant medications. We also examined how the anticoagulant medications were being managed and the bleeding outcomes associated with them. **Results:** The studies included a total of 2,136 patients, with prevalence rates ranging from 6.57% to 48,7%. The anticoagulant treatments used included vitamin K antagonists, direct oral anticoagulants (DOACs), and platelet aggregation inhibitors. All studies reported minimal risk of bleeding after dental procedures in patients on anticoagulant therapy, and local hemostasis was effective in managing post-operative bleeding. However, patients on vitamin K antagonists had an increased risk of bleeding when bridged with low molecular weight heparin. **Conclusions:** The prevalence of anticoagulant use has been rising, especially among older patients who often have underlying medical conditions. Therefore, dentists may encounter more patients receiving anticoagulation therapy. Studies showed that continuing anticoagulation during dental procedures did not increase the risk of bleeding in most cases. However, heparin bridging was associated with a higher incidence of bleeding. As a result, it is recommended to maintain oral anticoagulation with vitamin K antagonists and direct oral anticoagulants for most dental procedures, along with the use of local hemostatic agents to ensure patient safety.

Keywords: Dentistry; anticoagulants; bleeding risk; DOAC; vitamin K-antagonist.

RESUMEN

Introducción: Este estudio examina el uso de medicamentos anticoagulantes en pacientes sometidos a procedimientos dentales. El tratamiento dental para pacientes con terapia anticoagulante puede provocar complicaciones hemorrágicas, por lo que es esencial comprender la prevalencia y el tipo de anticoagulantes utilizados antes de los procedimientos dentales y cómo los dentistas manejan a estos pacientes durante los procedimientos dentales invasivos para garantizar la seguridad del paciente y los resultados óptimos del tratamiento. **Objectivos:** El estudio tiene como objetivo investigar la prevalencia y los tipos de terapia anticoagulante utilizados y las estrategias de manejo empleadas por los dentistas. **Metodología:** Para este estudio, analizamos 6 estudios de investigación diferentes. Estudiamos la prevalencia de pacientes que utilizan medicamentos anticoagulantes. También examinamos cómo se manejaban los medicamentos anticoagulantes y los resultados de sangrado asociados con ellos. **Resultados:** Los estudios incluyeron un total de 2.136 pacientes, con tasas de prevalencia que oscilaron entre el 6,57 % y el 48,7 %. Los tratamientos anticoagulantes utilizados incluyeron antagonistas de la vitamina K, anticoagulantes orales directos (DOAC) e inhibidores de la agregación plaquetaria. Los estudios informaron un riesgo mínimo de sangrado después de los procedimientos dentales en pacientes con terapia anticoagulante, y la hemostasia local fue efectiva para controlar el sangrado posoperatorio. Sin embargo, los pacientes tratados con antagonistas de la vitamina K tenían un mayor riesgo de hemorragia cuando se les administraba un puente con heparina de bajo peso molecular. **Conclusiones:** La prevalencia del uso de anticoagulantes ha ido en aumento, especialmente entre los pacientes mayores que a menudo tienen condiciones médicas subyacentes. Por lo tanto, los dentistas pueden encontrarse con más pacientes que reciben terapia anticoagulante. Los estudios demostraron que la continuación de la anticoagulación durante los procedimientos dentales no aumentó el riesgo de sangrado en la mayoría de los casos. Sin embargo, el puente de heparina se asoció con una mayor incidencia de hemorragia. Como resultado, se recomienda mantener la anticoagulación oral con antagonistas de la vitamina K y nuevos anticoagulantes orales para la mayoría de los procedimientos dentales, junto con el uso de agentes hemostáticos locales para garantizar la seguridad del paciente.

Palabras clave: Odontología; anticoagulantes; riesgo de sangrado; DOAC; antagonista de la vitamina K.

INDEX

1. INTRODUCTION

Anticoagulants are a type of drug used to prevent blood clots forming in subjects with high risk of thrombosis development (1). Anticoagulant use has grown throughout time, with older adults and people with specific medical disorders having a higher prevalence than others. According to recent studies, the anticoagulant prescription is increasing in general population and this trend is expected to continue in future (2).

Due to the prevalence of disorders like atrial fibrillation (AF), deep vein thrombosis (DVT), and pulmonary embolism that increase the risk of thrombosis, older adults are more prone to need anticoagulants (PE) (3). Also, patients are more likely to utilize anticoagulants as preventative measures if they have a history of a stroke, heart attack, or blood clots. Anticoagulants are a crucial part of medical therapy since these diseases are linked to a higher risk of morbidity and mortality (2).

Children do not often receive anticoagulant medication, but it may be required in some circumstances to avoid blood clot development. Congenital heart disease, deep vein thrombosis, pulmonary embolism, and systemic lupus erythematosus are a few disorders that may necessitate anticoagulant medication in children (4). Due to the increased risk of blood clots from various cancer treatments, children with cancer could also need anticoagulant therapy (5).

However, using anticoagulants has a number of concerns, including bleeding, particularly while undergoing invasive dental operations (6). Blood loss during dental operations might be problematic for people taking anticoagulant therapy. The bleeding may cause hematoma, delayed healing, and postoperative pain, all of which may have a significant impact on the patient's quality of life (7). The development of guidelines for the management of these patients, depending on

the kind of dental treatment, requires the identification of different anticoagulant types and their mechanisms of action (5).

There is a risk of bleeding difficulties before and after dental treatments if dentists do not take into account the patient's anticoagulation regimen, which is one of the most crucial measurements in dentistry (7). Because anticoagulants impair the coagulation cascade, its users are more likely to bleed. A dental procedure's high blood loss, hematoma formation, protracted postoperative bleeding, and the need for emergency intervention can all result from inadequate bleeding control. Uncontrolled bleeding may occasionally pose a life-threatening concern (6). Dentists must therefore be aware of the patient's anticoagulant treatment and take the necessary precautions to control bleeding during and after dental procedures (3).

