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Risk factors for bleeding after oral surgery in patients who continued using oral anticoagulant therapy

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ABSTRACT

Background. The authors assessed the incidence of postoperative bleeding in patients who were highly anticoagulated and in patients who underwent extensive oral surgical procedures and who continued using oral anticoagulant therapy.

Methods. The authors placed 125 patients receiving anticoagulant therapy into 1 of 3 groups. Group A had 54 patients who were highly anticoagulated (international normalized ratio [INR] $\geq$ 3.5) in whom up to 3 teeth were extracted. Group B had 60 patients with INR 2.0 to less than 3.5 in whom higher-risk dentoalveolar surgery (extraction of more than 3 teeth or other oral surgery procedure involving raising a mucoperiosteal flap, osteotomy, or biopsy) was performed. Group C had 11 patients whose INR values were 3.5 or higher and who required higher-risk dentoalveolar surgery. Eighty-five healthy participants who underwent surgical procedures similar to those performed in group A and group B were the control group.

Results. Two patients in group A (3.7%), 3 in group B (5.0%), and 2 in group C (18.2%) experienced postoperative bleeding. In the control group, a single bleeding event (1.2%) occurred. All cases of hemorrhage were mild and easily controlled using local hemostatic measures.

Conclusions. Dental extractions in patients who are highly anticoagulated (INR, 3.5-4.2), as well as more extensive oral surgical procedures in patients who are therapeutically anticoagulated, can be performed safely without interruption or modification of the therapy.

Practical Implications. Tooth extractions and even more extensive surgical procedures can be performed safely in patients who continue using anticoagulant therapy if proper local hemostatic measures are used and if no other coagulopathies are present.

Key Words. Anticoagulants; anticoagulant therapy; hemorrhage; hemostasis; oral surgical procedures; tooth extraction.

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Oral anticoagulants are used widely in prophylaxis and treatment of thrombosis in numerous diseases and conditions. These drugs, mostly coumarin derivatives, are vitamin K antagonists, acting by inhibiting vitamin K epoxide reductase, an enzyme necessary for cyclic interconversion of vitamin K. The lack of the active form of vitamin K prevents carboxylation of glutamic acid residues on coagulation factors II, VII, IX, and X.[1] The most common indications for oral anticoagulant therapy (OAT) are atrial fibrillation, mechanical prosthetic heart valves, deep vein thrombosis, pulmonary embolism, ischemic stroke, myocardial infarction, and valvular heart disease.[2]

The international normalized ratio (INR) is used to measure oral anticoagulants' effect. The therapeutic INR range is 2.0 to 3.0 in most cases.[2,3] For high-risk groups of patients, such as those with a mechanical mitral valve, the American Heart Association/American College of Cardiology recommends a higher INR range between 2.5 and 3.5.[2] For patients with mechanical heart valves, the British Committee for Standards in Haematology recommends a target INR up to 3.5,[3]

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whereas the European Society of Cardiology recommends a target INR up to 4.0, depending on prosthesis thrombogenecity and patient-related risk factors.[4]

Dental surgery in patients receiving OAT is always challenging. Cessation of OAT could cause a life-threatening thromboembolism.[5] Results from numerous reports show that dental extractions can be performed safely in patients receiving OAT if INR values are in the therapeutic range (< 4.0), providing that efficient local hemostatic measures are used.[5-16] The most commonly used local hemostatic agents are absorbable gelatin or collagen sponges, oxidized regenerated cellulose, fibrin glue, and antifibrinolytics applied directly into the wound or in the form of a solution as a mouthwash.

Although most research results have shown dental extractions to be safe without stopping OAT, a few cases of high-risk dentoalveolar surgery or dental surgical procedures in patients who are highly anticoagulated are available in the literature. Moreover, survey results have shown that approaches of oral and maxillofacial surgeons for treatment of patients taking oral anticoagulants are affected mostly by INR values and the extensiveness of surgical procedures.[17,18]

The aim of this study was to evaluate the incidence of postoperative bleeding after oral surgical procedures in patients with high INR values (≥ 3.5) and in patients who were treated with oral anticoagulants and were exposed to higher-risk dentoalveolar surgery. We compared these patients with a control group of healthy participants in whom we performed similar surgical procedures.

