



ORIGINAL ARTICLE

# Risk of postoperative bleeding following dental extractions in patients on antithrombotic treatment

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## KEYWORDS

Dental extraction;  
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Anticoagulant

**Abstract** *Introduction:* The risk of bleeding after dental extractions in patients taking antithrombotic medication is not well known. This study aims to investigate the incidence of postoperative bleeding following dental extractions in adult patients taking antithrombotic medication in Saudi Arabia.

*Methods:* This retrospective study included 539 patients aged 18–93 years who attended 840 appointments for dental extractions from January 2012 to June 2016 at a tertiary care hospital in Saudi Arabia. Patients who returned with a complaint of bleeding were treated with local hemostatic measures as outpatients.

*Results and Conclusion:* Only 1.7% of extraction appointments were associated with postoperative bleeding. The highest risk of bleeding was noted in patients receiving warfarin (3.88%), whereas those on clopidogrel had no significant risk of bleeding. Women were found to have the highest rate of bleeding, particularly those on newer oral anticoagulant medications.

Dental extractions can be safely done in adults receiving antithrombotic treatment, provided established guidelines are followed; therefore, dental professionals must exercise caution when planning invasive dental treatment for patients on continued antithrombotic therapy.

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## 1. Introduction

Hemostasis following dental extractions is achieved via coagulation. Patients with conditions such as atrial fibrillation, prosthetic heart valves, congestive heart failure, or venous thromboembolism (VTE<sup>1</sup>) are frequently placed on anticoagulants to prevent cardiovascular complications (e.g., fibrillation) (Rahman et al., 2014) with an increasing incidence (Hersi et al.,

<sup>1</sup> AF atrial fibrillation.

**Table 1** Antithrombotic medication dose modification schedule.

Medication	Lab test	Dose adjustment	Comments
Warfarin (Coumadin)	INR <sup>3</sup>	None	Treat if INR <sup>3</sup> ≤ 3.5. Patients with INR <sup>3</sup> > 3.5 have dose correction and INR <sup>3</sup> correction before surgery
Clopidogrel (Plavix)	None	None	
Aspirin	None	None	
Enoxaparin (Clexane®) once daily	None	Hold the a.m. dose; resume next day	Surgery at least 12 h after the last dose
Enoxaparin (Clexane®) twice daily	None	Hold the dose; take an evening dose if no bleeding	Surgery at least 12 h after the last dose
Heparin (unfractionated heparin)	None	None	
Rivaroxaban (Xarelto)	None	None	For patients with low-risk surgery
	GFR > 50	Withhold 1–2 days before procedure	For patients undergoing higher-risk surgery
	GFR < 50	Withhold 1–2 days before procedure	For patients undergoing higher-risk surgery
Dabigatran (Pradaxa)	None	None	For patients with low-risk surgery
	GFR > 50	Withhold 1–2 days before procedure	For patients undergoing higher-risk surgery
	GFR 30–50	Withhold 2–3 days before procedure	For patients undergoing higher-risk surgery
	GFR < 30	Withhold 2–5 days before procedure	For patients undergoing higher-risk surgery

2014). About 75% of patients with AF<sup>2</sup> in Saudi Arabia are treated with antithrombotic medications (Hersi et al., 2014). These patients receiving antithrombotic medications are at an increased risk of bleeding post-extraction.

Recent evidence from a meta-analysis suggests that the NOACs<sup>3</sup> or new oral anticoagulants (e.g., rivaroxaban and dabigatran) are potentially safer than the conventional anticoagulants for patients undergoing dental implant surgery (Shi et al., 2017). However, risk factors such as International Normalized Ratio (INR) were not controlled for in their analysis, and further controlled clinical studies are warranted. The American College of Chest Physicians evidence-based clinical practice guidelines (Douketis et al., 2012) recommend that all routine dental procedures, including extractions, scaling, and restorative treatments, should be completed without the interruption of warfarin therapy if local hemostatic agents are administered, and the INR is within the recommended therapeutic range.

A recent survey of Saudi medical and dental practitioners indicated that 64.6% of Saudi dentists sought medical consultation before treating patients on antithrombotic medications (Shah et al., 2015). These practitioners are uncertain about treating such patients. Although there are several current international guidelines (Steffel et al., 2018), the risk of postoperative bleeding for dental extractions remains largely undefined, and dental extractions are common for patients receiving antithrombotic therapy (AlSheef et al., 2020). To this end, we evaluated the association of post-extraction bleeding for patients receiving antithrombotic therapy following our customized guidelines.

