International Journal of Dental Research and Allied Sciences
2024, Volume 4, Issue 2, Page No: 27-35

Available online at: www.tsdp.net

ISSN: 3062-3502

Original Article

Bleeding Outcomes and Management in Tooth Extractions Among Patients on Direct Oral Anticoagulants: A Prospective Cohort Study

Elif Çelik[1], Ahmet Arslan[1]*, Fatma Şahin[1]

[1]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Bursa Uludağ University, Bursa, 16120, Turkey.

***E-mail** ✉ a.arslan474@gmail.com

Received: 15 May 2024; **Revised:** 15 August 2024; **Accepted:** 16 August 2024

ABSTRACT

This prospective study investigated the frequency and severity of bleeding during and after tooth extractions in patients taking direct oral anticoagulants (DOACs). Patients requiring at least one extraction were enrolled, with their DOAC therapy either continued or temporarily paused. Participants were grouped according to the number of teeth removed (≤3 or >3), the use of flap elevation, and whether osteotomy was performed. Bleeding was monitored during the procedure, at 20, 40, 60, and 80 minutes post-procedure, and daily for the first week. A total of 49 patients were included (rivaroxaban, n=17; apixaban, n=16; edoxaban, n=8; dabigatran, n=8), of whom 33 withheld DOACs before surgery. Extraction of more than three teeth, flap elevation, and osteotomy were associated with higher bleeding incidence ($p < 0.05$). Bleeding events were more frequent in patients on rivaroxaban and apixaban. Although DOAC therapy may increase the risk of bleeding across all perioperative phases, most events were minor and manageable. Temporarily stopping DOACs reduced bleeding during the procedure but had no significant effect on post-operative hemorrhage.

Keywords: Direct oral anticoagulants, Dental extraction, Oral surgery, Perioperative bleeding, Post-extraction hemorrhage, Anticoagulation management

How to Cite This Article: Çelik E, Arslan A, Şahin F. Bleeding Outcomes and Management in Tooth Extractions Among Patients on Direct Oral Anticoagulants: A Prospective Cohort Study. Int J Dent Res Allied Sci. 2024;4(2):27-35. https://doi.org/10.51847/0V5ekqXGIG

Introduction

Direct oral anticoagulants (DOACs) have become increasingly favored in recent years because of their predictable pharmacokinetics and perceived convenience over traditional anticoagulants, such as warfarin, by eliminating the need for routine dose adjustments [1]. These drugs achieve anticoagulation by selectively inhibiting specific components of the coagulation cascade, thereby preventing thrombus formation. Dabigatran functions as a direct thrombin inhibitor, whereas apixaban, rivaroxaban, and edoxaban target factor Xa [2].

Despite their clinical benefits, DOACs carry an inherent risk of bleeding, particularly in the perioperative period during dental surgical interventions like tooth extractions [3]. While management strategies for patients on vitamin K antagonists (VKAs) during dental procedures are well-established [4], evidence on DOACs remains limited. For VKAs, Perry *et al*. [5] proposed standardized management including INR assessment within 72 hours before the procedure, no intervention for INR values below 4, and the use of local hemostatic measures combined with 5% tranexamic acid mouthwash four times daily for 48 hours post-procedure. Douketis *et al*. [6] evaluated bleeding outcomes in 460 patients on oral anticoagulants undergoing dental interventions, finding no significant differences between warfarin and dabigatran groups, although urgent procedures were associated with higher bleeding or thromboembolic risks. Similarly, Valenzuela-Mencia *et al*. [7] suggested that DOAC users might have a higher likelihood of post-extraction

bleeding compared with healthy individuals, but limited data constrained the strength of these recommendations. Notably, single-tooth extractions generally present minimal post-operative bleeding risk, supporting the continuation of DOACs for such procedures [8]. Additionally, only a small proportion of patients require repeated local hemostatic interventions for persistent bleeding, indicating that routine modification of DOAC therapy is rarely necessary [9].

Managing post-operative bleeding in patients on DOACs necessitates balancing hemorrhage control with the risk of thromboembolism. Unlike VKAs, DOACs have rapid onset and shorter half-lives, complicating the reversal of anticoagulation [10]. Conventional reversal agents such as vitamin K or fresh frozen plasma are ineffective against DOACs, prompting the development of specific antidotes like idarucizumab for dabigatran and andexanet alfa for rivaroxaban and apixaban, which can quickly counteract anticoagulant effects in emergencies [11].

Decisions regarding the use of reversal agents must consider both bleeding severity and individual thrombotic risk [11]. For minor post-extraction bleeding, local interventions—such as direct pressure, topical hemostatic agents, and tranexamic acid rinses—are often sufficient, negating the need for systemic reversal [12]. However, in cases of significant or persistent hemorrhage, particularly in patients with high thromboembolic risk, administration of specific antidotes may be warranted to achieve prompt hemostasis and reduce morbidity and mortality [11].

