Postoperative bleeding associated with antiplatelet and anticoagulant drugs: A retrospective study

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Objective. To examine postoperative bleeding in patients taking antiplatelet and anticoagulant medications after invasive periodontal procedures.

Study Design. This 6-year retrospective study collected data from the electronic health records of patients who underwent invasive periodontal procedures at the College of Dentistry, University of Kentucky Lexington, from January 1, 2011 through April 1, 2017. Records were included when the medical history was current, an invasive periodontal procedure was performed, an antiplatelet or anticoagulant medication was taken, and a postoperative visit was documented.

Results. Four hundred and fifty-six patients (age range 22−89 years; mean age 66.1 years; 58% male) met the inclusion criteria and underwent 867 invasive periodontal procedures. Antiplatelet medications, warfarin, a direct oral anticoagulant, or a combination of these drugs were taken during 484 scaling and root planing procedures, 218 implant placements, 53 open flap debridements, 16 gingival grafts, 15 lateral windows, and 71 other. Medications were continued in 99.6% of patients during the procedure. Postoperative bleeding occurred after three procedures (0.35%) and resolved with local hemostatic measures. Medications were temporarily discontinued in four instances (range 1−5 days); none of these patients experienced postoperative bleeding.

Conclusions. Postoperative bleeding was infrequent in patients who underwent an invasive periodontal procedure while taking an antiplatelet or anticoagulant drug. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;128:243−249)

Antiplatelets and anticoagulants are used commonly by adults who have cardiovascular disease and by those who are at risk for thromboembolism. Although there is some concern about discontinuing these medications before general surgery,[1,2] antiplatelet medications[3-9] and warfarin (Coumadin) (when the international normalized ratio [INR] is <3.5) do not appear to pose a great risk of bleeding during routine dental procedures or simple tooth extractions.[10-15] However, less is known about these medications when used in combination and when newer anticoagulants are used.

Direct oral anticoagulants (DOACs), introduced in 2010, are being taken by an increasing number of people worldwide, particularly older adults.[16,17] The increased use of DOACs is the result of marketing and their advantages over warfarin (Coumadin), including shorter half-life and lack of a requirement for laboratory testing before planned invasive procedures. The two largest studies to date—Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) and Apixaban for Reduction in Stroke Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE)—have shown that postoperative bleeding rates after dental procedures are similar between patients taking warfarin and those taking dabigatran/apixaban.[18,19] However, reports from these two trials do not specify the type of dental procedures performed or the invasiveness of the procedures, and whether DOACs were temporarily discontinued before the dental procedures. Several smaller studies[1,20-24] provide some insight into the need for temporary discontinuation of DOACs before invasive dental procedures; however, this topic remains controversial.[25,26] A few reports state that it is unnecessary to discontinue a DOAC before minor surgical procedures (i.e., simple extractions).[22,27-29] Others have discontinued these medications, based on the type of procedure and the medical status of the patient.[20,21,30] Most reports, to date, are based on routine extractions, without any mention of the health status of the patient. Notably, data on postoperative complications after periodontal surgical procedures associated with DOAC use, especially in older adults and those with comorbidities, are limited.[22,31]

The aim of this study was to determine the frequency and severity of the postoperative bleeding events associated with antiplatelet and anticoagulant medication use in patients who underwent common periodontal procedures. We hypothesized that the frequency of

Statement of Clinical Relevance

This study showed very low risk of bleeding associated with antiplatelet and anticoagulant drug use during and after invasive periodontal procedures. The findings support the recommendation that these drugs not be discontinued before invasive periodontal procedures.

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postoperative bleeding would be low and of minor severity regardless of antiplatelet and anticoagulant use, combined use, periodontal procedure, or continuation of drug use.