Parenteral anticoagulants and oral anticoagulants are the two basic categories into which anticoagulants can be generally divided. Vitamin K antagonists (VKAs) like warfarin and direct oral anticoagulants (DOACs) like dabigatran, rivaroxaban, apixaban, and edoxaban are examples of oral anticoagulants (8). Unfractionated heparin, low molecular weight heparin (LMWH), and fondaparinux are examples of parenteral anticoagulants. These medications work through several ways to suppress the coagulation cascade and stop the development of blood clots (9).

For many years, VKAs have been used extensively in the administration of anticoagulant medication; however, since DOACs have been developed, their use has been declined (2). In comparison to VKAs, DOACs have a number of benefits, such as a shorter half-life, fewer food and medication interactions, and a more predictable pharmacokinetic profile. DOACs have been linked to bleeding issues after invasive dental procedures, therefore they are not without risk (1

The management of dental patients on anticoagulation therapy requires a balance between the risk of bleeding and the risk of thrombosis (7). Stopping anticoagulant therapy before a dental procedure can increase the risk of bleeding. The decision to stop or continue anticoagulant therapy should be made on an individual basis, taking into consideration the patient's medical history, the type of anticoagulant used, and the risk of bleeding associated with the dental procedure (11).

Anticoagulants are medications that interfere with the coagulation cascade, leading to the prevention or reduction of blood clot formation (5). They work by inhibiting the activity of various clotting factors or enzymes that are involved in the coagulation process. To have a better understanding of anticoagulants, the knowledge on how the coagulation cascade works is important (1).

1.1. Coagulation cascade

The coagulation cascade is a series of chemical reactions that occur in the body in response to injury, resulting in the formation of a blood clot. The cascade involves a complex interaction between various coagulation factors, which are proteins that are either produced by the liver or released from platelets and endothelial cells (12).

There are two main pathways in the coagulation cascade: the intrinsic pathway and the extrinsic pathway. Both pathways ultimately lead to the activation of a protein called prothrombin, which is converted to thrombin. Thrombin then converts another protein called fibrinogen into fibrin, which forms the basis of the blood clot (13).

The intrinsic pathway is initiated by damage to the blood vessel itself. This sets off a chain of reactions that involves several coagulation factors, including factor XII, factor XI, factor IX, and factor VIII. These factors activate each other in a cascade, eventually leading to the activation of factor X (12).

The extrinsic pathway, on the other hand, is initiated by the release of a protein called tissue factor from damaged tissue outside the blood vessel. Tissue factor then combines with factor VII, which activates factor X (13).

Once factor X is activated, it combines with other co-factors to form a complex known as the prothrombinase complex. This complex then activates prothrombin, which is converted to thrombin. Thrombin then converts fibrinogen to fibrin, which forms the basis of the blood clot (14).

There are also several other factors involved in the coagulation cascade, including factor XIII, which helps to stabilize the clot, and various inhibitors that help to regulate the process and prevent excessive clotting (12).

Overall, the coagulation cascade is a complex and tightly regulated process that involves numerous coagulation factors and steps (table 1.). Understanding this cascade is important for the management of bleeding disorders and the use of anticoagulants to prevent unwanted blood clots (12,14).

Table 1. Coagulation factor, their activation and function: comprehensive table (12,13,14)

Coagulation factor	Name	Activation	Function
I	Fibrinogen	Cleaved by thrombin	Forms fibrin threads in clot
II	Prothrombin	Cleaved by factor Xa and Va with Ca^{2+}	Forms thrombin
III	Tissue factor (TF)	Exposed due injury	Binds with factor VIIa to activate factor X
IV	Calcium ions (Ca^{2+})	N/A (not applicable)	Required for multiple coagulation factor
V	Proaccelerin	Cleaved by thrombin	Binds with factor Xa and Ca^{2+} to form prothrombinase
VII	Proconvertin	Activated by tissue factor (TF)	Binds with tissue factor and aclcium to activate factor X
VIII	Antihemophilic factor A	Activated by thrombin	Binds with IXa to activate factor X
IX	Antihemophilic factor B	Activated by factor XIa	Binds with VIIIa to activate factor X
X	Stuart-power factor	Activated by prothrombinase (V and Xa)	Converts prothrombin to thrombin
XI	Plasma thromboplastin antecedent (PTA)	Activated by contact with collagen	Binds with XIIa to activate factor IX
XII	Hageman factor	Activated by contact with collagen	Binds with prekallikrein to activate factor XI
XIII	Fibrin-stabilizing factor	Activated by thrombin	Crosslinks fibrin strands for stabilization

Different anticoagulants target different steps in the coagulation cascade to prevent the formation of a stable blood clot (14). For example, vitamin K-antagonist, (e.g. warfarin) inhibits the synthesis of clotting factors (15), while DOACs inhibit the activity of specific clotting factors, such as thrombin or factor Xa depending on the type of DOACs (16). Low molecular weight heparins (LMWHs) primarily inhibit the activity of factor Xa (17).

1.2. Low molecular weight heparin

One of the anticoagulants is low molecular weight heparin (LMWH) is a type of anticoagulant medication that inhibits blood clotting by enhancing the activity of antithrombin III, an endogenous anticoagulant protein, particularly clotting factor Xa (17). LMWH is a synthetic form of heparin that has a lower molecular weight than standard heparin, which allows it to be administered

subcutaneously instead of intravenously. The most commonly used LMWH are deltaparin, enoxaparin, tinzaprin, nadroparin and certoparin (18).

The coagulation cascade is a series of enzymatic reactions that occur in response to tissue damage, resulting in the formation of a blood clot to stop bleeding (12). LMWH interrupts this process by binding to antithrombin III, which inactivates thrombin and other coagulation factors, preventing the formation of blood clots (18).

LMWH is commonly used in the prevention and treatment of venous thromboembolism, deep in venous thromboembolism, deep vein thrombosis, and pulmonary embolism. In dentistry, LMW may be used in patients with a history of thromboembolic events or those undergoing oral surgical procedures that pose a risk for an important amount of bleeding, such as multiple tooth extractions (17).

LMWH is usually administered prophylactically, 2 hours before the surgical procedure, and continued for several days post-operatively. The dosage and duration of LMWH therapy depend on the patient's medical history and type of surgical procedure being performed (19).