The timing of dental extractions relative to DOAC dosing is also critical; because of the drugs' short half-life, brief discontinuation may lower bleeding risk without substantially increasing thrombotic risk [12].

Given the growing use of DOACs and the challenges they pose in balancing bleeding and thrombotic risks during dental surgery, evaluating post-operative hemorrhage in these patients is essential [13]. Despite the clinical importance, current evidence remains limited and management protocols are heterogeneous. Accordingly, this study aimed to investigate the bleeding risk associated with tooth extractions in patients receiving direct oral anticoagulants.

Materials and Methods

Study protocol

This investigation was conducted as a single-center, non-randomized clinical trial with a follow-up period of seven days. Ethical approval was obtained from the Institutional Review Board of the University Hospital of Pisa (Ethics Committee for the North-West Tuscany Area, approval no. 17796/2020). All procedures were carried out in accordance with the ethical principles of the Declaration of Helsinki for research involving human participants. The trial was prospectively registered on ClinicalTrials.gov under the identifier NCT06365242. Reporting of the study was aligned with the STROBE guidelines for observational studies [7]. The study design and patient flow are illustrated in **Figure 1**.

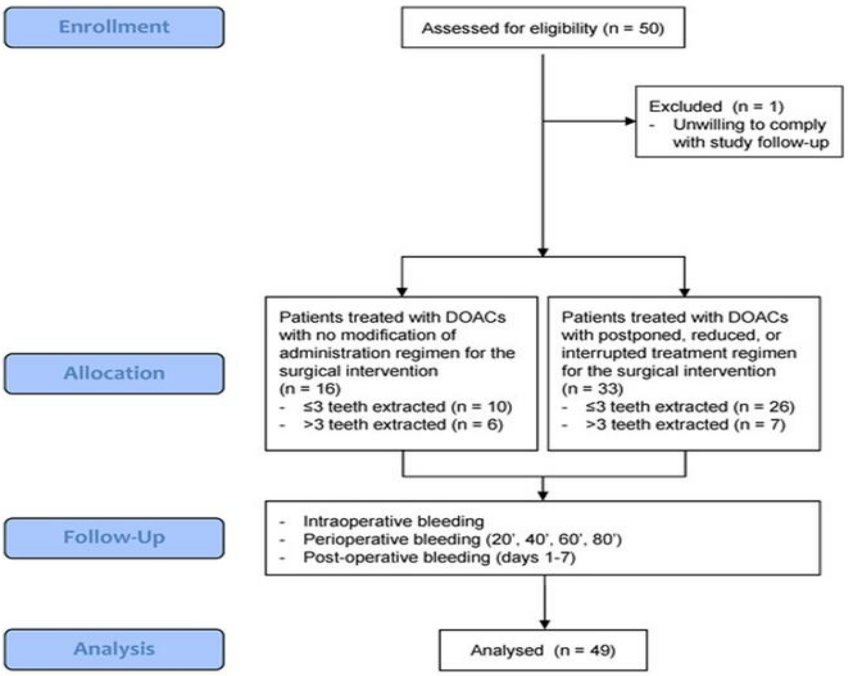

Figure 1. CONSORT 2010 flow diagram.

Patient recruitment

This study enrolled patients who were consecutively referred to the Unit of Dentistry and Oral Surgery for dental extractions between 2021 and 2023. Prior to participation, all patients provided written informed consent. To ensure privacy and regulatory compliance, all personal data were anonymized or encrypted.

Eligibility criteria included: adults over 18 years of age, ongoing treatment with direct oral anticoagulants (DOACs), requirement of at least one tooth extraction, and willingness to participate in the study. Patients were excluded if they were younger than 18, receiving antiplatelet therapy or vitamin K antagonists, or had known congenital or acquired bleeding disorders, such as hemophilia, coagulation factor deficiencies, von Willebrand disease, thrombocytopenia, or advanced liver disease.

All participants underwent baseline laboratory evaluations, including complete blood count, prothrombin time (PT), partial thromboplastin time (PTT), and INR.

Study grouping

Participants were assigned to groups based on the management of their DOAC therapy, as determined by their cardiologist:

- *Group 1:* Patients who continued their usual DOAC regimen without changes for the dental procedure.
- *Group 2:* Patients whose DOAC therapy was altered—either temporarily paused, reduced, or postponed—prior to the procedure according to clinical guidance from their cardiologist or primary care physician.

Patients were further categorized according to the specific DOAC prescribed (rivaroxaban, apixaban, edoxaban, or dabigatran). Additional data collected included systemic health status, DOAC dosage, body mass index (BMI), and smoking history. Vital signs, including blood pressure, heart rate, oxygen saturation, respiratory rate, body temperature, and blood glucose, were recorded on the day of surgery. All information was systematically recorded in a dedicated case report form (CRF).

Surgical procedure

Extractions were performed under standardized, minimally invasive conditions for all participants **(Figure 2)**.