METHODS

The Ethics Committee of the Dental Clinic of Vojvodina approved the study protocol, and we obtained written informed consent from all patients at the time of the procedure. We recruited consecutively patients whose dentists and physicians had referred them to the Department of Oral Surgery, Dental Clinic of Vojvodina, in Novi Sad, Serbia. The treating oral surgeon (B.B.) reviewed the medical charts of patients treated from March 2005 to June 2014. The study included patients receiving long-term OAT whose INR values were 3.5 or higher on the day of the procedure, as well as patients who were therapeutically anticoagulated who required higher-risk dentoalveolar surgery: extraction of more than 3 teeth or another oral surgery procedure involving raising a mucoperiosteal flap, osteotomy, or biopsy.

We placed the patients into 1 of 3 groups. Group A had patients who were highly anticoagulated (INR ≥ 3.5) in whom we extracted up to 3 teeth. Group B had patients with INR values of 2.0 to less than 3.5 in whom we performed higher-risk dentoalveolar surgery. Group C had patients whose INR values were 3.5 or higher and who required higher-risk dentoalveolar surgery. We excluded patients with INR greater than 4.5 and less than 2.0 on the day of the procedure, patients with liver and renal diseases, and patients taking medications that affect hemostasis (aspirin or other nonsteroidal anti-inflammatory drugs).

The same oral surgeon (B.B.) performed all surgical procedures on an outpatient basis. Local anesthesia was achieved by means of lidocaine 2% with 1:80,000 epinephrine, articaine 4% with epinephrine 1:200,000, or mepivacaine 3%. Patients with the risk of developing infective endocarditis received antibiotic prophylaxis according to the recommendations of the American Heart Association.[19]

We performed all procedures with minimal surgical trauma. We used absorbable collagen or gelatin sponges and oxidized regenerated cellulose as local hemostatic agents, along with wound suturing. In 1 case, after hard palate biopsy, we used thermocauterization for bleeding control because of the inability to use local hemostatic agents and suturing. We observed all patients for 2 hours after the procedures before dismissal and followed up 7 days after the procedures. The patients had regular checkups on the first, second, fifth, and seventh days after the procedure. We contacted patients unable to come for regular examinations by phone.

We advised all patients to continue with their medications and provided them with a list of postoperative instructions and the telephone number of a surgeon to be contacted in case of bleeding. We advised using paracetamol (acetaminophen) for pain relief. We removed the sutures between the fifth and seventh days.

The control group had 85 healthy participants. In 31 of these participants, we extracted up to 3 teeth (similar to group A); in 54 participants, we performed more complex surgical procedures (similar to groups B and C). In this group of patients, we used no local hemostatic agents. We determined bleeding to be an event by using the following criteria: the bleeding continued more than 12 hours, the patient had to call the surgeon or return to the dental practice or emergency department, the bleeding resolved with a large hematoma or ecchymosis within the oral soft tissues, or the patient required a blood transfusion.[20]

We analyzed the data regarding postoperative bleeding by using χ^2 and Fisher exact tests to evaluate the relative frequencies of postoperative bleeding in the patients in each group. We set the level of significance at .05. We processed the data by using software (SPSS, Version 22.0, IBM SPSS).

RESULTS

The study included 125 patients treated with oral anticoagulants. Table 1 shows the indications for OAT.

ABBREVIATION KEY. INR: International normalized ratio. **OAT:** Oral anticoagulant therapy.

TABLE 1

Indications for oral anticoagulant therapy.

