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# A Systematic Review of the Hemorrhage Risk for Patients on Antithrombotic Medication after Dental Procedures

<sup>1</sup>Cristian D Pirlog, <sup>2</sup>Alina M Pirlog, <sup>3</sup>Teodor Maghiar

## ABSTRACT

**Aim:** Antithrombotic medication represents a challenge for any dental practitioner due to the possible hemorrhage complications that can be associated with an important morbidity/ mortality risk. The objective of the present literature review is to establish which dental procedures have a risk to increase the incidence of hemorrhage in patients on antithrombotic therapy.

**Materials and methods:** A systematic review of the literature was conducted using MEDLINE, PubMed, and DiscoverEd databases. The inclusion criteria used were as follows: Current antithrombotic therapy, invasive dental procedures, and post-operative incidence of bleeding follow-up.

**Results:** A total of 14 clinical studies and 5 literature reviews were selected after the initial screening. The incidence of hemorrhage was assessed for dental implant placements, dental extractions, simple dental procedures, and periodontal treatment.

**Conclusion:** A well-coagulated patient can safely have invasive dental procedures in a hospital environment or nonhospital setting without having their antithrombotic therapy altered. Local hemostatic measures can offer a proper hemorrhage control.

**Keywords:** Antithrombotic medication, Dental extraction, Dental implants, Dental procedures, Incidence of hemorrhage.

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## INTRODUCTION

Anticoagulant and antiplatelet medications are treatments that are increasingly more used worldwide. Consequently, they are more common in patients presenting to the dental practitioner.<sup>1</sup> In recent years, in the United

<sup>1</sup>Department of Dentistry, Faculty of Medicine and Pharmacy University of Oradea, Oradea, Romania

<sup>2</sup>Department of General Medicine, Faculty of Medicine and Pharmacy, University of Oradea, Oradea, Romania

<sup>3</sup>Department of Urology, Faculty of Medicine and Pharmacy University of Oradea, Oradea, Romania

**Corresponding Author:** Cristian D Pirlog, Department of Dentistry, Faculty of Medicine and Pharmacy, University of Oradea, Oradea, Romania, Phone: +447951586870, e-mail: cristian\_daniel1986@yahoo.com

Kingdom, besides the popular anticoagulant warfarin and antiplatelet agents, such as aspirin and clopidogrel, new oral anticoagulants and antiplatelet therapies have been made available, such as apixaban, dabigatran, and rivaroxaban.

Antithrombotic medication has been prescribed for patients who present a high risk or have had a thrombotic event. The high-risk group of patients includes those who have had experienced deep vein thrombosis, pulmonary embolism, stroke, or have a cardiac arrhythmia that predisposes patients to clot formation.<sup>1</sup> As the number of antithrombotic medication prescriptions has increased in the last few years, the chances of having a patient in the dental surgery and taking them have increased considerably.<sup>1</sup> Combined therapy using both antiplatelet and anticoagulant medications increases the risk of spontaneous as well as postsurgical hemorrhage.<sup>1</sup>

Warfarin, a synthetic derivative of coumarin, is a vitamin K antagonist. It has been used as oral anticoagulants for more than 60 years.<sup>2</sup> Warfarin inhibits vitamin K reductase, resulting in an accumulation of inactive clotting factors, which will be reduced in line with the time of each disposal.<sup>2,3</sup> Warfarin is active *in vivo* and needs only 4 to 5 days for its anticoagulant effect to be developed.<sup>2,3</sup> It presents a long half-life of 40 hours, requiring in most cases 5 days for prothrombin time to normalize after stopping.<sup>2,3</sup> The international normalized ratio (INR) is used to monitor the effects of warfarin on coagulation.<sup>2,3</sup> The high end of the therapeutic range of INR is considered to be between 3.5 and 4.4 Patients with the INR above the therapeutic range have an increased risk of oral hemorrhage.<sup>4</sup> Therefore, warfarin therapy should be adjusted by the general medical practitioner or anticoagulation service to achieve the therapeutic range.<sup>5</sup> It was recommended to check the INR of a patient under warfarin therapy 24 hours before the dental invasive procedure.<sup>5</sup>