MATERIALS AND METHODS

A retrospective study design was employed based on data extracted from the electronic health record (AxiUm, Coquitlam, British Columbia, Canada) of patients who took antiplatelet medications, warfarin, or one or more of the DOACs, and received a periodontal procedure at the University of Kentucky College of Dentistry between January 1, 2011 and April 1, 2017. Procedures were performed by a variety of clinicians, including dental students, residents, general dentists, and dental specialists. We included patients who had evidence of using any of the following medications: dabigatran (Pradaxa), rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Savaysa), aspirin, clopidogrel (Plavix), ticlopidine (Ticlid), ticagrelor (Brilanta), abciximab (Reopro), epitifibatide (Integtilin), tirofibran (Aggrastat), dipyridamole (Persantine), warfarin (Coumadin/Jantoven) during the designated treatment dates and had one or more of the following Current Dental Terminology procedures documented: D4342, D4341, D4245, D4261, D4260, D7951, D7952, D7950, D6010, D4249, D4230, D7286, D7285, D7960, D6101, D6102, D6011, D7280, D4241, D4240, D4273, D4277, and D4275. Dental extractions were not included because we have previously published findings on this study population regarding that procedure.[23] We excluded patients whose record did not indicate that they (1) took one of the study medications, (2) underwent a periodontal procedure between the dates listed, (3) had a postoperative appointment after the procedure, or (4) their medical history was updated within 1 year before the procedure.

Data from records that met the above criteria with regard to age, race, gender, antiplatelet/DOAC/warfarin medication(s), INR, drug dosage(s), drug indication, smoking status, other medication(s) taken, medical comorbidities, physician consultation, antiplatelet/anticoagulant medication discontinuation, date of surgery, specialty of the provider, procedure completed, management of bleeding, outcome at follow-up, and explanation of any outcome were extracted (by R.R.) and recorded on an Excel spreadsheet. All data were de-identified before collection and entry on the spreadsheet. The study was performed with approval from the University of Kentucky institutional review board.

Data analysis

Data entered into a spreadsheet were reviewed for entry errors by a second independent investigator (C.M.). The primary outcome was bleeding frequency and complications in patients who took these medications. Secondary considerations were severity of the bleeding episodes, frequency of continuation or discontinuation of medications before periodontal surgery, and how often information regarding physician consultation was completed. Data were tabulated and analyzed for each variable, and correlations were determined between the groups. Differences in bleeding complications between groups of patients taking different medications were determined by Fisher's exact test. Drug type (i.e., antiplatelet, warfarin, DOAC) and age comparisons were analyzed using analysis of variance (ANOVA). A P value of 0.05 was used as the cutoff level for significance.

A power analysis (i.e., 90% power) revealed a sample size of 48 in the anticoagulant group and 394 in the antiplatelet group would demonstrate significance at the 0.05 level based on Fisher's exact procedure (one sided test) assuming bleed rates were 10%[1,11,27] and 0.5%[12,32] respectively, as reported in the current literature.

RESULTS

Screening identified 817 records, and 456 met the inclusion criteria. Three hundred and sixty-one records were excluded because (1) the medical history was not updated within 1 year ($n = 228$) or (2) the record did not annotate use of study medications (n = 133). The study cohort (age range 22−89 years; mean age 66.1 years; 58% males; 90% white/non-Hispanic patients) took antiplatelet medications, warfarin, DOACs, or a combination of these medications and underwent 867 periodontal procedures (Table I). All included patients were seen at a follow-up visit (average 8 days). Aspirin and a combination of aspirin and clopidogrel were the most commonly used medications, followed by warfarin. There were 50 patients who took both an antiplatelet and anticoagulant medication. Those who took anticoagulants were significantly older (by 4−7 years) than those who took antiplatelets ($P = .003$), but there was no significant difference in the mean age of patients taking warfarin compared with those taking a DOAC, as determined by ANOVA.

A majority of patients had medical comorbidities (84.04%) and 23.99% were smokers (Table II). Neither comorbidity nor smoking was related to postoperative bleeding. The patient's antiplatelet/anticoagulant medication was temporarily discontinued in four instances (0.46%) before the periodontal procedure, and few procedures (n = 23 [2.65%]) were associated with a medical consultation.