LMWH has a shorter half-life compared to DOAC, which means that its anticoagulant effect can be more easily reversed if needed. Also, LMWH does not require routine monitoring of blood levels, unlike vitamin K-antagonists that require frequent monitoring of international normalized ratio (INR) (18).

LMWH may need to be interrupted before dental procedures if the patient's bleeding risk is deemed too high. This decision should be made in consultation with the patient's primary care physician or hematologist (20).

1.3. Vitamin K-antagonist

Vitamin K-antagonist anticoagulants, such as warfarin, are widely used for the prevention and treatment of thromboembolism, atrial fibrillation, and mechanical heart valves. Warfarin works by inhibiting the synthesis of vitamin K-dependent clotting factors in the liver, namely factors II, VII, IX and X (21). This results in the inhibition of the coagulation cascade and a decreased risk of thrombus formation. Warfarin has a narrow therapeutic range, and the dose must be carefully monitored to maintain the target international normalized ratio (INR) (22). The target INR varies depending on the indication for anticoagulation and ranges from 2.0-3.0 for most indications. The INR is calculated by comparing the patient's prothrombin time (PT) - a measure of how long it takes for a patient's blood to clot, to the PT of a normal individual. This ratio is then adjusted based on a variety of factors, including the patient's age, sex, and medical history (2).

Regulatory monitoring of a patient's INR levels is important to ensure that the patient is receiving the correct dose of anticoagulant medication (15). If the INR is higher than 3, it means that the patient's blood is clotting more slowly than normal, which can increase the risk of bleeding (5).

Dental procedures in patients on warfarin therapy require special attention, as they carry a risk of bleeding complications (23). The decision to continue or interrupt warfarin therapy before a dental procedure depends on the individual patient's risk of bleeding and thromboembolism, as well as the invasiveness of the procedure. In general, dental procedures are classified as low, moderate, or high risk on their invasiveness and bleeding potential (11).

Low-risk dental procedures, such as routine dental cleanings, simple fillings and single tooth extractions, can be performed without interruption of the warfarin therapy (7). However, the dentist should be aware of the patient's INR and take

appropriate measures to control bleeding, such as local hemostatic measures. These measures include the application of pressure, suturing, and the use of topical hemostatic agents such as oxidized cellulose, collagen, tranexamic acid, and fibrin sponge. (24).

Moderate-risk dental procedures, such as complex extractions, implant placement, and periodontal surgery, may require temporary interruption of warfarin therapy. The decision to interrupt therapy should be made in consultation based on patient's individual risk of bleeding and thromboembolism (10). In general, warfarin therapy should be interrupted 3 to 5 days before the procedure, and the patient's INR should be monitored closely. Bridging therapy with heparin or low molecular weight heparin may be considered to prevent thromboembolism during the interruption period (20).

High-risk dental procedures, such as extensive soft tissue surgery, multiple tooth extractions, and jaw reconstruction, may require temporary interruption of warfarin therapy and hospitalization for closer monitoring (24). In these cases, warfarin therapy should be interrupted 5 to 7 days before the procedure, and bridging therapy with heparin or low molecular weight heparin should be considered. The decision should be made in consultation with the patient's physician (25).

1.4. Direct oral anticoagulants (DOACs)

Direct oral anticoagulants (DOACs) are the newer class of anticoagulants that have gained popularity due to their ease of use, predictable pharmacokinetics, and lower risk of bleeding complications compared to traditional anticoagulant therapies such as warfarin (6). DOACs include factor II (dabigatran), and factor Xa (rivaroxaban, apixaban, and edoxaban) blockers, and are approved for various indications such as stroke prevention in patients with nonvalvular atrial

fibrillation, treatment and prevention of venous thromboembolism after orthopedic surgery (26).

In recent years, there has been increasing interest in the use of DOACs in dentistry, as dental procedures can pose a risk of bleeding complications in patients on anticoagulation therapy (6). The use of DOACs in dentistry has several advantages over traditional anticoagulant therapies, including a lower risk of bleeding complications, less need for monitoring, and fewer drug interactions (8).

It is important to know that while DOACs have a lower risk of bleeding complications compared to traditional anticoagulant therapies, there is still a risk of bleeding with any anticoagulant therapy (6). Therefore, it is recommended that patients on DOAC therapy undergo a comprehensive medical evaluation prior to any dental procedure to assess their bleeding risk and determine whether any modifications to their anticoagulant therapy are necessary. Additionally, patients on DOAC therapy should be closely monitored for any signs of bleeding during and after dental procedures (27).

In conclusion, DOACs are a promising option for anticoagulation therapy in patients undergoing dental procedures (28). While they have a lower risk of bleeding complications compared to traditional anticoagulant therapies, appropriate patient selection monitoring, and management of bleeding complications are essential in ensuring their safe and effective use (3). Further research is needed to better understand the optimal management of patients on DOAC therapy undergoing dental procedure (19).

1.5. Direct oral anticoagulants vs Vitamin K-antagonist vs Low molecular weight heparin

Direct oral anticoagulants, vitamin K-antagonists, and low molecular weight heparin are used for prevention and treatment of thromboembolism. However,

there are several differences between these three classes of anticoagulants in terms of their pharmacology, mechanism of actions, monitoring and reversal agents (2,17).

1.5.1. Pharmacology:

DOACs, as previously mentioned, include dabigatran, rivaroxaban, apixaban, and edoxaban. These agents have a direct inhibitory effect on either thrombin (dabigatran) or factor Xa (rivaroxaban, apixaban, edoxaban) (12), and their anticoagulant effects are rapid, predictable, and dose dependent. DOACs are orally administered and have a shorter half-life than VKAs, with a half-life ranging from 5-17 hours (8).

VKA anticoagulants, such as warfarin, act by inhibiting vitamin K-dependent clotting factors II, VII, IX, and X (12). These agents are orally administered and have a delayed onset of action requiring several days to reach therapeutic levels. VKAs have a longer half-life than DOACs, ranging from 20-60 hours (10).