## 2. Material and Methods

Patient eligibility criterion for the present study was that they underwent dental extraction(s) under local anesthesia while concurrently receiving antithrombotic medications at the den-

tal outpatient clinics in King Fahad Medical City in Saudi Arabia between January 2012 and June 2016.

Patients receiving the following antithrombotic medications were in line with our institutional protocols and guidelines: warfarin (vitamin K antagonist), clopidogrel (antiplatelet P2Y12 inhibitor), heparin, and low molecular weight heparin [enoxaparin] (anticoagulants), or new oral anticoagulants (NOACs<sup>3</sup>) [dabigatran (a direct thrombin inhibitor) and or rivaroxaban (a direct-acting Factor Xa inhibitor)] (Table 1).

Forty-three patients were excluded for the following reasons: if patients were younger than 18 years, if patients receiving warfarin had an INR test result > 3.5 (for that visit), if patients did not follow the medication protocol, if patients were receiving their antithrombotic medications from another institution, if patients possessed had additional comorbidities that affect bleeding (liver dysfunction, renal failure, thrombocytopenia, or hemophilia), if patients underwent dental extractions under general anesthesia, or if patients returning with a complaint of bleeding had no evidence of bleeding detected on clinical oral examination (see Table 2).

The antithrombotic medication routine was continued throughout all dental appointments to minimize thrombosis risk, as per our institutional guidelines. Patients with a higher bleeding risk were defined as those having five or more dental extractions at one appointment. Patients receiving warfarin underwent INR testing within 24 h before their procedure, and those with an INR > 3.5 were referred to the anticoagulation clinic for adjustment of their dosage. Only two patients required a warfarin dose modification before extraction, and neither experienced bleeding postoperatively.

Patients receiving warfarin (with an INR ≤ 3.5), clopidogrel or aspirin continued to have their dental extraction with no medication adjustment (Grines et al., 2007). Patients on enoxaparin, rivaroxaban, and dabigatran had dosing modifications if indicated, according to the risk of bleeding during surgery and renal function (Brown et al., 2013; Cockcroft, 1976; Winter et al., 2012).

<sup>2</sup> VTE venous thromboembolism/VTE venous thromboembolism.

<sup>3</sup> INR international normalized ratio.

**Table 2** Patient characteristics per visit.

Characteristic	n 840 (%)
Age at time of procedure	
< 30 years	92 (11.0)
31–40 years	95 (11.3)
41–50 years	214 (25.5)
51–60 years	211 (25.1)
> 60 years	228 (27.1)
Gender	
Male	446 (53.1)
Female	394 (46.9)
Patient medical conditions	
Cardiac	480 (57.1)
VTE <sup>2</sup>	150 (17.9)
Cancer	86 (10.2)
Stroke	32 (3.8)
APS <sup>4</sup>	9 (1.1)
Other	83 (9.9)
Antithrombotic medication	# visits, n (%)
Warfarin	225 (26.8)
Enoxaparin	264 (31.4)
Clopidogrel	265 (31.5)
Rivaroxaban	42 (5.0)
Dabigatran	13 (1.5)
Heparin	31 (3.7)

All patients were treated under local anesthesia at the dental outpatient clinics and given a follow-up appointment. The majority of patients taking enoxaparin were inpatients (89.4% n = 236/264). These patients were referred for dental extractions while receiving antithrombotic medications and were admitted for reasons other than dental treatment. Hospitalized patients are routinely given antithrombotic medications because of the high prevalence of venous thromboembolism among hospitalized patients (Geerts et al., 2001).

The diagnosis of postoperative bleeding was based on Lockhart et al. with a minor modification (Lockhart et al., 2003) as we defined an event as bleeding continuing > 5 h, bleeding necessitating the patient's return to a dentist or a medical facility for treatment, bleeding resulting in a large hematoma or ecchymosis in the oral soft tissues, or bleeding requiring a blood transfusion.

All patients were given a follow-up appointment. Patient dental records were reviewed for evidence of postoperative bleeding according to our definition. Patients not seen at the clinic had their medical records reviewed to identify any follow-ups in the Emergency Department or other clinics. Thirty-two patients had no documented visits and were contacted via telephone to ascertain if they had experienced any postoperative bleeding. Two patients (0.23%) could not be contacted and were lost to follow-up.

### 2.1. Statistical analysis

Baseline characteristics were presented as the mean  $\pm$  standard deviation for continuous variables and count (percentage) for categorical variables. Categorical variables were analyzed using chi-squared tests. All statistical tests were two-tailed.  $P < 0.05$  was considered statistically significant. Data were analyzed using Excel 2010 software.