Table III shows the frequency of periodontal procedures performed in relation to the medication taken. Scaling and root planing (n = 484 [55.82%]) was the most common procedure, followed by placement of a dental implant (n = 218 [25.14%]). The remaining procedures (n = 165 [19.03%]) represent a variety of soft

Table I. Medications and demographic characteristics

	AP	*Plavix*	*Warf*	*DOAC*	*AP + Plavix*	*Plavix + Warf*	*AP + Warf*	*AP + Plavix + Warf*	*AP + Plavix + DOAC*	*AP + DOAC*	*AP + Warf + DOAC*	*Total*
N (Procedures)	617	30	55	13	102	2	33	1	2	5	7	867
Male (N)	341	14	31	10	66	2	25	1	2	4	7	503
Female (N)	276	16	24	3	36	0	8	0	0	1	0	364
Race (%)*	88.5%	90%	92.7%	100%	95.1%	100%	100%	100%	100%	100%	100%	90.4%
Mean Age (Range)	62.8 (22–82)	66.2 (50–80)	67.4 (38–54)	73.3 (64–82)	63.2 (44–83)	79.0 (78–80)	70.2 (59–83)	63.0	67.5 (66–69)	70.2 (66–78)	67.2 (62–74)	66.1

*Calculated as a percent white/non-Hispanic.
AP, antiplatelet; *DOAC*, direct oral anticoagulant; *Warf*, warfarin.

Table II. Percentage of study population (n) with comorbidities

Medical comorbidities	84.04% (694)
Smoker	23.99% (208)
Kidney disease	3.34% (26)
Documented reason for medication	
Atrial fibrillation	5.42% (47)
Deep venous thrombosis	0.69% (6)
Pulmonary embolism	1.04% (9)
Acute coronary syndrome	17.58% (145)
Not reported	75.39% (619)

tissue and osseous surgical procedures, including grafting, sinus augmentation, hard and soft tissue biopsies, and implant-related procedures.

Overall, the occurrence of postoperative bleeding episodes was very low (n = 3 [0.35%]), and no embolic complications were observed. Analysis by Fisher's exact test demonstrated no difference in postoperative bleeding frequencies between specific medication groups. Two bleeding episodes occurred after dental implant placement. Details regarding the implant group and bleeding are provided in Table IV. There were 218 total implant procedures involving 176 patients. In 10 instances, medical consultations were completed, and none had medications discontinued. In the two implant procedures with postoperative bleeding complications, one patient took warfarin and the other took warfarin and daily low-dose aspirin. Both had preoperative INRs measured within two days of the procedures, and the results were within normal limits. The implant bleeding episodes occurred five and seven days postoperatively and required a revisit to the dentist. Both were treated with routine hemostatic procedures, and no additional complications were observed.

A third bleeding episode occurred in the right palate donor site of an 84-year old male after a free gingival graft. This patient was taking aspirin and continued to take it during the procedure. On day 5, he noted oral bleeding and accidentally took an excessive amount of anti-hypertension medication that resulted in a severe drop in blood pressure and syncope. The bleeding was brought under control by the time the patient presented to the hospital, and no additional procedures were needed to achieve hemostasis.

DISCUSSION

Dental practitioners are encountering an increasing number of older patients who take antiplatelet and anticoagulant medications and need invasive periodontal therapy.[16,33] Although a significant amount of research findings have been published on the pharmacologic properties of antiplatelet and anticoagulant medications,[28,34,35] the bleeding outcomes in

Table III. Medications taken by patients per procedure in relation to bleeding events

	Antiplatelets			*Anticoagulants*								
Procedure	*AP*	*Clop*	*AP + Clop*	*AP + Warf*	*AP + Clop + Warf*	*AP + DOAC*	*AP + Clop + DOAC*	*AP + Warf + DOAC*	*Warf*	*Clop + Warf*	*DOAC*	*Total*
Scaling and root planing	359	18	54	8[#]	1	3	2	6	26	0	7	484
Implantation	154	8	24	14*	0	1	0	0	14†	1	2	218
Open flap debridement	46	2	3	0	0	0	0	0	2	0	0	53
Free gingival graft	12‡	0	2	1	0	0	0	0	0	0	1	16
Lateral window	11	1	2	0	0	1	0	0	0	0	0	15
Vertical sinus lift	8	1	1	0	0	0	0	0	1	0	0	11
Other¶	27	0	16§	10	0	0	0	1	12‖	1	3	70
Total	617	30	102	33	1	5	2	7	55	2	13	867

*Bleeding episode 7 days after dental implant placement at site #12/#13. INR 2.8 at the time of the procedure and at follow-up appointments. Patient reported postoperatively to dental clinic where cautery and lidocaine were used for hemostasis.