LMWH is an effective drug for both treating and preventing thromboembolic diseases. Enoxaparin and dalteparin are two examples of LMWHs. These are usually administered through a subcutaneous injection, normally in the abdomen or thigh (18). They work by enhancing the activity of antithrombin III, a naturally occurring protein that prevents many blood clotting factors, most prominently factor Xa. The half-life of LMWH is dose dependent, and it usually varies from 4-10 hours (17).

1.5.2. Mechanism of action:

DOACs, VKAs and LMWHs have a different mechanism of action, with DOACs and LMWH having a more targeted approach. DOACs and LMWHs directly inhibit specific clotting factors, while VKAs indirectly inhibit multiple clotting factors by blocking vitamin K-dependent clotting factors synthesis. This can

result in a delay in the anticoagulant effect, as the body gradually depletes its reserves of vitamin K-dependent clotting factors (5,20,27).

1.5.3. Monitoring:

There are various monitoring requirements for various blood-thinning drugs (17). DOACs don't need their anticoagulant levels to be checked on a regular basis. The reason for this is that DOACs can be used safely and efficiently without routine laboratory testing due to their predictable pharmacokinetic profile and broad therapeutic window (6). Nonetheless, laboratory testing can be used to determine the patient's anticoagulation status in some circumstances, such as emergency surgery or when patients experience bleeding (29).

Nonetheless, VKAs call for routine anticoagulation level monitoring through a lab test known as the International Normalized Ratio (INR) (17). The INR calculates a normal number by measuring how long it takes for blood to clot (15). To maintain the desired anticoagulation level, the dose of warfarin, the most widely used VKA, is adjusted using the INR. Depending on the reason for anticoagulation, the goal INR may change, however for the majority of patients, it usually ranges between 2.0 and 3.0 (5).

Anticoagulation level monitoring is not necessary for LMWHs on a regular basis. However, in some instances, such as in patients with renal impairment, obese people, or women who are pregnant, laboratory tests can be carried out to determine the patient's anticoagulation status (17).

1.5.4. Antidotes:

Patients on anticoagulant therapy who have bleeding issues or need immediate surgery must carefully evaluate whether to reverse their anticoagulation. There are reversal medications for DOACs, VKAs, and LMWH, however they each have a different mechanism of action (30).

Idarucizumab is a monoclonal antibody that binds to the DOAC dabigatran, which is used to prevent and cure blood clots, and counteracts its anticoagulant properties. Apixaban, rivaroxaban, and edoxaban, three other DOACs used to prevent blood clots, can all be reversed by the recombinant protein andexanet alfa (31).

Vitamin K is a nutrient that the body naturally produces and is necessary for the liver to produce clotting factors (30). VKAs like warfarin can have their effects reversed by administering vitamin K. The blood product known as prothrombin complex concentrate (PCC) contains the clotting factors II, VII, IX, and X. Patients who are bleeding as a result of taking VKAs can utilize PCC to replace these clotting factors (31).

Protamine sulphate is a drug that can counteract the anticoagulant effects of LMWH. This drug has the ability to counteract the anticoagulant effects of LMWH and heparin. By attaching to the heparin molecules, it inhibits the anticoagulant effects of those molecules. Protamine sulphate can bind to and neutralise numerous LMWH molecules, making it extremely powerful at undoing the effects of LMWH (31).

It is important to keep in mind that DOACs and VKAs have distinct action mechanisms when comparing these reversal agents, necessitating the use of various kinds of reversal agents (30,31). Whereas VKAs prevent the formation of numerous coagulation factors in the liver by preventing the activity of vitamin

K, DOACs directly inhibit one or more clotting factors (17). In contrast to DOACs and VKAs, LMWHs function through a distinct mechanism since they predominantly decrease the activity of Factor Xa, a specific clotting factor (12).

1.6. Justification

The use of anticoagulants is a critical component in managing a wide range of medical conditions, including cardiovascular diseases, deep vein thrombosis, and pulmonary embolism. Dental procedures, on the other hand, often involve minor to moderate invasions of the oral cavity, which can lead to bleeding. Therefore, dentists must carefully evaluate their patients' medical history and medication use to avoid excessive bleeding during and after dental procedures.

Despite the well-established importance of anticoagulant management in dental treatment, little is known about the prevalence and types of anticoagulants used before dental procedures. Understanding the current landscape of anticoagulant use in dental patients is essential to improving dental care quality and avoiding potential complications that may arise from uncontrolled bleeding. Current study will provide an insight into the current clinical practices and inform future guidelines for the management of patients on anticoagulant therapy undergoing dental procedures.

1.7. Hypothesis

H0: Patients under anticoagulant treatments have a higher risk of bleeding comparing to patients under no anticoagulant treatment.

H1: There is a high prevalence of anticoagulation therapy among elderly subjects.

H2: The prevalence of patients on anticoagulation therapy receiving dental treatment without interruption varies by the type of dental procedure, with more invasive procedures (e.g. implant placement) being associated with higher rates of anticoagulant interruption.

2. OBJECTIVES

Main objectives

I. Describe the prevalence of patients that dentists may expect that could be receiving anticoagulation treatment.

Secondary objectives

II. Review the recommended interventions over anticoagulant therapy in patients that need dental treatment

III. Analyze the risk of bleeding on patients under different type of anticoagulation treatments.

3. MATERIALS AND METHODS

Science-related publications and previously completed studies were used to perform this review. The following online resources were examined up:

- PubMed, accessed on February 15, 2023
- Medline, accessed on February 15, 2023 (https://www.nlm.nih.gov/medline/medline_overview.html)
- Google Scholar, accessed on November 20, 2022
- Library CRAI Dulce Chacon, accessed on January 29, 2023

Specific search terms were used to find papers about the use of anticoagulation in dental therapy. Searches were made using the following words: “anticoagulation therapy”, “implant”, “oral surgery”, “warfarin”, “DOAC”, “odontology”, “rivaroxaban”, “tooth extraction”, “management”, “prevalence anticoagulation”, “postoperative bleeding”, “ LMWH”,

“warfarin”, “coagulation cascade”, “antidote of anticoagulants”, “anticoagulation emergency”. The words "AND" and "OR" were utilized as boolean operators to identify articles that applied to this review. To ensure that just relevant information was used, articles were screened using exclusion and inclusion criteria.