### 3. Results

A total of 539 patients with a mean age of  $51.3 \pm 15.2$  years underwent 840 appointments for dental extractions. Men had 1,066 teeth extracted (mean = 2.4 teeth per patient) and women had 914 teeth extracted (mean = 2.31) ( $P > 0.05$ ). Patient medical conditions requiring antithrombotic medications included cardiac disease (57.1%, n = 480), history of venous thromboembolism (17.9%, n = 150), cancer (10.2%, n = 86), history of cerebrovascular accident (3.8%, n = 32), presence of antiphospholipid syndrome (APS<sup>4</sup>) (1.1%, n = 9) and other diseases (9.9%, n = 83). There was no difference in the frequency of patients treated for cardiac disease, VTE<sup>1</sup>, cancer, or stroke ( $P > 0.05$ , Chi-squared test).

There was a change in the frequency of medications used by year (Fig. 1) (Chi-squared test,  $P < 0.0001$ ). The use of clopidogrel decreased after 2012, the use of warfarin decreased after 2013, and the use of enoxaparin increased after 2013. The use of dabigatran and rivaroxaban began in 2014, with rivaroxaban quickly becoming the third most commonly used drug after enoxaparin and clopidogrel. NOACs<sup>3</sup> comprised about 25% of antithrombotic medications prescribed to this group of patients in 2016.

A total of 1980 teeth were extracted. A mean of  $2.4 \pm 2.01$  (range: 1–15) teeth were removed per patient visit. A total of 461 visits (54.9%) resulted in the removal of one tooth per session. Only 62 (7.4%) of the appointments consisted of five or more dental extractions (representing a higher-risk of bleeding) (Vaneshree and Ozayr, 2016). Perioperative local hemostatic measures were taken in just over half the cases (Fig. 2).

Upper molars, particularly the first and second molars, were more commonly involved in bleeding (Fig. 3). These teeth may be more associated with bleeding and lower molars more associated with dry sockets. (Vaneshree and Ozayr, 2016)

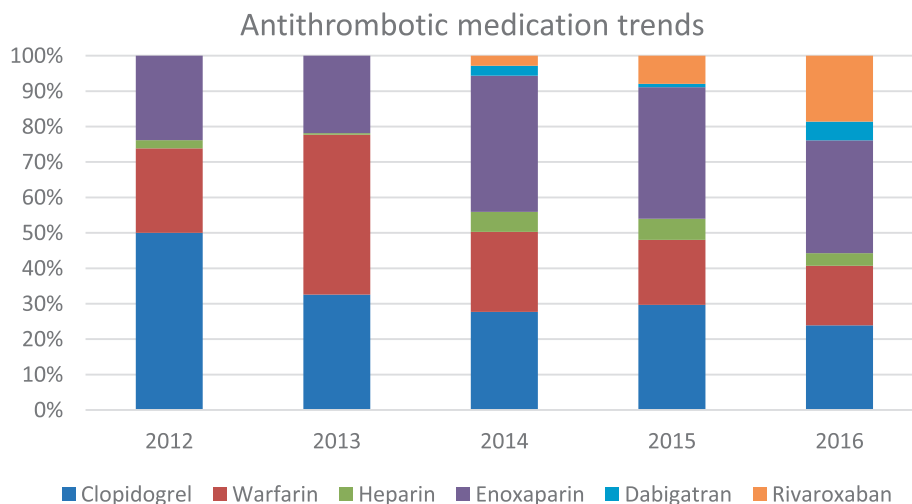
The mean follow-up period for outpatients was 2.5 days (mode 7 days). Only 14 (1.7%) cases involved bleeding (Table 3). Six additional patients returned with a chief complaint of bleeding but displayed no evidence of bleeding on clinical examination and therefore required no treatment. Patients with bleeding had an average of  $2.4 \pm 2.03$  (range: 1–7) teeth extracted, similar to those without bleeding. There was no change in the occurrence of bleeding by year ( $P = 0.263$ ), although the bleeding rate in 2013 approached significance ( $P = 0.067$ ).

Bleeding was not uniformly distributed among drugs administered ( $p = 0.009$ ). Warfarin was associated with more (Chi-square test with multiple comparisons,  $p < 0.0001$ ), and clopidogrel was associated with less ( $p = 0.011$ ) bleeding than other drugs. Nearly 85.7% (n = 12/14) of bleeding occurred in female patients ( $p = 0.001$ ). All returning patients were treated as outpatients with local hemostatic measures. None of the patients were admitted or had a blood transfusion for this event. No complications related to thrombosis or emboli were found.