INDICATION FOR ORAL ANTICOAGULANT THERAPY	GROUP A (INR* ≥ 3.5) (N = 54)	GROUP B (INR = 2.0 TO <3.5 AND HIGHER-RISK DENTOALVEOLAR SURGERY) (N = 60)	GROUP C (INR ≥ 3.5 AND HIGHER-RISK DENTOALVEOLAR SURGERY) (N = 11)
Prosthetic Valve Replacement	14	20	3
Prosthetic Valve Replacement and Ischemic Cardiovascular Disease	5	3	1
Prosthetic Valve Replacement and Atrial Fibrillation	5	1	2
Atrial Fibrillation	5	9	1
Atrial Fibrillation and Valvular Heart Disease	8	5	2
Atrial Vibrillation and Ischemic Cerebrovasular Disease	2	3	1
Atrial Fibrillation and Ischemic Cardiovascular Disease	0	2	0
Ischemic Cardiovascular Disease	3	1	0
Ischemic Cerebrovascular Disease	0	4	0
Ischemic Cardiovascular Disease and Ischemic Cerebrovascular Disease	1	2	0
Ischemic Cerebrovascular Disease and Deep Vein Thrombosis	1	2	0
Deep Vein Thrombosis, Including Pulmonary Embolism	8	7	1
Dilated Cardiomyopathy and Ischemic Cardiovascular Disease	2	1	0

* INR: International normalized ratio.

Group A had 54 patients (52 receiving acenocoumarol, 2 receiving phenprocoumon) with a mean (standard deviation [SD]) INR value of 3.72 (0.21; range, 3.50-4.20). In this group, there were 38 male and 16 female participants, with a mean (SD) age of 65 (9.7) years. In this patient group, we performed single-tooth extraction in most cases (Table 2). In 8 patients in this group, we performed the procedure by using local anesthetic without a vasoconstrictor (mepivacaine 3%).

Group B had 60 patients, 36 male and 24 female, with a mean (SD) age of 65.7 (10.3) years. Fifty-seven of them received acenocoumarol, and 3 received warfarin. The mean (SD) INR value was 2.57 (0.38; range, 2.0-3.37). Table 3 shows the types and number of surgical procedures, as well as INR values, in this group. We provided local anesthesia without a vasoconstrictor in 6 patients in this group who underwent simple dental extractions.

Group C had 11 patients, 7 male and 4 female, with a mean (SD) age of 67.5 (8.3) years. All patients in this group received acenocoumarol. The mean (SD) INR value was 3.71 (0.18; range, 3.52-4.17). Table 4 provides data regarding the types of surgical procedures and INR values in this group of patients. We performed all procedures in this group by using local anesthetics with a vasoconstrictor.

There were 85 participants in the control group, 52 male and 33 female, with a mean (SD) age of 64.5 (9.8) years. In 31 of these participants, we extracted up to 3 teeth in a fashion similar to that used in group A (1 tooth removed in 16 patients, 2 teeth removed in 12 patients, and 3 teeth removed in 3 patients). Fifty-four participants underwent more complex surgical procedures similar to those used in the patients in groups B and C. The procedures were 27 cases of 4 to 7 teeth removed, 8 cases of surgical removal of a tooth and/or third-molar surgery, 5 cases of surgical removal of a tooth or third-molar surgery with simple dental extraction, 2 cases of periapical surgery, 2 cases of cystectomy with or without tooth extraction, 3 cases of buccal exostosis removal with or without dental extraction, 3 cases of single-tooth extraction and oroantral communication closure, 1 case of surgical removal of an impacted maxillary canine, and 3 cases of soft-tissue procedures with or without dental extraction.

TABLE 2

Group A: oral surgical procedures and international normalized ratio values.

NO. OF TEETH EXTRACTED	NO. OF PATIENTS	MEAN INR* (SD)† [RANGE]
1	28	3.73 (0.21) [3.50-4.20]
2	21	3.69 (0.19) [3.50-4.07]
3	5	3.80 (0.20) [3.55-4.10]

* INR: International normalized ratio.
† SD: Standard deviation.

TABLE 3

Group B: oral surgical procedures and international normalized ratio values.