Aspirin is an antiplatelet that inhibits the cyclooxygenase-1 enzyme, which converts arachidonic acid to thromboxane A2, the ligand for the homonymous platelet receptor.<sup>6</sup> Used in the long term, it helps to prevent heart attacks, strokes, and blood clot formation.<sup>6</sup> The drug has analgesic, antiinflammatory, and antipyretic effects. It inhibits the formation of a highly effective platelet aggregator and a vasoconstrictor. Since the platelets do not synthesize proteins, the effect remains demonstrable as long as the affected thrombocytes live (7–10 days).<sup>6</sup> Clopidogrel is a prodrug that is oxidized into an active metabolite in a two-step process by hepatic cytochromes.<sup>7</sup> This metabolite irreversibly blocks the adenosine diphosphate receptor and reduces platelet activity by 50 to 60%.<sup>7</sup> There are no major differences in terms of bleeding between aspirin and clopidogrel monotherapy.<sup>8</sup> After cessation of aspirin or clopidogrel, bleeding time and global platelet activity return to baseline levels in 5 days.<sup>8</sup>

Dabigatran is a selective, reversible, direct oral inhibitor of thrombin. It is converted into the active compound by plasma esterases.<sup>9</sup> Peak plasma concentration is reached between 1 and 2 hours after intake.<sup>9</sup> In healthy volunteers, the terminal half-life is approximately 9 hours following a single dose and 12 to 17 hours after repeated dosing.<sup>9</sup>

A steady-state level is reached after 2 or 3 days of administration.<sup>10</sup> One-third of the circulating drug is bound to plasma proteins. The drug is mainly cleared by the kidneys. The interruption protocol for dabigatran should take into account the incidence of hemorrhage and type of surgery.<sup>11</sup> Thrombin time should be measured 6 to 12 hours before surgery in patients at high risk of bleeding or if major surgery is planned.<sup>11</sup> Rivaroxaban is a direct oral inhibitor of factor Xa. Peak plasma concentrations are reached 2 to 4 hours after intake.<sup>12</sup> Rivaroxaban has no direct effect on platelet aggregation, but indirectly inhibits platelet aggregation induced by thrombin.<sup>12</sup> The terminal elimination half-life is between 5 and 13 hours.<sup>12</sup>

Various observational studies and meta-analyses have attempted to provide evidence on the risk of prolonged oral hemorrhage and thromboembolic events following dental procedures.<sup>13,14</sup>

Wahl<sup>15</sup> suggested that if anticoagulation was withheld before dental treatment, there was an incidence of 1% of patients suffering a serious thromboembolic complication. However, there has been a criticism of this finding as the length of time that the anticoagulant was stopped was either longer than normal practice or unknown.<sup>16</sup> Furthermore, no local hemostatic measures were detailed in the study.

Local hemostatic measures for dental procedures that are likely to cause bleeding include packing any open sockets with hemostatic material and placing sutures.<sup>17</sup> For all patients taking anticoagulant or antiplatelet medication, hemostasis should be achieved using local measures before the patient being discharged from care.

An additional local hemostatic measure is the 5% tranexamic acid mouthwash. It is commonly used in combination with an oral hemostatic measure to achieve hemostasis.<sup>18</sup> Tranexamic acid acts as an antifibrinolytic agent by blocking the binding of plasmin to fibrinogen. It is used for a short period of time before and after the surgery to prevent major blood loss.<sup>19</sup> Tranexamic acid is

used in dentistry in the form of a 5% mouth rinse after extractions or surgery in patients with prolonged bleeding time, from acquired or inherited disorders.<sup>19</sup>

By systematically reviewing the available literature, the direct relationship between antithrombotic medication and prolonged oral hemorrhage following dental procedures was analyzed. This can aid the dental practitioner to make the decision whether to continue or stop the antithrombotic medication. It can also suggest where future research on this topic should be focused. The review covered data in the available literature and analyzed cases with prolonged oral hemorrhage following dental procedures that were published from 1998 to 2016.