†Bleeding episode 5 days after dental implant placement at site #30. INR between 2.1 and 3.5 before surgery. INR 4.1 at revisit. Physician withheld medication 2 days once bleeding occurred.

‡Bleeding episode same day of free gingival graft. Patient had a syncope episode after taking higher than the prescribed dose of blood pressure medications. Patient was taken to the emergency room and placed on intravenous fluids. We believe the hospital visit occurred after the bleeding episode. Bleeding was under control by the time the patient reported to the hospital.

§Denotes 1 procedure with medication discontinued.

‖Denotes 2 procedures with medications discontinued.

¶Open flap debridement, osseous surgery, free gingival graft, lateral window sinus augmentation, vertical sinus augmentation, soft tissue biopsy, connective tissue graft, hard and soft tissue biopsy, crown lengthening, block graft, peri-implant debridement and osseous surgery, frenectomy and second stage dental implant surgery.AP, aspirin; Clop, clopidogrel; DOAC, direct oral anticoagulant; Warf, warfarin.

Table IV. Characteristics associated with implant procedures

Medication	*No. of patients*	*# Implant procedures*	*Consults*	*# Postoperative bleeding events*	*Management*	*Discontinuation of medication*
Aspirin	122	154	1	0	NA	No
Clopidogrel	8	8	0	0	NA	NA
Aspirin + clopidogrel	18	24	6	0	NA	0
Aspirin + warfarin	14	14	3	1*	7 days postoperatively patient reported to clinic. Cautery and lidocaine used for hemostasis. INR consistently around day 2.8 of surgery and at all follow-up visits. No preoperative consultation or medication discontinuation	0
Aspirin + DOAC	1	1	0	0	NA	0
Clopidogrel + warfarin	1	1	0	0	NA	NA
Warfarin	10	14	No	1‡	INR between 2.1 and 3.5 on day of surgery. INR 4.1 at revisit 5 days later. Physician withheld medication for 2 days once bleeding occurred. No preoperative consultation or medication discontinuation.	No
DOAC	2	2	0	0	NA	0
Pradaxa	0	0	NA	NA	NA	NA
Savaysa	0	0	NA	NA	NA	NA
Eliquis	0	0	NA	NA	NA	NA
Xarelto	2	2	0	0	NA	0
Total	**176**	**218**	**10**	**2**		**0**

*Sites #12, #13.

‡Site #30.*DOAC,* direct oral anticoagulant.

patients undergoing invasive periodontal procedures, including dental implantation, have not been adequately investigated. In this report, we sought to determine the frequency and severity of bleeding after invasive periodontal procedures in patients who were taking an antiplatelet and/or anticoagulant medication. Overall, the findings from this retrospective study demonstrated that (1) the frequency of bleeding episodes was low and not significantly different among the three study groups (antiplatelet vs warfarin vs DOAC) or in patients who had medical comorbidities; (2) discontinuation of antiplatelet and anticoagulant drugs before invasive periodontal procedures was infrequent and not needed; and (3) physician consultation was not needed to achieve hemostasis.