ORAL SURGICAL PROCEDURE*	NO. OF PATIENTS	MEAN INR† (SD)‡ [RANGE]§
Four-tooth Extraction	25	2.57 (0.44) [2.0-3.37]
Five-tooth Extraction	8	2.51 (0.36) [2.0-3.15]
Six-tooth Extraction	2	2.16 [2.08-2.25]
Seven-tooth Extraction	1	2.72
Eight-tooth Extraction	1	2.66
Periapical Surgery	1	2.40
Third-molar Surgery, Surgical Extraction of 1 Tooth, and Extraction of 2 Teeth	1	2.26
Single-tooth Extraction and Oroantral Communication Closure	3	2.60 (0.38) [2.18-2.90]
Removal of Buccal Exostosis	1	2.20
Removal of Buccal Exostosis and Soft-tissue Biopsy	1	2.80
Surgical Removal of 1 Tooth and Extraction of 3 Teeth	1	2.90
Surgical Removal of 1 Tooth	4	2.56 (0.27) [2.20-2.85]
Surgical Removal of 1 Tooth and Single-tooth Extraction	1	2.01
Abscess Incision and Single-tooth Extraction	1	3.15
Third-molar Surgery	1	2.39
Surgical Removal of Impacted Maxillary Canine	1	2.93
Surgical Removal of 1 Tooth and Extraction of 2 Teeth	1	2.32
Cystectomy and 3-tooth Extraction	1	3.20
Cystectomy and 2-tooth Extraction	1	3.20
Foreign Body Removal as Part of Amalgam Restoration	1	2.80
Soft-tissue Biopsy	2	2.77 [2.33-3.2]
Frenectomy	1	2.53

* If it is not indicated otherwise, simple dental extraction was performed.
† INR: International normalized ratio
‡ SD: Standard deviation.
§ If only 1 patient was treated, just the mean INR is listed. If 2 patients were treated, both the mean INR and the range are listed.

We saw postoperative bleeding in 2 of 54 patients (3.7%) in group A. In the first case, minor bleeding occurred on the second day after single-tooth extraction in a patient whose INR was 4.10. The bleeding was stopped by means of compression. The second case was a patient who came back to the clinic several hours after extraction of 2 teeth. The patient's INR was 3.52. We successfully managed the bleeding by inserting oxidized regenerated cellulose and resuturing the wound.

In group B, we saw postoperative bleeding in 3 of 60 patients (5%). The first patient, with an INR of 2.57 in whom 5 teeth had been extracted, manifested bleeding on the day of the procedure. We stopped the hemorrhage after inserting oxidized regenerated cellulose and resuturing the wound. The second case of bleeding occurred after closure of an oroantral communication in a patient with an INR of 2.73. Bleeding started the night after the procedure and was managed successfully after wound revision by inserting oxidized regenerated cellulose and resuturing. The third patient had an INR of 2.51 and manifested postoperative bleeding the day after extraction of 4 mandibular incisors. Bleeding ceased after resuturing. In 2 patients of this group, we observed cheek hematoma; in 1 patient after closure of an oroantral communication and in the other after extraction of a highly positioned impacted maxillary canine. Hematomas probably were caused by the need for extensive buccal flap mobilization. Both hematomas were absorbed spontaneously in a few days, with no further complications.

In group C, there were 2 bleeding complications (18.2%). We observed the first of these complications in a patient with an INR of 3.72 who underwent third-molar surgery. We stopped the bleeding by means of compression. In the same patient, we noted a large skin hematoma extending from the mandibular angle down to the clavicle postoperatively. The hematoma was absorbed spontaneously in a few days, with no further complications. The second patient with bleeding came for a regular checkup the day after the removal of 4 maxillary teeth. His INR was 3.6 at the time of the procedure. He complained of several bleeding episodes during the night. We noted coagulum extending over the wounds with fresh bleeding during the checkup. The hemorrhage stopped after removal of the coagulum, insertion of oxidized regenerated cellulose, and resuturing of the wound. In the control group, we noted 1 bleeding event (1.2%) in a patient who underwent third-molar surgery.