The aim of the study was to research which invasive dental procedures combined with antithrombotic medication were more prone to cause oral hemorrhages, and furthermore, whether antithrombotic medication should be stopped during invasive dental procedures.

## MATERIALS AND METHODS

The available literature data research published between 1998 and 2016 on the MEDLINE, PubMed, and DiscoverEd was analyzed. The search was not only limited to English studies but also Russian, French, German, Romanian, Ukrainian, Spanish, Italian, and Hungarian research.

Search terms included anticoagulants, antiplatelet, antithrombotic, dentistry, oral surgical procedures, hemostatic measures, invasive dental procedures, and oral. Searches were limited to articles involving human subjects.

The systematic reviews and meta-analyses were included if patients were under anticoagulant or antiplatelet medication, if patients had dental procedures performed while the practitioner was aware of the patients' current medication, and if patients were followed up for the incidence of oral hemorrhage.

Researchers were excluded if no dental procedure was carried out, if patients were not followed up after the procedure for a sufficient amount of time, if there were no control groups to compare the study group, and if papers were guidelines and any expert opinions.

# RESULTS

In the first search, a total of 217 studies were identified (Flow Chart 1). The inclusion and exclusion criteria were applied to obtain the relevant studies. Following the screening process, 14 clinical studies and 5 literature reviews were selected (Flow Chart 1). Due to the heterogeneity of the key parameters, aggregation of statistical data was not possible. Therefore, a descriptive analysis of selected studies was conducted.

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The majority of the papers referred to specific drugs, such as warfarin, rivaroxaban, and dabigatran (Table 1). There were 12 articles focusing on warfarin as the main antithrombotic medication administered (Table 1). Two studies assessed the incidence of hemorrhage for rivaroxaban and dabigatran (Table 1). Furthermore, mentioned in the papers were low-molecular-weight heparin, thrombocyte aggregation inhibitors, and platelet aggregation inhibitors (Table 1).

## Warfarin

Bacci et al<sup>20</sup> enrolled patients into two groups: One receiving warfarin, the other not under any antithrombotic medication. After implant surgery, sutures and compressive gauze soaked with tranexamic acid were placed. There was no major postoperative bleeding and no

Clinical studies	Number of patients	Antithrombotic medication	Dental procedure	Groups	Postoperative procedures
Bacci et al <sup>20</sup>	159	Warfarin	Dental implant surgery	Group I—50 patients receiving warfarin therapy Group II—109 nonmedicated patients	Local hemostatic measures were taken, such as sutures and compressive gauze soaked with tranexamic acid. There were no complications identified
Bajkin et al <sup>21</sup>	214	Oral anticoagulation therapy	Simple dental extractions	Group I—109 patients under oral anticoagulation therapy Group II—105 patients under low-molecular-weight heparin	Local hemostatic measures were taken, such as resorbable collagen sponges without suturing. There were no complications identified
Bajkin et al <sup>22</sup>	213	Aspirin, warfarin	Dental extractions	Group I—71 patients under anticoagulant therapy Group II—71 patients under warfarin therapy Group III—71 patients under aspirin therapy	Local hemostatic measures were taken. No complications identified
Bajkin et al <sup>23</sup>	210	Warfarin	Dental extractions	Group I—54 patients under warfarin therapy with INR > 3.5 Group II—60 patients under warfarin therapy with INR 2–3.4 Group –III—85 not medicated patients	Local hemostatic measures were taken. There were no complications identified
Broekema et al <sup>24</sup>	206	Vitamin K antagonists, thrombocyte aggregation inhibitors	Dentoalveolar surgery including dental extractions, apicectomy, and implant placement	Group I—103 patients taking vitamin K antagonists and thrombocyte aggregation inhibitors Group II—not medicated patients	Local hemostats measures were taken, such as sutures, compressive gauzes, and a tranexamic acid mouthwash. There were no complications reported
Clemm et al <sup>25</sup>	564	Platelet aggregation inhibitors, vitamin K inhibitors, new oral	Dental implant placement, sinus floor augmentation, bone grafting	Group I—patients under platelet aggregation inhibitors therapy, vitamin K inhibitors therapy, new oral anticoagulants therapy Group II—not medicated	Two patients were hospitalized, one from group II and one from group I Local hemostatic measures
Cannon and Dharmar <sup>26</sup>	70	Warfarin	Minor oral surgical procedure	Group I—patients had warfarin stopped before the procedure Group II—patients kept taking warfarin during the procedure	were taken Local hemostatic measures were taken. There were no complications reported