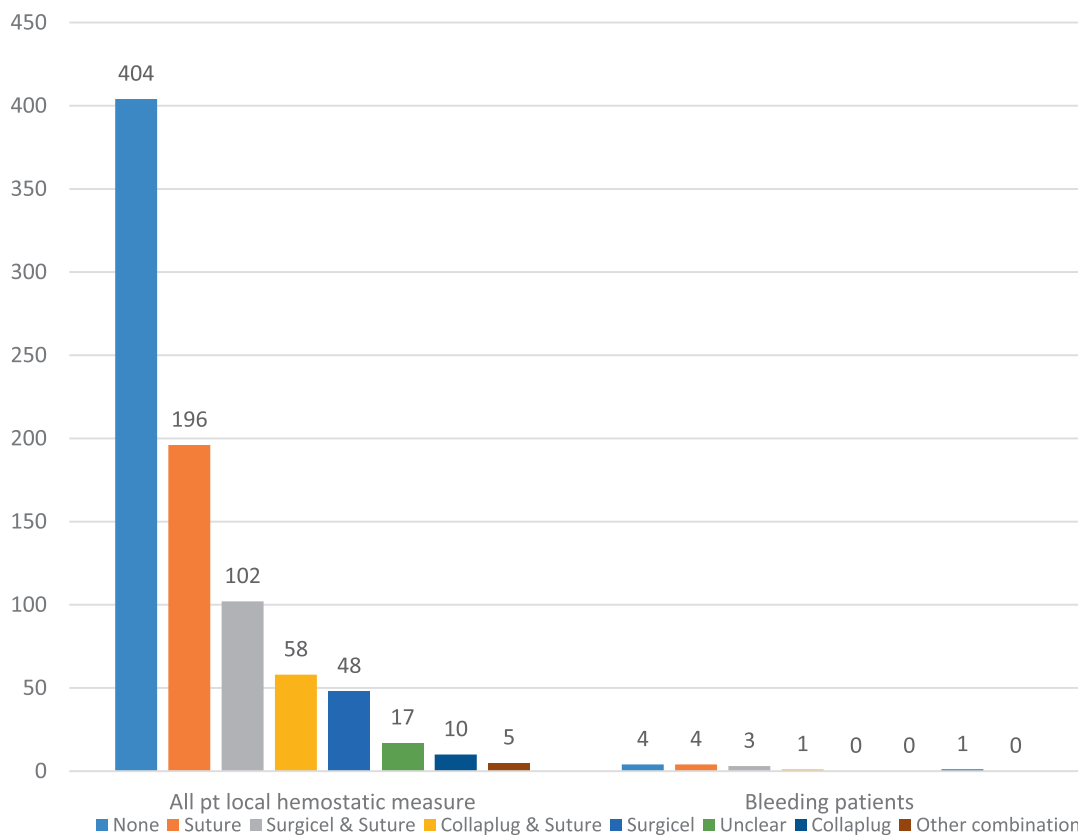
### 4. Discussion

In the present study, only 1.7% of the appointments resulted in postoperative bleeding. Patients on warfarin medication were

<sup>4</sup> APS antiphospholipid syndrome.