The final search formula was as follows: (“anticoagulant” OR “antithrombotic” OR “DOAC” OR “vitamin K antagonist” OR “warfarin”) AND (“dentistry” OR “dental procedures” OR “oral surgery”)

Inclusion Criteria:

- Academic journals
- Articles published from 2012 to the present time
- Articles available in complete text
- Literature review articles
- Retrospective cohort studies
- Prospective studies
- Studies that were done in human subjects

Exclusion Criteria:

- Articles that were published before 2012
- Studies that were not done in human subjects
- Irrelevant to the subject of anticoagulation

Ethics:

- This study did not require ethical approval as it was a review of previously published studies.

4. RESULTS

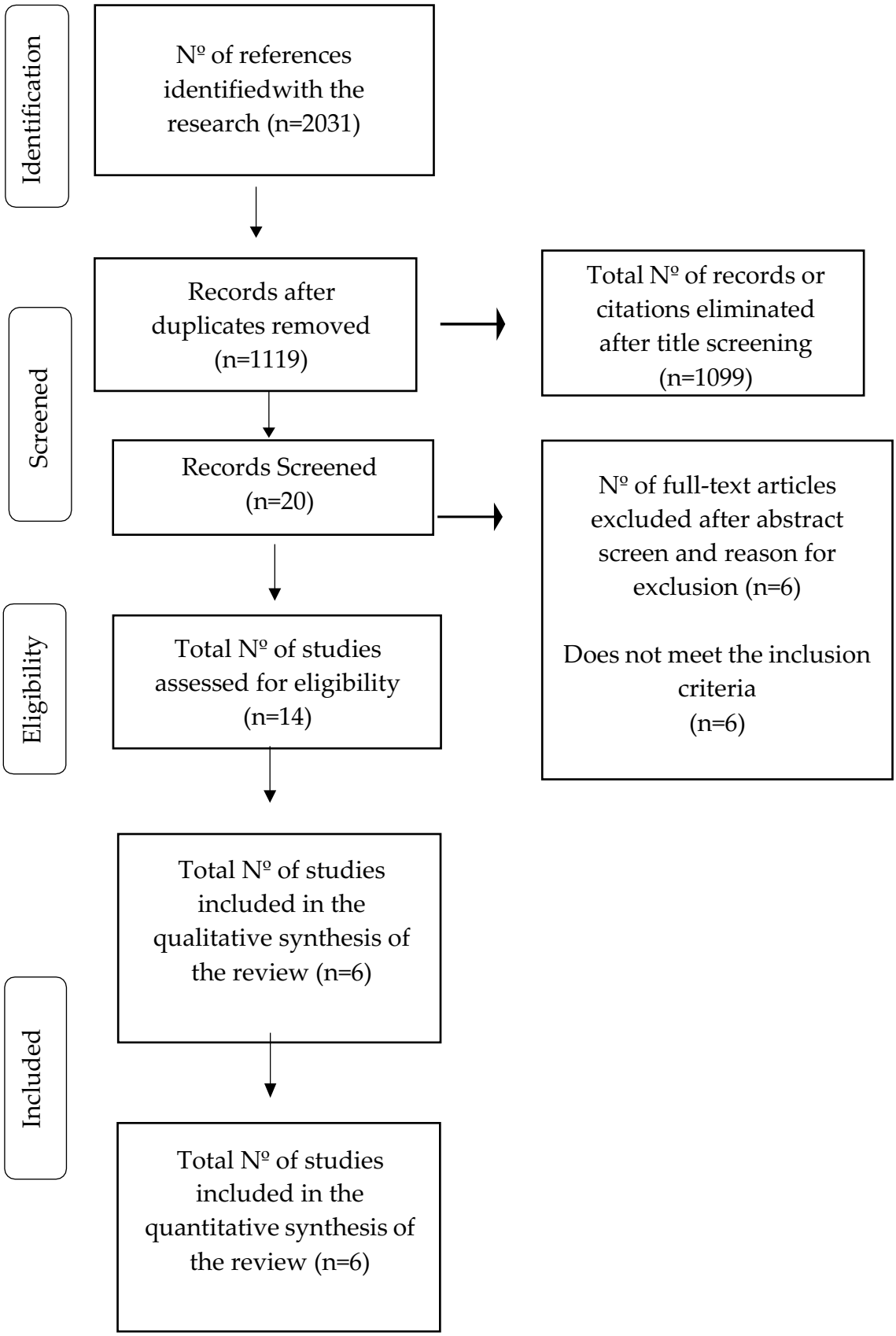
Identification
Nº of references identifiedwith the research (n=2031)
Screened
Records after duplicates removed (n=1119)
Total Nº of records or citations eliminated after title screening (n=1099)
Records Screened (n=20)
Nº of full-text articles excluded after abstract screen and reason for exclusion (n=6)
Does not meet the inclusion criteria (n=6)
Eligibility
Total Nº of studies assessed for eligibility (n=14)
Total Nº of studies included in the qualitative synthesis of the review (n=6)
Included
Total Nº of studies included in the quantitative synthesis of the review (n=6)

Table 2. Data collection table. Analyzing different studies regarding their prevalence on the use of anticoagulation