Although patients whose INR values were 3.5 or greater and who required higher-risk dentoalveolar surgery (group C) had a higher incidence of postoperative bleeding, we found no statistically significant difference in comparing this patient group with groups A and B ($\chi^2 2 = 3.702$, $P = .157$; Fisher exact test, $P = .179$). We found no statistically significant differences in postoperative bleeding in comparing group A with the control group of 31 participants who underwent a similar number of tooth extractions ($\chi^2 1$, Yates $= 0.116$, $P = .733$; Fisher exact test, $P = .531$) and in comparing groups B and C with the control group of 54 patients with similar surgical procedures ($\chi^2 1$, Yates $= 0.162$, $P = .687$; Fisher exact test, $P = .62$ and $\chi^2 1$, Yates $= 2.448$, $P = .118$; Fisher exact test, $P = .072$, respectively).

DISCUSSION

The main problem in patients receiving OAT is whether to alter or stop OAT and risk thromboembolism or to let the patient continue OAT and risk hemorrhage during or after the dental procedure. Results from several studies have shown that minor dentoalveolar surgery can be performed safely without interruption of OAT in patients who are therapeutically anticoagulated.[5-16] However, there is a lack of evidence concerning the safety of high-risk dentoalveolar surgery in patients who continued using OAT, as well as about the safety of dentoalveolar surgery in patients who are highly anticoagulated.[15] van Diermen and colleagues[21] recommended discussion with the patient's physician if the patient's INR is higher than 3.5 and if more complicated or invasive surgical procedures are planned (level of evidence A, recommendation class I).

Depending on the INR values, different protocols for dentoalveolar surgery are available in the literature. According to the guidelines developed by the Academic Centre for Dentistry Amsterdam, in the Netherlands, the INR must be 3.5 or lower for most dentoalveolar surgical procedures including no more than 3 extractions at the same time, surgical removal of third molars, periodontal treatment, apicoectomies, incision of an abscess, or placement of a maximum 3 implants.[16] Aframian and colleagues[7] in a review article stated that for patients within the therapeutic INR range of 3.5 or lower, OAT need not be modified or discontinued for simple single dental extractions. However, the authors concluded that there is not enough evidence for such recommendations for more complicated and invasive oral surgical procedures, especially in patients with higher INR levels.[7] Authors of a study published in 2014 advocated that an INR of 3.0 or even lower in patients with comorbidities should be the upper limit for tooth extractions.[22]

Bleeding incidence is expected to be higher in patients with higher INR values. However, contradictory data is available in the literature.

Investigators in several studies did not confirm the association of postoperative bleeding and higher INR values.[11,23-27] Most of these authors stated that prolonged bleeding is more likely to occur after extractions of teeth with severe periodontitis because of the greater degree of local inflammation than in patients with high INR values. To the contrary, other authors reported the influence of high INR values on postoperative bleeding.[28]

In our study, we included 54 patients who were highly anticoagulated (INR, 3.5-4.2) in whom we performed simple dental extraction of up to 3 teeth. The incidence of postoperative bleeding was 3.7% (2 of 54 patients).

In the current literature, there is no strong evidence concerning the influence of the type of surgical procedure and the number of extracted teeth on postoperative bleeding. Results from a study of patients who were awaiting liver transplants who had altered hemostatic function showed that the incidence of postoperative bleeding depends on the extensiveness of the oral surgical procedure.[29] Almost all authors emphasize the importance of minimally traumatic surgical procedures in patients receiving OAT.