**Fig. 1** Frequency of antithrombotic medication used per patient visit by year.

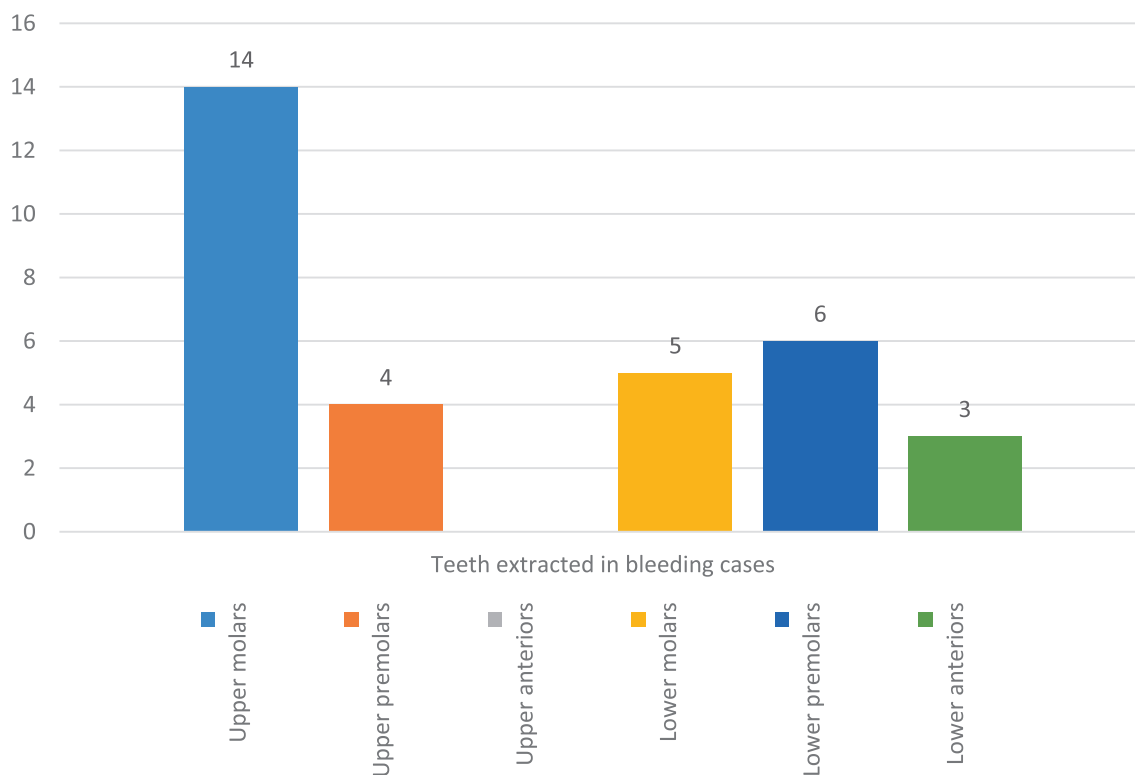


**Fig. 2** Perioperative local hemostatic agents used for all patients vs those with bleeding.

at the highest risk of bleeding (3.88%), whereas patients on clopidogrel had a near-zero risk of bleeding when compared to other drugs. Women were found to be at greatest risk of postoperative bleeding following extractions compared to men. This finding is more concerning because men and women were almost equally represented in the present study (53.1% vs. 46.9%, respectively). A meta-analysis of risk factors supports sex gender differences in bleeding during treatment with newer oral anticoagulants (Alotaibi et al., 2013). It is also consistent with previous studies demonstrating that women are

generally more predisposed to bleeding complications than men, possibly due to associated factors such as BMI, creatinine clearance, and anatomic differences (Ahmed and Dauerman, 2013). Conducting more extensive clinical studies on women under anticoagulant therapy and identifying the main factors for those experiencing bleeding following invasive dental procedures are important.

A review of dental extractions in patients on antithrombotic therapy was comparable with our study population and suggested that while bleeding is an associated risk, it is less



**Fig. 3** Location of extracted teeth in bleeding cases.

**Table 3** Characteristics of 14 patients with bleeding.

Patient Characteristics						
Medical condition	Medication	Gender	No. of teeth extracted during the visit	Age (years)	Immediate postoperative measures	Additional measures
Cardiac	Heparin	F	2	54	Suture	Surgicel® and suture
Cardiac	Warfarin (INR <sup>3</sup> 2.6)	F	1	53	Suture	CollaPlug®
Cardiac	Warfarin (INR <sup>3</sup> 2.8)	F	1	42	Gauze only	Surgicel®, suture, tranexamic acid
APS <sup>4</sup>	Warfarin (INR <sup>3</sup> 3)	F	1	39	Surgicel® and suture	Collaplug®
Cardiac	Warfarin (INR <sup>3</sup> 2.6)	F	4	69	Collaplug® and suture	Suture
VTE <sup>2</sup>	Enoxaparin	F	2	66	Suture	Surgicel® and suture
VTE <sup>2</sup>	Warfarin (INR <sup>3</sup> 3.2)	F	3	18	Surgicel® and suture	Surgicel®, suture, tranexamic acid
VTE <sup>2</sup>	Warfarin (INR <sup>3</sup> 2.4)	F	1	18	Collaplug®	“local measures“
Cancer	Enoxaparin	F	7	64	Suture	Gauze pack only
Stroke	Warfarin (INR <sup>3</sup> 2.3)	M	1	47	Gauze pack only	Surgicel® and suture
Cardiac	Warfarin (INR <sup>3</sup> 2.4)	F	1	65	Suture	Surgicel®
Cardiac	Warfarin (INR <sup>3</sup> 1.1)	F	2	31	Gauze pack only	Surgicel® and suture
VTE <sup>2</sup>	Enoxaparin	F	6	70	Gauze pack only	Suture
Cardiac	Clopidogrel	M	1	54	Surgicel® and suture	Local measures in the Emergency Department

F = female; M = male.