Table	1.	Clinical	studies	and	literature	reviews	identified	in	the	systematic	research
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(Cont'd...) Clinical Number of Antithrombotic studies patients medication Dental procedure Postoperative procedures Groups Devani Warfarin Group I-32 patients had Local hemostatic measures 65 Dental extractions et al<sup>27</sup> warfarin therapy stopped were taken, such as sutures Group II-33 patients kept and surgical pack. There were taking warfarin therapy no complications reported Gómez-57 Rivaroxaban Dental implant Group I-18 patients Local hemostatic measures Moreno placement were under treatment with were taken including et al<sup>28</sup> rivaroxaban nonabsorbable sutures and a Group II-39 not medicated gauze impregnated with 5% tranexamic acid. There were patients no complications identified Gómez-71 Surgery was conducted Dabigatran Dental implant Group I-29 patients under treatment with dabigatran Moreno placement 12 hours after the last dose of et al29 Group II-42 not medicated dabigatran. Medication was resumed 8 hours after the patients procedure. Local hemostats measures were taken: Nonabsorbable sutures, gauze impregnated with 5% tranexamic acid. There were no complications reported Local hemostatic agents Karsli 40 Warfarin, Dental extractions Group I-patients under warfarin therapy et al<sup>30</sup> warfarin were used. There were no Group II-patients under warfarin bridged with complications identified in any low-molecularbridged with low-molecularof the groups weight heparin, weight heparin therapy warfarin Group III-patients taking bridged with warfarin bridged with unfracunfractionated tionated heparin therapy Group IV-not medicated heparin patients Mauprivez 51 Direct oral Dental extractions Group I-31 patients under Local hemostatic measures et al<sup>31</sup> anticoagulants direct oral anticoagulant were taken. There were no Vitamin K complications identified therapy antagonists Group II-20 patients taking vitamin K antagonists Morimoto 139 Warfarin Periodontal Group I-patients taking Local hemostatic measures et al32 treatment warfarin therapy were taken, such as insertion of Group II-not medicated oxidized cellulose, compression, and suturing. There were no patients complications reported Zanon 500 Anticoagulant Dental extractions Group I-250 patients under Local hemostatic measures et al33 therapy anticoagulant therapy were taken that include: Group II-250 nonmedicated fibrin sponge, silk suture, patient and a gauze saturated with tranexamic acid. There were no complications noted Number of papers Literature included in Antithrombotic Postoperative procedures or the review medication reviews Dental procedure Groups or meta-analyses conclusion 13 papers No meta-analyses were Local hemostatic measures Muñoz-Dabigatran Any invasive Corcuera of which 1 dental treatment conducted were taken. The conclusion et al34 randomized was to assess and treat each clinical trial. case individually 9 narrative