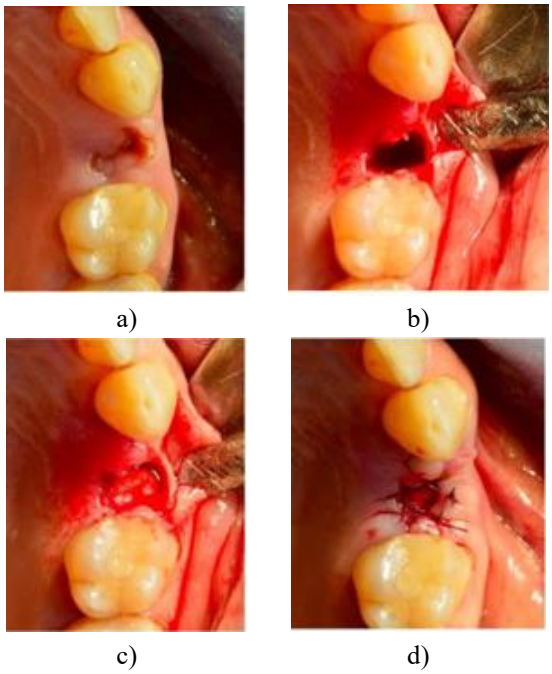

Figure 2. Tooth 2.5 requiring extraction (a), flap elevation and tooth removal (b), collagen sponge application (c), and suture placement (d).

Surgical procedure

Tooth extractions were performed under standardized conditions using local anesthesia (2% mepivacaine with 1:100,000 epinephrine). Elevators and forceps were used for all extractions, with a full-thickness flap raised in cases of complex or difficult extractions **(Figure 2)**. Patients in both DOAC management groups were further categorized based on the number of teeth removed: ≤3 teeth or >3 teeth. This cut-off was chosen according to previous studies, which suggest that extracting up to three teeth generally carries a low bleeding risk [14].

After extraction, the alveolar sockets were carefully debrided and irrigated with saline, followed by placement of a collagen sponge. Soft tissues were then repositioned and secured using single interrupted absorbable sutures. No additional hemostatic interventions were routinely applied at this stage. Post-operative antibiotic therapy (amoxicillin 2 g/day or clindamycin 1.2 g/day for penicillin-allergic patients) was prescribed as clinically indicated based on systemic health, with no evidence suggesting that antibiotic co-administration increased bleeding risk in patients on DOACs [15, 16], unlike what has been reported for warfarin [17]. Analgesia was managed with acetaminophen 1 g as needed.

Bleeding assessment

Intra-operative bleeding was defined as any active hemorrhage that impaired visibility of the surgical field. Peri-operative bleeding was monitored within the

first 80 minutes after the procedure, recorded at 20-minute intervals, and defined as oozing or active bleeding not controllable by standard local measures or gauze compression. When bleeding occurred, gauze soaked with tranexamic acid was applied; persistent bleeding after 20 minutes prompted the use of oxidized cellulose and additional sutures. In cases of prolonged hemorrhage, diathermocoagulation was performed.

Post-operative bleeding was defined as bleeding or oozing beyond 12 hours post-surgery that resulted in hematoma formation, required clinical intervention, or led to hospitalization.

Follow-up

Patients were provided with detailed instructions for post-operative wound care and asked to complete a daily questionnaire for the first week. The questionnaire recorded the number of bleeding episodes, interventions employed, and any additional analgesic use. At 7 days post-extraction, patients returned for a follow-up assessment to evaluate wound healing, suture removal, and the presence of complications such as edema, pain, suppuration, or alveolar osteitis. Post-operative bleeding assessments were conducted by a clinician not involved in the surgical procedures.

Sample size calculation

The study aimed to determine the incidence of bleeding events following tooth extractions in patients on different DOACs. Based on Berton *et al*. [8], who reported a 20% incidence of bleeding requiring additional intervention, a minimum of 28 participants was required to achieve 90% power at a 0.05 significance level. To account for potential dropouts, the study aimed to enroll 50 patients.

Statistical analysis

Data analysis was performed by a dental researcher with expertise in biostatistics who was not involved in patient care or data collection. Continuous variables were summarized as means ± standard deviations, and the Shapiro–Wilk test was used to assess normality. Depending on distribution, parametric or non-parametric tests were applied. Group comparisons for quantitative or ordinal variables were performed using the Kruskal–Wallis test, while post-hoc analyses employed the Mann–Whitney U test or Wilcoxon signed-rank test. Categorical variables were analyzed using the chi-squared test or Fisher's exact test. Statistical analyses were conducted using XLStat 2023.1.4 (Addinsoft, Paris, France). Only case report forms (CRFs) with at least 95% completeness were included, and missing data were addressed using regression imputation.