In our study cohort involving 867 procedures, 749 procedures were performed in patients who were taking an antiplatelet (i.e., aspirin, clopidogrel or a combination of both). There were more than 400 scaling and root planing procedures, 186 dental implant procedures, 14 free gingival grafts, and 24 sinus augmentation procedures performed in patients taking antiplatelets, and only 1 bleeding episode (0.16%) was observed (see Table III). This rate is lower than that reported in similar studies,[36,37] although comparable studies examined mostly minor surgical procedures and extractions and had much fewer study patients. Other studies involving minor surgical procedures and extractions have reported similar bleeding rates as that in our study.[8,12,32] The single bleeding episode we documented occurred in a patient who had had a free gingival graft taken from the palate, resulting in bleeding from the donor site five days postoperatively. Bleeding was controlled by using local hemostatic measures. The patient was hospitalized, but the hospitalization was related to excess blood pressure medication taken.

Warfarin was associated with 55 periodontal surgical procedures, and warfarin combined with an antiplatelet (aspirin and/or clopidogrel) was taken in association with 36 procedures. Two bleeding events (2.4%) were documented. This rate is similar to those reported in comparative studies,[4,14,38-40] although several of the prior studies only examined extractions. One study evaluated bleeding episodes in patients taking warfarin while undergoing periodontal procedures.[10] That study showed similar results to ours, i.e., a 1.3% postoperative bleeding rate.

A single DOAC medication was taken in association with 13 invasive periodontal procedures, and together with other antiplatelet drugs (n = 7), or aspirin and warfarin (n = 7). There were no postoperative bleeding complications associated with DOAC use in this patient cohort (n = 27). These results are similar to our prior findings involving dental extractions[23] but lower than the findings from a large prospective study that reported a postoperative bleeding rate of 3.4% in patients taking DOACs who underwent periodontal procedures[31] and much lower than the 5.9% to 11% postoperative bleeding rates reported in other studies.[1,41,42]

Whether the antiplatelet or anticoagulant was continued or temporarily discontinued did not appear to alter the surgical outcome, even though this information was infrequently annotated in the electronic health records of our study cohort. When the medication was temporarily discontinued (antiplatelet, n = 1; warfarin, n = 3), the amount of time varied between 1 and 5 days. This variability suggests that some clinicians may be unaware of the current recommendation regarding not discontinuing antiplatelets and anticoagulants for periodontal procedures.[43] When the INR is within the therapeutic range of 2.0 to 3.5, experts recommend that the management protocol include the use of local hemostatic measures (e.g., sutures, pressure, gelatin sponges, oxidized cellulose, chitosan hemostatic products, or tranexamic acid soaked sponges), where appropriate.[44] Accumulating data from this and other studies[23,25,45] suggest that a similar protocol is advisable for most patients who are taking DOACs when periodontal procedures are performed.

Medical consultations were infrequently recorded with patients taking an antiplatelet medication or an anticoagulant (n = 23). Twelve medical consultations were obtained when a patient took an antiplatelet medication, and 11 medical consultations were obtained before surgery in the warfarin group. In the DOAC group, no medical consultations were recorded, nor were any of the DOAC medications discontinued before surgery.

Overall, this study has the advantage of a large sample size of diverse patients who took antiplatelet and/or anticoagulant drugs and underwent an invasive periodontal procedure in an institutional environment. The procedures were well documented, detailed, and varied, which is an advantage over previous large studies.[18,19] However, the study is limited by its retrospective study design, reliance on the practitioners' documentation, lack of a comparison group of healthy patients or patients whose anticoagulant was interrupted, exclusion of 361 records because of incomplete data in the health record, and the possibility that postoperative bleeding may have occurred in a setting where the patient went to a facility other than the study setting. This limits the accuracy, completeness, and interpretation of the existing data set. Also, it is important to consider that patients being treated in a university setting may be unique from those seeking care in private practice settings, as well as the fact that a limited number of patients

took a DOAC in this study cohort. Thus, our ability to make accurate interpretations of the use of DOACs associated with bleeding events was restricted by these small numbers.

CONCLUSIONS

This study revealed that there is a low occurrence of postoperative bleeding events in patients undergoing invasive periodontal procedures, regardless of the use of an antiplatelet or anticoagulant, continuation or discontinuation of the medication, presence of a medical comorbidity, or smoking status. The study also revealed that further study of DOAC use during oral surgical procedures is warranted.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.oooo.2019.04.005.

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