literature reviews, 1 case series, 2 clinical cases

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Literature	Number of papers	Antithromhotic			Postoperative procedures or
reviews	the review	medication	Dental procedure	Groups or meta-analvses	conclusion
Nematullah et al <sup>35</sup>	5 trials with a total of 553 patients	Warfarin	Minor dental procedures	Interrupting warfarin therapy usual dose was not associated with an increased risk for clinically significant non-major bleeding (RR, 0.71; 95% Cl: 0.39–1.28; p = 0.65; l2 = 0%) or an increased risk for minor bleeding (RR, 1.19; 95% Cl: 0.90–1.58; p = 0.22; l2 = 0%)	Continuing warfarin therapy does not increase the incidence of hemorrhage
van Diermen et al <sup>36</sup>	Two systematic reviews	Antithrombotic medication	Simple dental procedures	No meta-analyses were conducted	Do not interrupt oral antithrombotic medication, not even dual antiplatelet therapy
Wahl et al <sup>37</sup>	8,104	Warfarin	Dental procedures	Group I—5,431 patients under anticoagulation therapy Group II—2,673 patients had warfarin dose reduced or withdrawn	Group I—31% of the patients required more than local home- ostasis to control hemorrhage Group II—22 patients had embolic complications and there were six fatal events recorded
Yang et al <sup>38</sup>	Six studies included in the literature review with a total of 591 patients	Oral anticoagulation therapy	Dental extractions	There was no significant difference in the bleeding risk between patients continuing or discontinuing oral anticoagulant therapy while undergoing dental extractions (risk ratio, 1.31; 95% CI, 0.79, 2.14; $p > 0.05$ ). There was also no significant difference in bleeding risk 1 day (risk ratio, 0.91; 95% CI, 0.35, 2.37; $p > 0.05$ ) and 7 days (risk ratio, 1.47; 95% CI, 0.83, 2.59; p > 0.05) after the dental extraction	Patients continuing oral anticoagulant therapy do not have an increased risk of bleeding after dental extractions compared with patients who discontinue oral anticoagulant therapy

(Cont'd...)

RR: Relative risk; CI: Confidence interval

significant difference between the groups bleeding risk. The authors concluded that patients under warfarin therapy can safely undergo dental implant placement without any change of regimen if an effective local hemostatic procedure was in place.

Bajkin et al<sup>21-23</sup> compared the postoperative hemorrhage for groups who were taking warfarin and aspirin with patients not medicated after dental extractions. The same local hemostatic measures were taken for both groups. The authors concluded that the patients can undergo dental extraction procedures without any change of their treatment and, if reasonable, local hemostatic procedures were taken, such as resorbable collagen sponges.

Cannon and Dharmar<sup>26</sup> and Devani et al<sup>27</sup> looked into the differences between one group of patients who had their anticoagulant regimen stopped before the minor surgical procedure and another group who continued with their anticoagulant therapy. None of the patients including both groups had any serious bleeding complications. The studies suggested that patients can safely undergo routine minor oral surgical procedures without alteration to their therapeutic anticoagulation regimen if local hemostatic procedures were used, such as sutures and surgical packing.

Morimoto et al<sup>32</sup> assessed the bleeding risk after periodontal surgical treatment. The authors had two groups: One under warfarin therapy and one control group without medication. Same aftercare protocol was followed, consisting of insertion of oxidized cellulose, compression, and sutures. The conclusion of the study was that subgingival and supragingival scaling can be safely performed in patients on warfarin and antiplatelet therapy. Periodontal surgery can be performed in patients with INR <3.0 with proper local hemostatic procedures.

Two meta-analyses, Nematullah et al<sup>35</sup> and Yang et al,<sup>38</sup> concluded that there was no significant difference in the bleeding risk between patients continuing or discontinuing oral anticoagulant therapy while undergoing dental extractions. Furthermore, Yang et al<sup>38</sup> suggested that there was no difference in the bleeding risk 1 and 7 days after dental extractions.

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Wahl et al<sup>37</sup> separated patients receiving warfarin therapy into two groups: One kept their warfarin dose as per therapeutic INR respectively; the other group had their warfarin dose reduced or withheld. The authors concluded that from the first group 31% required more than local hemostasis to control the hemorrhage. In the second group, there were 22 embolic complications and 6 fatal events.

Broekema et al<sup>24</sup> studied the bleeding risk in patients under vitamin K antagonists' therapy *vs* nonmedicated patients following dental extractions, apicectomy, and implant placement. Patients were given standard postoperative care and those taking vitamin K antagonists used tranexamic acid mouthwash postoperatively. None of the patients has developed a severe complication that required intervention.

Clemm et al<sup>25</sup> enrolled patients into two groups. In group I, the patients were taking platelet aggregation inhibitors, vitamin K inhibitors, or new oral anticoagulants, and in group II, there were not medicated patients. Both groups had dental procedures, such as dental implant placement, sinus floor augmentation, and bone grafting. After the dental procedures, two patients were hospitalized, one from group II and one from group I. The authors concluded that anticoagulation therapy should be continued in patients undergoing implant surgery and bone grafting procedures if local hemostatic measures were taken.