Results and Discussion

Patient characteristics

A total of 49 patients (21 females, 42.9%) completed the study, undergoing a combined total of 136 tooth extractions. One patient was excluded due to non-compliance with the follow-up protocol. The mean age of participants was 72.2 ± 8.3 years. Regarding anticoagulant therapy, 17 patients were on rivaroxaban (16 receiving 20 mg/day, 1 receiving 15 mg/day), 16 patients were on apixaban (9 receiving 10 mg/day, 7 receiving 5 mg/day), 8 patients received edoxaban (6 on 60 mg/day, 2 on 30 mg/day), and 8 patients were on dabigatran (5 taking 300 mg/day, 3 taking 220 mg/day). The average duration of DOAC therapy among participants was 38 ± 27 months. A detailed summary of demographic and clinical characteristics is provided in **Table 1**.

Table 1. Demographic data.

Variables	Total Sample (n = 49)	Rivaroxaban (n = 17)	Apixaban (n = 16)	Edoxaban (n = 8)	Dabigatran (n = 8)	p Value
Age (years; mean [SD])	72.2 (8.3)	72 (5.6)	72.8 (9.7)	70.8 (11)	73.1 (8.3)	0.807
Gender (females [%])	21 (42.9)	9 (53.0)	6 (37.5)	4 (50.0)	2 (25.0)	0.560
BMI (kg/m^2; mean [SD])	28.3 (5.5)	29.2 (4.2)	28 (5.3)	26.4 (2.1)	32.7 (8.6)	0.133
Non-smokers [%])	43 (87.8)	12 (70.6)	8 (50.0)	5 (62.5)	2 (25.0)	0.133
Systolic pressure (mean [S]D)	133 (23.8)	134.4 (21.3)	125.7 (26.3)	136.5 (12.5)	140 (31.6)	0.299
Diastolic pressure (mean [SD])	79 (11.5)	82.6 (12.5)	76.6 (11.7)	75.3 (8.0)	79.3 (11.4)	0.293
Body temperature (mean [SD])	36.4 (0.4)	36.1 (0.4)	36.4 (0.3)	36.7 (0.3)	36.3 (0.3)	0.026
Glycemia (mean [SD])	121.4 (49.0)	119.3 (30.0)	98 (11.4)	119.9 (28.7)	173.9 (93.9)	0.004
Heart rate (mean [SD])	77.6 (14.4)	75.8 (10.1)	72.3 (11.1)	83 (24.5)	74.4 (15.0)	0.712

Of the 49 patients included, 33 (67%) temporarily discontinued DOAC therapy prior to surgery, with an average interruption period of 28.5 ± 13.0 hours. The decision to pause treatment was made by cardiologists for 14 patients, by general practitioners for 4 patients, by other specialists in 11 cases, and 4 patients independently chose to withhold their medication. All patients abstained from DOACs for at least 24 hours following the extraction procedure.

The primary indications for anticoagulant therapy included atrial fibrillation (55.1%), deep vein thrombosis (24.5%), ischemic cardiomyopathy (18.3%), pulmonary embolism (16.3%), valvular disorders (12.2%), and heart failure (8%). Comorbidities were common, with 40.8% of patients diagnosed with hypertension and 24.5% with type II diabetes. The mean body mass index (BMI) was 28.3 ± 5.5 kg/m², consistent with an overweight population. Six patients (12.2%) were active smokers, while 24 (49%) were former smokers. Baseline vital signs were: systolic blood pressure 133 ± 23.8 mmHg, diastolic blood pressure 79 ± 11.5 mmHg, heart rate 77.6 ± 14.4 bpm, oxygen saturation 96 ± 1.7%, respiratory rate 15 ± 2 breaths/min, body temperature 36.4 ± 0.4 °C, and blood glucose 121.4 ± 49 mg/dL. Statistically significant baseline differences were observed for body temperature and glycemia.

Laboratory analyses **(Table 2)** revealed that patients receiving rivaroxaban had a significantly higher prothrombin time (PT) ratio compared with those on apixaban (p = 0.038) and edoxaban (p = 0.03). Additionally, rivaroxaban-treated patients showed a significantly prolonged partial thromboplastin time (PTT) relative to other DOAC groups (p = 0.001). The mean estimated glomerular filtration rate (eGFR) was 82.6 mL/min, indicating mild renal impairment among the cohort.

Table 2. Blood testing values and comparison between groups.