Reference	Sample size	Indication for anticoagulant treatment	Type of anticoagulation	Prevalence of anticoagulation	Dental treatment	Bridging used	Interruption of anticoagulant	Intra-operative management	Bleeding/ adverse effect	Conclusion
Clemm et al. 2015	Total n = 564 (anticoagulated patients, test group n = 117) (non-anticoagulated patients, control group n = 447)	Atrial fibrillation, artificial heart valves, myocardial infarction , venous thromboembolism, pulmonary embolism, cardiovascular prophylaxis	DOAC (dabigatran, rivaroxaban, apixaban), platelet aggregation inhibitor, vitamin K-antagonist (warfarin)	20,7%	Implant placement, bone grafting	Vitamin K - antagonist discontinued for 3 days with LMWH bridging	None	Non-absorbable sutures and sterile gauze soaked in tranexamic acid 5%	Increased risk of bleeding in patients using vitamin K– antagonist with LMWH bridging	If the least invasive technique is used, it is possible to continue taking VKAs and NOACs during implant procedures, although individuals who are on VKAs might experience an increase in moderate post-procedural bleeding. Despite implant surgery is an intrusive process, the risk of bleeding is low.
Gomez-Moreno et al. 2016	Total n = 57 (anticoagulated patients, test group n = 18) (non-anticoagulated patients control group n = 39)	Atrial fibrillation, deep vein thrombosis, pulmonary embolism	DOAC (rivaroxaban)	31,6%	Implant placement	None	None	Non-absorbable sutures and sterile gauze soaked in tranexamic acid 5%	Patients under anticoagulation treatment presented moderate amount of bleeding	The number of bleeding problems between rivaroxaban patients and a systemically healthy control group did not differ in the study in a statistically meaningful way.

Table 2. Data collection table. Analyzing different studies regarding their prevalence and the use of anticoagulation.

Reference	Sample size	Indication for anticoagulant treatment	Type of anticoagula-tion	Prevalence of anticoagula-tion	Dental treatment	Bridging used	Interruption of anticoagulant	Intra-operative management	Bleeding/ adverse effect	Conclusion
Manor et al. 2020	Total n = 193 (anticoagulated patients, test group n = 72) (non-anticoagula-ted patients, control group n = 121)	Not mentioned in the study	Vitamin K – antagonist (warfarin) DOAC (rivaroxaban, dabigratan, apixaban) platelet aggregation inhibitor	38%	Implant insertion, bone grafting, dental extraction	None	None	Non-absorbable sutures and sterile gauze soaked in tranexamic acid 5%	In the test group a total of 4 patient had postoperative bleeding, which were under double anticoagulant medication,and 7 of the control group, bleeding was solved with local hemostasis.	Patients on anticoagulant therapy had a minimal risk of bleeding after receiving dental implants when local hemostasis was in established. However when bleeding incidents do happen, they can be locally controlled. Prior to oral surgery, anticoagulant therapy does not need to be modified.
Schmitt et al. 2019	Total n = 838 (anticoagulated patients, test group n = 235) (non-anticoagula-ted patients, control group n = 603)	Cardiovascular prophylaxis, thromboembo-lism, stent implantation, atrial fibrillation, cardiac arrhythmia	Platelet aggregation inhibitors, vitamin K – inhibitors, low molecular weight heparin, DOAC	28%	Tooth extraction, osteotomy	In 12 patients vitamin K – inhibitors were bridged with LMWH	Not mentioned in the study	Non-absorbable sutures and sterile gauze soaked in tranexamic acid 5%, hemostyptic filler, bipolar electrocoagula tion	There were 15 moderate postoperative bleeding events: 4 in the AT group and 11 in the non-AT group.	Patients who are still receiving anticoagulant therapy have a minimal risk of postoperative bleeding following tooth extractions and osteotomies, and local hemostatic treatments can be used to stop the bleeding.

Table 2. Data collection table. Analyzing different studies regarding their prevalence and the use of anticoagulation

Reference	Sample size	Indication for anticoagulant treatment	Type of anticoagula-tion	Prevalence of anticoagula-tion	Dental treatment	Bridging used	Interruption of anticoagulant	Intra-operative management	Bleeding/ adverse effect	Conclusion
Okamoto et al. 2018	Total n = 289 (anticoagula-ted patients, test group n = 19) (non-anticoagula-ted patients control group n = 270)	Cardiovascular disease (not specified)	Vitamin K-antagonist (warfarin) Platelet aggregation inhibitor	6,57%	Implant placement	None	None	Not mentioned in the study	There was 5 moderate postopetarive bleeding event among anticoagulated patients and 20 among non-anticoagulated patients	Implant placement for patients on anticoagulation therapy can be safely managed if their INR is effectively controlled, and the use of local hemostatic agents is sufficient in managing post-operative bleeding
Buchben-der et al. 2021	Total n = 195 (anticoagula-ted patients test group n = 95) (non-anticoagula-ted patients control group n = 100)	Hypertension, coronary heart disease, stent implant, artificial heart valve, bypass, myocardial infarction, cerebral microangiopath y, cardiac pacemaker	DOAC (apixaban, rivaroxaban, dabigatran, edoxaban) Platelet aggregation inhibitor (clopidogrel, ticagrelor) Vitamin K-antagonist	48,7%	Dental extractions	None	None	Non-absorbable sutures and sterile gauze soaked in tranexamic acid 5%	Mild post-opetarive bleeding occurred in 25 anticoagulated patients. Moderate post-operative bleeding occurred in 1 patient who was under anticoagulation treatment and ten different co-medications. 4 teeth were extracted.	Continuing anticoagulation for high-risk surgeries is reasonable, despite increased postoperative bleeding that is typically mils. Effective perioperative management of anticoagulated patient necessitates interdisciplinary teamwork

5. DISCUSSION

Patients with a range of medical disorders frequently receive anticoagulant therapy to prevent thrombotic and embolic events (10). Nonetheless, anticoagulant therapy can raise the risk of bleeding, particularly during invasive dental treatments. As a result, the management of anticoagulated patients undergoing dental procedures needs comprehensive examination of the patient's underlying medical condition, the kind of anticoagulant therapy, and the potential risks and advantages of discontinuing anticoagulant therapy (8).

According to Costa-Tort et al. every year, the percentage of people needing anticoagulant medication increases globally, in Spain this affects 1.9% of the population. According to current estimates, between 800,000 and 1,000,000 people in Spain are presently receiving long-term treatment with anticoagulant medicine of some kind (32). Corresponding to this, there has been a rise in the use of antiplatelet medications, notably as a secondary preventative therapy for atherosclerotic disease and since percutaneous coronary procedures and stent implantations are performed so frequently (26). This expansion has led to an increase in the number of dental patients receiving antithrombotic therapy, with older patients, who frequently have underlying systemic pathologies, being the most frequently impacted group (8).