## Rivaroxaban

Gómez-Moreno et al<sup>28</sup> evaluated the incidence of bleeding complications after dental implant placement in patients under rivaroxaban therapy. The first group of patients was on treatment with rivaroxaban for more than 6 months, whereas the second group consisted of healthy subjects. Postoperative, nonabsorbable sutures were used, and all patients were given gauze impregnated with 5% tranexamic acid to bite on for 30 to 60 minutes. There was no statistically significant difference between the groups, and the relative risk was 0.919 based on the pooled groups. The research conclusion was that dental implant surgery in patients taking rivaroxaban can be performed safely if local hemostatic measures are taken without the need to modify or interrupt anticoagulant medication.

## Dabigatran

Gómez-Moreno et al<sup>29</sup> evaluated the incidence of hemorrhage complications after dental implant placement in patients under dabigatran therapy. Seventy-one patients were divided into two groups: 29 taking dabigatran for more than 6 months before the implant surgery and a control group of 42 healthy subjects. There was no statistically significant difference found between the groups, with a relative bleeding risk of 0.675 based on the pooled groups. The authors concluded that dental implant surgery in patients taking dabigatran can be performed safely provided that 12 hours have passed since the last dose of dabigatran and local hemostatic measures are applied. Normal dosage can be resumed 8 hours after implant surgery.

A literature review conducted by Muñoz-Corcuera et al<sup>34</sup> selected 13 papers all assessing the incidence of hemorrhage after dental invasive procedures. The author concluded that patients under dabigatran therapy should be assessed and treated as individual cases and local hemostatic measures should be delivered following dental procedures.

## **Platelet Aggregation Inhibitors**

Bajkin et al,<sup>22</sup> Broekema et al,<sup>24</sup> and Clemm et al<sup>25</sup> concluded that patients under platelet aggregation inhibitors therapy can safely undergo invasive dental procedures without any change of regimen if local hemostatic measures are applied. There were no complications reported by all three researches.

# DISCUSSION

There has been a lot of debate around the optimal management of patients under anticoagulant therapy undergoing dental procedures.<sup>39</sup> The attention of the scientific world has been orientated toward warfarin<sup>40</sup> due to its widespread use. The main focus point was to determine if during dental procedures that have an incidence of bleeding, warfarin dose should be stopped, reduced, or continued. The results of the present literature review indicated that if continuing normal warfarin administration during and postdental procedures, the incidence of bleeding was not increased. There were no statistical or clinical differences in hemorrhage following dental procedures between patients under anticoagulant medication and patients who were not medicated. Furthermore, patients who continued warfarin therapy did not experience major hemorrhage in any of the articles in this literature review. The follow-up period after the dental procedures was between 1 and 7 days, the timeframe during which most procedure-related oral hemorrhagic events occur.38 In contrast, reducing or withholding the warfarin dose was associated with embolic complications and fatal events.37

The recent introduction of new oral anticoagulant medications, rivaroxaban and dabigatran, has revealed the need for more scientific reports about their use in conjunction with dental procedures. The incidence of bleeding in patients taking rivaroxaban and dabigatran therapy following dental implants placement was not statistically significantly higher than in the control groups. For a patient under rivaroxaban or dabigatran therapy, the recommendation in case of undergoing invasive dental procedures was to delay or miss the morning dose on the day of their treatment.<sup>5</sup> Further study would be necessary to clarify if the results can be attributed to any dental procedure or just dental implant placement.

Platelet aggregation inhibitors, such as aspirin, offered no increase in the incidence of hemorrhage after invasive dental procedures. Furthermore, patients under therapy with aspirin and warfarin have not been associated with any hemorrhagic complications after invasive dental procedures.

The interactions between platelet aggregation inhibitors and new oral anticoagulant medications should be further researched as there were not sufficient data to draw a conclusion regarding the incidence of hemorrhage.