Variables (Mean [SD])	Total Sample (n = 49)	Rivaroxaban (n = 17)	Apixaban (n = 16)	Edoxaban (n = 8)	Dabigatran (n = 8)	p Value
Red blood cells (10^6/mm^3)	4.33 (0.38)	4.31 (0.37)	4.51 (0.66)	4.06 (0.69)	4.43 (0.60)	0.313
Hemoglobin (g/dL)	12.55 (2.07)	12.29 (2.09)	13.35 (1.99)	12.13 (1.64)	13.28 (1.73)	0.431
Platelets (10^3/mm^3)	216.47 (58.46)	226.00 (53.53)	233.0 (64.99)	217.50 (110.71)	236.13 (55.48)	0.728
PT ratio	1.34 (0.17)	1.37 (0.15)	1.25 (0.22)	1.18 (0.12)	1.20 (0.18)	0.014
INR	1.31 (0.15)	1.31 (0.15)	1.25 (0.23)	1.25 (0.03)	1.21 (0.09)	0.318
aPTT (sec)	36.57 (3.75)	37.06 (3.89)	32.06 (3.52)	32.14 (3.41)	46.95 (8.75)	<0.001
aPTT ratio	1.04 (0.14)	1.06 (0.13)	1.02 (0.08)	1.22 (0.01)	1.51 (0.31)	<0.001
Fibrinogen (mg/dL)	367.07 (81.52)	366.33 (55.80)	351.5 (86.41)	351.20 (63.83)	403.29 (101.92)	0.299
Creatinine (mg/dL)	0.98 (0.36)	0.98 (0.35)	0.92 (0.27)	0.87 (0.26)	1.07 (0.29)	0.062
Estimated glomerular filtration rate	82.61 (10.63)	77.23 (13.48)	84.46 (13.43)	84.59 (16,92)	90.31 (21.17)	0.646

Tooth extraction characteristics

In this cohort, the majority of patients (36 out of 49, 73.5%) underwent extraction of three or fewer teeth. Procedures involving ≤3 teeth were associated with a lower incidence of peri-operative bleeding. Notably, differences in post-operative bleeding related to the number of teeth removed were observed only at the 20-minute (T2) and 7-day (T7) evaluations. Extraction of neighboring teeth did not appear to influence hemorrhage rates.

Complex procedures, defined by either flap elevation or osteotomy, accounted for 57.1% of all extractions, with flap elevation performed in 26.5% and osteotomy in 30.6% of cases. Patients undergoing flap elevation experienced higher peri-operative bleeding, reaching statistical significance at 20 minutes post-procedure. Furthermore, post-operative bleeding was consistently elevated across all follow-up time points in cases requiring flap elevation.

Intra-operative bleeding

During the extraction procedures, 27 patients (55.1%) experienced intra-operative bleeding. This included 12 patients on apixaban, 9 on rivaroxaban, and 3 each on edoxaban and dabigatran. When more than three teeth were extracted, bleeding occurred in 69.2% of cases, compared to 50% for extractions of three or fewer teeth (p < 0.001). No significant association was found

between the continuation or temporary suspension of DOAC therapy and intra-operative bleeding.

Peri-operative bleeding

Within the first 20 minutes post-extraction, 28 patients (57.1%) exhibited peri-operative bleeding. The distribution by anticoagulant was as follows: 14 on apixaban, 6 on edoxaban, 5 on rivaroxaban, and 3 on dabigatran. Patients on apixaban demonstrated significantly higher bleeding rates at 20 minutes compared to those on rivaroxaban **(Table 3)**. Additionally, peri-operative bleeding was more common in posterior tooth extractions than anterior ones (81% vs. 64%) and in complex extractions compared to simpler procedures (26% vs. 13%).

Table 3. Peri-operative bleeding and comparison between groups.

Bleeding	Total Sample (n = 49)	Rivaroxaban (n = 17)	Apixaban (n = 16)	Edoxaban (n = 8)	Dabigatran (n = 8)	p Value
20′ min (n [%])	28 (57.1)	5 (29.4)	14 (87.5)	6 (75.0)	3 (37.5)	0.010
40′ min (n [%])	19 (38.8)	6 (35.3)	7 (43.75)	4 (50.0)	2 (25.0)	0.731
60′ min (n [%])	14 (28.6)	5 (29.4)	4 (25.0)	3 (37.5)	2 (25.0)	0.928
80′ min (n [%])	8 (16.3)	5 (29.4)	3 (18.75)	0 (0.0)	0 (0.0)	0.157

At 40 minutes post-procedure, 19 patients (38.8% of the cohort) continued to exhibit peri-operative bleeding, including 7 on apixaban, 6 on rivaroxaban, 4 on edoxaban, and 2 on dabigatran. By 60 minutes, bleeding persisted in 14 patients (28.6%), with 5 on rivaroxaban, 4 on apixaban, 3 on edoxaban, and 2 on dabigatran. At 80 minutes, only 8 patients (16.3%) demonstrated ongoing bleeding—5 on rivaroxaban and 3 on apixaban. No significant differences in peri-operative bleeding were observed at any time point when comparing patients who temporarily suspended DOAC therapy with those who continued their usual regimen.

Post-operative bleeding

The highest incidence of post-operative bleeding occurred on the first day, affecting 23 patients (46.9%), distributed as 11 on rivaroxaban, 7 on apixaban, 4 on edoxaban, and 1 on dabigatran. By the second day, 11 patients (22.4%) experienced bleeding (7 rivaroxaban, 3 apixaban, 1 edoxaban), and on day 3, 4 patients (8.2%) had bleeding episodes (distributed among rivaroxaban, apixaban, and edoxaban). Between days 4 and 7, bleeding was observed exclusively in patients on rivaroxaban, with two episodes on days 4 and 5 and one episode on days 6 and 7. No statistically significant differences were noted during this later period.