Ward and Smith[17] in a review article stated that there are not enough studies that included a significant number of patients receiving anticoagulant therapy concerning moderate and high-risk dentoalveolar surgery, so it cannot be concluded strongly whether it is safe to perform surgery of such extensiveness while maintaining therapeutic INR levels. The results of the survey these authors conducted showed that most oral and maxillofacial surgeons suggested that their patients stop OAT to achieve minimal therapeutic or subtherapeutic INR levels if high-risk surgery is planned. The same authors found that most surgeons supported continuing OAT if 3 to 5 teeth had to be extracted.[17] Scully and Wolff[30] deemed that uncomplicated extraction of up to 3 teeth is safe if the INR is less than 3.5 in the absence of other bleeding risk factors, whereas Chugani[31] stated that periodontal flap surgery, implant placement, and apicoectomy are not recommended in patients with INR values between 3.0 and 4.0.

Some authors tried to classify oral surgical procedures in patients receiving OAT in accordance with the degree of surgical trauma and risk of postoperative bleeding.[23,32] Ferrieri and colleagues[32] categorized all surgical procedures as either low–risk procedures, which included uncomplicated extraction of up to 4 teeth, or high-risk procedures, which included single surgical extraction, uncomplicated extraction of 5 or more teeth, biopsies, or implant placement. Results from retrospective studies published in 2012 showed that different types of oral surgical procedures can be performed safely in patients who continued OAT.[14,15]

TABLE 4

Group C: oral surgical procedures and international normalized ratio values.

ORAL SURGICAL PROCEDURE*	NO. OF PATIENTS	MEAN INR† (SD)‡ [RANGE]§
Four-tooth Extraction	4	3.77 (0.30) [3.52-4.17]
Two-tooth Extraction and Soft-tissue Biopsy	1	3.56
Third-molar Surgery	1	3.72
Surgical Removal of 1 Tooth	3	3.67 (0.12) [3.56-3.80]
Surgical Removal of 2 Teeth	1	3.70
Removal of Buccal Exostosis	1	3.74

* If it is not indicated otherwise, simple dental extraction was performed.
† INR: International normalized ratio.
‡ SD: Standard deviation.
§ If only 1 patient was treated, just the mean INR is listed.

In our study, higher-risk dentoalveolar surgery was considered extraction of more than 3 teeth or another oral surgery procedure involving raising a mucoperiosteal flap, osteotomy, or biopsy. We noted postoperative bleeding in 3 of 60 patients (5%). The results showed higher-risk dentoalveolar surgery can be performed safely in patients who are therapeutically anticoagulated.

Along with INR values and the degree of surgical trauma, an important factor that can influence postoperative bleeding is inflammation of dental tissues. Our study results help confirm this fact because most of the hemorrhage occurred after extractions of teeth with severe periodontitis. In multiple tooth extractions, bleeding was not present at every site; it was more common at sites with a greater degree of local inflammation.

Our study has some potential drawbacks and limitations: its retrospective design and relatively small sample size. We treated the patients by using different local anesthetics. Vasoconstrictors in local anesthetics can affect intraoperative bleeding. However, we managed all intraoperative bleeding easily, so we think that the use of different local anesthetics did not influence this study's results substantially.

In the group of patients with INR greater than 3.5 in whom higher-risk dentoalveolar surgery was performed (group C), there were 2 bleeding complications (18.2%), which is higher than the bleeding incidence in groups A and B but without a statistically significant difference. However, this number of patients is too small to obtain firm conclusions, so further research is necessary to prove the safety of high-risk dentoalveolar surgery in patients who are highly anticoagulated. Besides, we performed single or 2-tooth extraction in most patients in group A (patients who were highly anticoagulated with INR of 3.5 or greater). Further research is also necessary to prove the safety of extraction of 3 or more teeth in this patient group.

CONCLUSIONS

Our study results suggest that simple dental extractions are safe in patients who are highly anticoagulated (INR, 3.5-4.2), as well as more extensive oral surgical procedures in patients who are highly anticoagulated if efficient local hemostatic measures are provided and if no other coagulopathies are present. However, firm conclusions about the safety of high-risk dentoalveolar surgery in patients who are highly anticoagulated cannot be made based on this study's results because of the small number patients. ■

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