The studies selected for this literature review included invasive dental treatment carried out in the hospital and nonhospital setting. This literature review should be valid and offer valuable information for dental practitioners working in both settings. Invasive dental procedures that have a risk of increasing the incidence of hemorrhage have been identified and classified as low risk and high risk.

The low-risk dental procedures considered more likely to cause an oral hemorrhage were simple extractions, incision and drainage of intraoral swellings, root surface instrumentation, and subgingival scaling.<sup>5</sup>

The high-risk dental treatments that can increase the hemorrhage incidence were considered to be complex extractions, periodontal surgery, dental implant surgery, periradicular surgery, crown lengthening, gingival recontouring, and biopsies.<sup>5</sup> Both groups' dental procedures were normally encountered and dealt by a dental practitioner in both settings.

There were some risks of bias identified in all the studies. The most important bias identified was that dental practitioners were not blinded. This would have been avoided if the dental practitioner that carried the follow-up appointment was conducted by a different dental practitioner rather than the one that carried out the procedure, with no knowledge of the groups. Furthermore, additional potential bias has been identified in the patients' comorbidities as conditions, such as liver disease, chronic renal failure, and hematological diseases can increase the bleeding risk and change the hemostatic procedures. In addition, the operator's surgical skills, the complexity of the dental procedure, and the willingness of the patient to report any hemorrhagic events were considered as a potential bias.

The current literature review offered a good solid database of articles as it included studies from eight

languages. The inclusion and exclusion criteria were selected so that the resulting articles would offer valuable information on the subject and the database search results reproduced. Any guidelines or expert opinions were excluded from the search. Articles were only considered if patients were under antithrombotic medication and were followed up for the incidence of oral hemorrhage.

The standard care for patients taking warfarin was regular INR monitoring.<sup>41</sup> All the studies that have analyzed the incidence of bleeding included patient with their INR between 1.5 and 4. This was considered the therapeutic range in which any dental treatment can be carried out without reducing or withholding the dose of warfarin.

There was one article that enrolled patients with their INR above 3.5 without disrupting warfarin therapy.<sup>23</sup> Local hemostatic measures were taken and no increase in the incidence of hemorrhage reported. Further study was required to evaluate the upper value of the INR when warfarin administration should be discontinued and the length of its cessation. In addition, when warfarin was discontinued what other adjuvants should be administered during dental treatment to offer a good outcome.

Nine articles<sup>21-24,27-30,38</sup> assessed the incidence of bleeding after dental extractions while patients were under warfarin therapy. There were no major complications reported with none of the patients hospitalized.

Excluding one article, all the postoperative hemorrhages were controlled with local measures, such as resorbable or nonresorbable sutures and gauze impregnated with 5% tranexamic acid. There was one article<sup>37</sup> which found that one-third of the patients required more than just local hemostatic measures. It was not clear what those measures were as the authors did not offer any information relating to this. In addition, there was no information if patients had be hospitalized following their dental invasive procedures.

Five studies<sup>26,34-37</sup> reached the same conclusion regarding minor dental procedures. They all recommended that the anticoagulant therapy should not be stopped or altered as there was no increased risk of hemorrhage during or after the procedure.

For periodontal surgical treatment, the anticoagulant therapy should not be altered and local hemostatic measures, such as insertion of oxidized cellulose, compression, and suturing should obtain the necessary local coagulation.

Furthermore, reviewing the incidence of bleeding during and after dental implant placement, there was no increased risk of hemorrhage if local hemostatic procedures were taken. Five studies<sup>20,24,25,28,29</sup> recommended not to alter the anticoagulant dose and postoperatively to apply sutures with a gauze impregnated with 5% tranexamic acid.

# CONCLUSION

A well-coagulated patient can safely have routine dental procedures that present a low or high risk of hemorrhage, such as periodontal surgical treatment, dental extractions, apicectomy, and dental implant placement without altering antithrombotic therapy. In addition, local hemostatic measures, such as sutures, gauzes, and 5% tranexamic acids should be available in all hospital and nonhospital setting. In this manner, oral hemorrhage should be managed successfully.

Finally, further research should be focused on patients with the INR outside the therapeutic range and new hemostatic alternatives were found to prevent any embolic complications.

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