When stratified by DOAC type, statistically significant differences were identified at 20 minutes (T1) and 40 minutes (T2) between patients on rivaroxaban and dabigatran ($p = 0.016$ at T1, $p = 0.023$ at T2). Although not statistically significant, there was a tendency for early post-operative bleeding (T1–T2) in patients who maintained DOAC therapy, whereas delayed bleeding (T3–T7) was more frequently observed in those who temporarily withheld their medication **(Table 4)**.

Table 4. Post-operative bleeding rates and comparison between suspension or continuation of OAC therapy.

Bleeding	DOAC Continued (n = 16)	DOAC Suspended (n = 33)	p Value
T1 (n [%])	8 (50.0)	15 (45.6)	0.357
T2 (n [%])	5 (31.3)	6 (18.2)	0.304
T3 (n [%])	1 (6.3)	3 (9.1)	0.733
T4 (n [%])	1 (6.3)	1 (3.0)	0.587
T5 (n [%])	0 (0.0)	2 (6.1)	0.315
T6 (n [%])	0 (0.0)	1 (3.0)	0.482
T7 (n [%])	0 (0.0)	2 (6.1)	0.315

The present study indicates that approximately half of patients on DOAC therapy experienced intra- or early peri-operative bleeding following tooth extractions, with the peak of post-operative hemorrhage occurring on the first day after surgery. Whether DOACs were continued or temporarily withheld did not significantly alter bleeding outcomes, provided that appropriate local hemostatic interventions were applied. This finding aligns with the pharmacological characteristics of DOACs, including predictable pharmacokinetics and relatively short half-lives, suggesting that routine discontinuation may not be necessary for most dental procedures.

Patients undergoing extraction of more than three teeth in a single session exhibited higher rates of bleeding across all intra-, peri-, and post-operative time points, with significant differences observed except at the earliest measurement (T1). This supports previous literature identifying three teeth as a practical threshold

for low-risk extractions [14]. Other studies have suggested that for procedures involving fewer than four teeth, DOAC therapy can generally be maintained if local hemostatic measures are employed [18]. Timing extractions at least 4 hours after the last DOAC dose has also been recommended to minimize bleeding, and avoidance of multiple contiguous premolar or molar extractions in a single session has been suggested [19]. Interestingly, in our cohort, removal of adjacent teeth did not emerge as a significant risk factor.

The type of anticoagulant appeared to influence bleeding risk. Rivaroxaban was associated with higher bleeding rates, likely due to its effect on prolonging prothrombin and partial thromboplastin times [20, 21]. In contrast, apixaban, as a highly selective factor Xa inhibitor acting on both free and bound FXa, demonstrates a more controlled anticoagulant effect [22]. Overall, bleeding events in this study occurred in roughly 50% of patients, whereas prior reports have documented lower incidences: Yagyuu *et al*. observed 10.4% post-extraction bleeding in DOAC-treated patients [23], and Hiroshi *et al*. reported rates of 1.65% for dabigatran and 3.41% for rivaroxaban [24]. Patel *et al*. documented post-operative bleeding in 13% of cases, with half being self-limiting, concluding that modification of DOAC regimens should be individualized [25].

Evidence regarding the need to modify DOAC therapy before dental surgery remains conflicting. Early approaches advocated either discontinuation 24 hours before the procedure or continuation of therapy, whereas more recent perspectives suggest that timing adjustments may suffice in invasive procedures [26]. Although the thromboembolic risk from short-term DOAC interruption is low, temporary cessation should generally be reserved for patients with high anticipated bleeding risk. For low-risk procedures, interruption is often unnecessary, and heparin bridging is discouraged due to increased bleeding without reduction in thromboembolic events [27].

Guidelines for timing extractions relative to DOAC dosing vary. Van Diermen *et al*. recommend scheduling procedures 1–3 hours after the last dose [28], while the European Heart Rhythm Association advises targeting trough drug concentrations approximately 12 hours post-dose [29]. Brennan and colleagues found comparable bleeding rates among apixaban (39%), rivaroxaban (37%), and dabigatran (27%) when therapy was continued, though patients on rivaroxaban who took the morning dose on the day of extraction were more likely to experience bleeding, with pre-extraction rivaroxaban levels roughly double those in patients who had taken their last dose the previous evening [30].

Overall, our findings support the safety of performing tooth extractions in patients on DOAC therapy using local hemostatic measures, without routinely interrupting or modifying anticoagulant regimens, as these drugs do not appear to substantially elevate post-extraction bleeding risk [8, 23, 31, 32]. Nevertheless, considerable variability exists in clinical practice regarding temporary DOAC discontinuation, ranging from 12 to 120 hours prior to surgery [33], highlighting the ongoing uncertainty and need for individualized decision-making.