A recent study done in the general population has shown that the prevalence of anticoagulant therapy among adults has moved from 9.2% in 2011 to 11.5% in 2019 (33). It is important to note that estimating the exact prevalence of anticoagulant use in the general population can be challenging due to a lack of available data on this subject. Furthermore, while some studies have investigated the prevalence of certain populations under anticoagulant treatment, it can still be difficult to estimate how many of these individuals will present to a dental office (1). This is because factors such as access to dental care, personal

preferences, and oral health status can all influence an individual's decision to seek dental treatment (10).

The prevalence of anticoagulant therapy in patients undergoing dental procedures can vary depending on the population studied and the type of dental procedure. Based on the information provided by the studies reviewed in table 2, the overall prevalence of anticoagulation among patients undergoing dental procedures ranged from 6.57% to 48.6% (34,35).

The lowest prevalence was reported in the study by Okamoto et al., which included 289 patients and reported a prevalence of anticoagulant treatment of 6.57% among patients undergoing implant placement, with the anticoagulation being used vitamin K-antagonist being warfarin and platelet aggregation inhibitor (35). The highest prevalence was reported in the study by Buchbender et al., which included 195 patients and reported a prevalence of anticoagulant treatment of 48.7% among patients undergoing dental extractions, with the anticoagulation treatment being used DOAC (rivaroxaban, dabigatran, edoxaban), platelet aggregation inhibitors such as clopidogrel and ticagrelor and Vitamin K-antagonist (34).

Clemm et al. (2015) reported a prevalence of 20.7% among 564 patients undergoing implant placement, with the anticoagulant treatment used being DOAC, vitamin K-antagonist, and platelet aggregation inhibitors (36). The prevalence of anticoagulation of Gómez-Moreno et al. being 31,6% among 57 patients who underwent implant placement, under anticoagulant treatment of direct oral anticoagulant (rivaroxaban) (37).

In the study of Manor et al., which included 193 patients, 38% were under anticoagulation treatment with vitamin K-antagonist (warfarin), DOAC (rivaroxaban, dabigatran, apixaban) and platelet aggregation inhibitor (38). On the other hand, in the study of Schmitt et al.2019 in which 838 patients were

included, the prevalence of anticoagulation was 28%, being the type of anticoagulants, platelet aggregation inhibitors, vitamin k-antagonist, LMWH and DOAC (23).

Due to the uncertainty surrounding the number of patients receiving anticoagulation therapy, it is imperative for dentists to take a comprehensive medical history. Given these limitations, it is important for dental professionals to be aware of the potential for increased bleeding risk in patients taking anticoagulants and to take appropriate precautions when performing dental procedures (19). This may include measures such as minimizing trauma to oral tissues, using local hemostatic agents, and coordinating with the patient's healthcare provider to adjust anticoagulant therapy as needed. In order to safely and successfully manage patients who are taking these medications, it is crucial for dentists and other healthcare professionals to be knowledgeable about the many types of anticoagulants and their indications (9).

Anticoagulants are drugs that stop blood clots from forming or becoming larger. Patients with particular medical disorders, such as deep vein thrombosis, pulmonary embolism, stroke, or heart attack, which enhance their risk of blood clot development, have prescribed them (17). These drugs are crucial in keeping these patients from developing life-threatening problems, but they can also make bleeding more likely, especially during invasive medical procedures (6).

Chahine et al. (2019) conducted a study to investigate the use of anticoagulant treatment before frequent dental procedures. The study included 6,062 patients who underwent dental operations and consisted of 20 studies written between 1985 and 2018. The results of the study showed that warfarin and direct oral anticoagulants (DOACs), such as dabigatran, rivaroxaban, and apixaban, were the most commonly prescribed anticoagulation treatments for the patients included in the research (10).

The studies mentioned in table 2 have evaluated a range of anticoagulant agents, including traditional vitamin K-antagonists, DOACs and platelet aggregation inhibitors and their bleeding outcomes.

Traditional vitamin K antagonists, such as warfarin, have been widely used for stroke prevention in patients with cardiovascular diseases, such as atrial fibrillation (32). As we can observe in table 2, vitamin K-antagonist was prescribed for patients in all the studies (23,34–36,38), except in the study of Gomez-Moreno et al., in which only DOAC (rivaroxaban) was used (37).

Vitamin K-antagonists work by inhibiting the production of vitamin K-dependent clotting factors, which are necessary for blood clotting (10). While warfarin has been effective in reducing the risk of stroke in these patients, it requires examining the patient's international normalized ratio (INR) frequently to make sure the dosage is adequate (15), to avoid extreme bleeding complications the INR must be lower than 4 according to studies (10,39). There are a number of extensively discussed methods for managing vitamin K antagonists before oral surgery, suspension for a number of days, temporary bridging with heparin, dosage reduction without bridging or unchanged dosages, and local hemostatic interventions all contribute to hemostasis. Due to its short half-life, heparin has the advantage of having strong controllability (19).

Those who are highly anticoagulated are more likely to bleed during dental operations (10). As seen in the study of Manor et al. where the four patients in the test group experienced postoperative bleeding after implant placement were taking two types of anticoagulant medications, the bleeding was solved by applying local hemostasis measurements (38).

According to the study of Clemm et al. traditional vitamin K antagonists such as warfarin have been associated with higher risk of bleeding compared to newer oral anticoagulants (36). This is likely due to the fact that warfarin requires

frequent monitoring of the patient's INR levels and dosing adjustments, which can be challenging to manage and can increase the risk of bleeding complications (15). Also, in the study Clemm at al. it was noted that patients who are on continuous warfarin therapy and undergo dental surgery have a six percent higher risk of minor postoperative bleeding (36).

The higher bleeding outcome of patients under warfarin was also seen in the study done by Schmitt et al. 2019 out of the 80 patients who were under continuous vitamin K-antagonist therapy 9 (11.3%) of them presented post-operative bleeding events (23). Whereas from the control group which consisted of 603 individuals under no anticoagulation treatment only 4 (0.7%) presented post-operative bleeding. In both of the groups postoperative bleeding was controlled under local hemostatic measures (23).