In our cohort, rivaroxaban and apixaban were associated with higher bleeding risk. Temporary suspension of DOAC therapy did not reduce post-operative bleeding. Surgical procedures involving flap elevation were linked to increased bleeding at 20 minutes post-operation and across the T1–T7 period, while intra- and peri-operative bleeding were also elevated in cases requiring osteotomy at 20 and 40 minutes after the procedure.

Although definitive conclusions cannot be drawn due to the relatively small sample size, our findings suggest that bleeding in patients on DOAC therapy tended to be more frequent following extractions of posterior teeth compared to anterior teeth, as well as in complex procedures relative to simpler ones.

This study has several limitations. First, the modest sample size and uneven distribution across DOAC types limited the ability to establish a standardized clinical protocol. Bleeding risk was evaluated for the cohort as a whole, without further stratification by specific anticoagulant, because patient numbers for each medication were unequal. Selection bias may have occurred, as pre-operative DOAC management varied, with most patients pausing their anticoagulant therapy but not according to a uniform protocol. The timing of tooth extractions relative to the last DOAC dose was not accounted for, given that patients took their medications at different times of day, which precluded scheduling procedures according to drug half-lives. Additionally, anticoagulant intensity at the time of surgery and post-operatively was not measured using DOAC-specific assays, such as calibrated anti-Factor Xa or other Anti-Xa tests, representing another limitation. Variability in surgical factors—including the number of teeth removed, flap elevation, and osteotomy—may also limit the comparability of cases and the generalizability of the results.

Despite these limitations, the study provides valuable insights into the dynamics of post-operative bleeding in patients on different DOACs, aided by careful post-

operative monitoring. Further research with larger, more balanced samples and standardized protocols is needed to develop clear, evidence-based guidelines for the safe management of anticoagulated patients during dental procedures. Such evidence would enhance patient safety and provide clinicians with greater confidence in managing anticoagulation in oral surgery.

Conclusion

In this cohort, patients receiving direct oral anticoagulants exhibited similar rates of intra-operative, peri-operative, and post-operative bleeding. Observed bleeding events were generally mild and effectively controlled with local measures such as gauze compression. Temporary suspension of DOAC therapy did not significantly affect peri-operative or post-operative bleeding. Nevertheless, larger studies with more balanced patient groups are needed to confirm these findings and guide standardized management strategies for anticoagulated patients undergoing dental extractions.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Lee JY, Park SH, Kim DM, Ko KA, Park JY, Lee JS, et al. Risk of post-operative bleeding after dentoalveolar surgery in patients taking anticoagulants: A cohort study using the common data model. Sci Rep. 2024;14(1):7787.
2. Darwish G. The effect of direct oral anticoagulant therapy (DOACs) on oral surgical procedures: A systematic review. BMC Oral Health. 2023;23(1):743.
3. Ono S, Ishimaru M, Yokota I, Konishi T, Okada A, Ono Y, et al. Risk of post-extraction bleeding with direct oral anticoagulant compared with warfarin: Retrospective cohort study using large scale claims data in Japan. Thromb Res. 2023;222(1):24–30.
4. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, et al. The 2018 European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Eur Heart J. 2018;39(16):1330–93.
5. Perry DJ, Noakes TJC, Helliwell PS; British Dental Society. Guidelines for the management of patients on oral anticoagulants requiring dental surgery. Br Dent J. 2007;203(7):389–93.
6. Douketis JD, Healey JS, Brueckmann M, Fraessdorf M, Spyropoulos AC, Wallentin L, et al. Urgent surgery or procedures in patients taking dabigatran or warfarin: Analysis of perioperative outcomes from the RE-LY trial. Thromb Res. 2016;139(1):77–81.
7. Valenzuela-Mencia J, Serrera-Figallo M, Torres-Lagares D, Machuca-Portillo G, Sánchez-Fernández E, Valmaseda-Castellón E, et al. Clinical practice guideline of the Spanish Society of Oral Surgery for oral surgery in patients with coagulation disorders. Med Oral Patol Oral Cir Bucal. 2024;29(1):e58–e66.
8. Berton F, Costantinides F, Rizzo R, Franco A, Contarin J, Stacchi C, et al. Should we fear direct oral anticoagulants more than vitamin K antagonists in simple single tooth extraction? A prospective comparative study. Clin Oral Investig. 2019;23(8):3183–92.
9. Woolcombe SA, Ball RE, Patel JP. Managing direct oral anticoagulants in accordance with the Scottish Dental Clinical Effectiveness Programme guidance for patients undergoing dentoalveolar surgery. Br Dent J. 2022;232(9):547–54.
10. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, et al. 2019 AHA/ACC/HRS focused update of the 2014 guideline for the management of patients with atrial fibrillation. Heart Rhythm. 2019;16(8):e66–e93.
11. Nisi M, Carli E, Gennai S, Gulia F, Izzetti R. Hemostatic agents for the management of bleeding risk associated with oral anticoagulant therapy following tooth extraction: A systematic review. Appl Sci. 2022;12(21):11017.
12. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344–9.
13. Abayon M, Kolokythas A, Harrison S, Elad S. Dental management of patients on direct oral anticoagulants: Case series and literature review. Quintessence Int. 2016;47(8):687–96.

14. Lupi SM, Rodriguez YBaena A. Patients taking direct oral anticoagulants (DOAC) undergoing oral surgery: A review of the literature and a proposal of a peri-operative management protocol. Healthcare (Basel). 2020;8(3):281.
15. Sanborn D, Sugrue A, Amin M, Mehta R, Farwati M, Deshmukh AJ, et al. Outcomes of direct oral anticoagulants co-prescribed with common interacting medications. Am J Cardiol. 2022;162(1):80–5.
16. Yagi T, Mannheimer B, Reutfors J, Ursing J, Giunta DH, Kieler H, et al. Bleeding events among patients concomitantly treated with direct oral anticoagulants and macrolide or fluoroquinolone antibiotics. Br J Clin Pharmacol. 2023;89(2):887–97.
17. Mar PL, Gopinathannair R, Gengler BE, Chung MK, Perez A, Dukes J, et al. Drug interactions affecting oral anticoagulant use. Circ Arrhythm Electrophysiol. 2022;15(4):e007956.
18. Lababidi E, Breik O, Savage J, Engelbrecht H, Kumar R, Crossley CW. Assessing an oral surgery specific protocol for patients on direct oral anticoagulants: A retrospective controlled cohort study. Int J Oral Maxillofac Surg. 2018;47(8):940–6.
19. Cocero N, Basso M, Grosso S, Carossa S. Direct oral anticoagulants and medical comorbidities in patients needing dental extractions: Management of the risk of bleeding. J Oral Maxillofac Surg. 2019;77(3):463–70.
20. Firriolo FJ, Hupp WS. Beyond warfarin: The new generation of oral anticoagulants and their implications for the management of dental patients. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012;113(4):431–41.
21. Little JW. New oral anticoagulants: Will they replace warfarin? Oral Surg Oral Med Oral Pathol Oral Radiol. 2012;113(5):575–80.
22. Granger CB, Alexander JH, McMurray JJV, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981–92.
23. Yagyuu T, Kawakami M, Ueyama Y, Imada M, Kurihara M, Matsusue Y, et al. Risks of postextraction bleeding after receiving direct oral anticoagulants or warfarin: A retrospective cohort study. BMJ Open. 2017;7(8):e015952.
24. Hiroshi I, Natsuko SY, Yutaka I, Masayori S, Hiroyuki N, Hirohisa I. Frequency of hemorrhage after tooth extraction in patients treated with a direct oral anticoagulant: A multicenter cross-sectional study. PLoS One. 2022;17(4):e0266011.
25. Patel JP, Woolcombe SA, Patel RK, Obisesan O, Roberts LN, Bryant C, et al. Managing direct oral anticoagulants in patients undergoing dentoalveolar surgery. Br Dent J. 2017;222(4):245–9.
26. Cabbar F, Cabbar AT, Coşansu K, Çekirdekçi EI. Effects of direct oral anticoagulants on quality of life during periprocedural management for dental extractions. J Oral Maxillofac Surg. 2019;77(5):904–11.
27. Johnston S. An evidence summary of the management of patients taking direct oral anticoagulants (DOACs) undergoing dental surgery. Int J Oral Maxillofac Surg. 2016;45(5):618–30.
28. Van Diermen DE, van der Waal I, Hoogstraten J. Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013;116(6):709–16.
29. Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, et al. European Heart Rhythm Association practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation. Europace. 2013;15(5):625–51.
30. Brennan Y, Gu Y, Schifter M, Crowther H, Favaloro EJ, Curnow J. Dental extractions on direct oral anticoagulants vs. warfarin: The DENTST study. Res Pract Thromb Haemost. 2020;4(2):278–84.
31. Mauprivez C, Khonsari RH, Razouk O, Goudot P, Lesclous P, Descroix V. Management of dental extraction in patients undergoing anticoagulant oral direct treatment: A pilot study. Oral Surg Oral Med Oral Pathol Oral Radiol. 2016;122(5):e146–55.
32. Caliskan M, Tükel HC, Benlidayi ME, Deniz A. Is it necessary to alter anticoagulation therapy for tooth extraction in patients taking direct oral anticoagulants? Med Oral Patol Oral Cir Bucal. 2017;22(6):e767–73.
33. Miller SG, Miller CS. Direct oral anticoagulants: A retrospective study of bleeding, behavior, and documentation. Oral Dis. 2018;24(2):243–8.