Anticoagulated patients can be challenging to manage during surgical procedures, such as oral surgery. There are risks associated with both continuing anticoagulation medication and stopping or temporarily pausing it. If medication is stopped, there is a risk of developing blood clots which can be dangerous (19). However, if the medication is continued, there is a risk of bleeding during and after the surgery which can be uncomfortable and may delay healing (39). Most of the time, bleeding can be controlled using local measures. This means that deciding whether to stop or continue anticoagulation medication during oral surgery is a controversial issue (40).

In the study of Clemm et al. (table 2) on anticoagulated patients undergoing dental implant surgery, including implant placement and bone grafting procedures. They compared the bleeding complications among patients who were using different types of anticoagulants. The study showed that there was a higher risk of bleeding in patients who underwent bridging therapy before the surgery (12.5%) compared to the previously mentioned patients who continued

to take vitamin K antagonists (6.7%), those taking platelet aggregation inhibitors had an even lower risk (1.4%). The control group had the lowest risk of bleeding (0.6%) (36).

The researchers of Schmitt et al. compared two subgroups of patients who were taking vitamin K inhibitors during dental implant surgery: those who continued their medication and those who temporarily switched to low-molecular-weight heparin. There were no statistically significant differences in bleeding frequency between any of the pairwise comparisons of these subgroups. The study also showed that the Bridging group had a higher risk of postoperative bleeding (25%) compared to the group who continued vitamin K inhibitors (9.4%) (23).

On the other hand, in the study of Buchbender et al. (table 2) where dental extractions were performed, results showed that postoperative bleeding happened in 12.9% of patients (22 out of 170) in the control group, 25.9% of patients (44 out of 170) in the vitamin K antagonist group, and 48.1% of patients (65 out of 135) in the Bridging group. When the groups were compared using statistical analysis, there were significant differences found between the control group and the Bridging group. The probability of postoperative bleeding occurring, and the number of bleeding events were also much higher in the Bridging group compared to the vitamin K antagonist group (34).

The discontinuation of anticoagulants may result in serious thromboembolic problems, thus if possible, these medications shouldn't be stopped in the case of minor surgery. The use of VKAs in surgical procedures like tooth extraction or implant placement is still supported by a considerable literature review (19).

While vitamin K antagonists have been a popular choice as an anticoagulant, direct oral anticoagulants (DOACs) have emerged as a newer option with their own set of benefits and drawbacks (25). Direct oral anticoagulants, such as dabigatran and rivaroxaban, are becoming more commonly used in the United

States and European Union (16). Studies have demonstrated that these targeted direct oral anticoagulants offer clear advantages over the older, cheaper anticoagulant warfarin (6).

The authors of a study conducted in 2012 (Firriolo and Hupp et al.), suggested that if an oral surgical procedure, such as implant placement, direct oral anticoagulant should be temporarily discontinued. They recommended that dabigatran should be stopped at least 24 hours before elective surgery, or even longer in certain cases (16). On the contrary in the study of Gomez-Moreno et al. (table 2), which was conducted in 2016, during the period of follow-up after surgery, only 1 patient out of 18 who were being treated with uninterrupted rivaroxaban, experienced minor bleeding on the day after implant placement. The bleeding was managed by having the patient bite down on gauze soaked in tranexamic acid for an hour in the surgical area (37).

As well as in a study conducted by the same authors (Gomez-Moreno et al. 2018), it was found that patients receiving dental implants and being treated with the oral anticoagulant dabigatran did not experience a higher occurrence of bleeding compared to control patients, despite the continued use of the medication without interruption (28).

In a study Curto et al. classified dental treatments into two categories based on the likelihood of bleeding (42). The first category comprises procedures that pose a low risk of bleeding, such as oral surgeries that last for less than 45 minutes. The second category includes procedures that pose a medium to high risk of bleeding, such as oral surgeries that last for more than 45 minutes. The authors (Curto and Albaladejo et al.) suggested that, for procedures that fall into the second category, patients being treated with apixaban and dabigatran should discontinue the medication for a minimum of 24 hours and 48 hours respectively.

In case the period of drug suspension is prolonged, it may be necessary to consider bridging therapy with low molecular weight heparin (29).

One can say that it is unlikely for patients to experience thromboembolic complications while continuing their anticoagulation treatment during tooth extractions or oral surgeries such as implant placements, as long as local measures are taken to prevent bleeding (23,34–38). The frequency of bleeding is low in patients with controlled anticoagulation treatment, and any bleeding that occurs after the procedure can be adequately controlled using local measures. It is recommended that anticoagulation treatment should be continued during tooth extractions and osteotomies, as long as the most minimally invasive surgical approach is considered, and practitioners are capable of managing any bleeding complications that may arise (10,34–37). To prevent treatment errors and fatal complications, effective communication among the dentists, patients, general physicians, and the cardiologist is essential (10).

6. CONCLUSION

The following conclusions can be drawn from the findings:

I. The number of patients taking anticoagulation treatment who visit dentists can vary depending on the area, and it is not easy to predict. Despite some research examining the occurrence of anticoagulant treatment in certain groups, it remains challenging to estimate how many of these patients will come to the dentist. This is due to different factors such as oral health, preferences, and access to dental care affecting people's decision to seek dental care. Further research is needed to explore this issue more thoroughly.

II. For most dental procedures, patients taking VKAs and NOACs should continue their medication. Stopping and restarting oral anticoagulants can be challenging for both the doctor and the patient and increases the risk of blood clots. Therefore, it is recommended to use a multidisciplinary approach when managing patients receiving anticoagulant therapy during dental procedures.

III. Based on the findings of this review, it can be concluded that the use of bridging with LMWH in anticoagulated patients may increase the risk of bleeding. Conversely, in patients with well-regulated anticoagulation therapy, the risk of bleeding is minimal. Further research may be necessary to fully understand the risks and benefits of bridging therapy in different patient populations.

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