Collaplug: collagen dental dressing.

Surgicel: oxidized regenerated cellulose.

serious than the complications of thromboembolism. Altering antithrombotic dosing was not recommended unless the prescribing physician supported this adjustment. Following existing guidelines, ensuring the patient had an INR within the

recommended range before minor dental surgery was recommended. Local hemostatic measures were discovered to be sufficient to control bleeding (Mingarro-de-Leon et al., 2014). Approximately half of the patients in this review had a local

hemostatic agent placed immediately post-extraction (51.9%); however, it is preferable to use local hemostatic agents as a general recommendation for all dentists extracting teeth from patients receiving antithrombotic medications.

Patients who had extractions while receiving warfarin had an INR of <3.5, and only two (0.86%) patients required medication adjustment to reach this level. Guidelines from North America, the UK, and Australia recommend patients on warfarin therapy to have a therapeutic INR of 2 to 3 for most indications or 2.5 to 3.5 for specific mechanical heart valves. (Perry et al., 2007; Douketis et al., 2012; Nematullah et al., 2009; Scottish Dental Clinical Effectiveness Programme, 2015) The British Committee for Standards in Haematology, British Society for Haematology Committee, British Dental Association, and the National Patient Safety Agency consensus was that an INR of 2 to 4 did not warrant adjustment and was found to be associated with a very low-risk of bleeding in patients undergoing outpatient dental surgery (Perry et al., 2007).

New oral anticoagulants (Miller et al., 2012; van Diermen et al., 2013) are increasingly used for the prevention of thromboembolic disease in patients with non-valvular atrial fibrillation (Firriolo and Hupp, 2012; Heidbuchel et al., 2013). These drugs do not require routine monitoring of coagulation or dosing adjustments based on laboratory tests, although the dosing is related to glomerular filtration rate (GFR). Several drug–drug interactions can affect the activity of NOACs<sup>3</sup> and the associated risk of bleeding, such as verapamil, quinidine, amiodarone, dronedarone, and ketoconazole for dabigatran; likewise, quinidine, ketoconazole, HIV protease inhibitors and erythromycin for rivaroxaban. Patients taking these drugs may be at increased risk for bleeding during dental extractions. Evaluation of anticoagulant effects with these drugs is not routinely available and requires special testing (Heidbuchel et al., 2013).

Some variation in what is considered a risk factor for bleeding has been reported. Some considered surgical tooth extraction (i.e., involving elevation of mucoperiosteal flap) and multiple tooth extractions to be at high risk for bleeding (Martinez and Tsakiris, 2015). However, the number of teeth we extracted in patients with bleeding was comparable with the number extracted in patients without bleeding.

In the tertiary hospital setting, dentists conducting minor oral surgery procedures on patients under warfarin and clopidogrel medications normally have extensive experience with such medications. It is not uncommon to encounter patients on anticoagulants presenting for dental treatment in general dental clinics. However, the more recent introduction of NOACs<sup>3</sup> is in relatively small numbers of patients compared with the older medications and has complicated patient care in general dentistry. A previous survey found that 27% of US oral surgeons routinely discontinued warfarin before low-risk procedures (Ward and Smith, 2007). Serious complications such as emboli and mortality have been reported in 0.8% of 3,500 patients stopping warfarin (Wahl et al., 2015). The same team found that <1.3% of 950 patients undergoing 2,400 oral surgery procedures experienced bleeding (Wahl, 2000).

In Saudi Arabia, dentists usually have specialized postgraduate training (Al-Dlaigan et al., 2011; Al-Dlaigan et al., 2012). This specialization or focus can lead to a less active role in the management of patients on anticoagulants. Of particular con-

cern, only a small percentage of dentists (17.8%) and medical practitioners (28.8%) adhere to the guidelines developed for the management of patients on antithrombotic medication in dental settings<sup>5</sup> (AlSheef et al., 2020). This statistic indicates that both professions need to be educated further and encouraged to adhere to evidence-based guidelines developed to manage such patients (Shah et al., 2015).

There were several limitations to the present study. Data retrieval was limited by the information documented in the patient charts. Because of the small study population, treatment with NOAC<sup>3</sup> medications made the detection of increased or decreased risk of bleeding difficult; hence, a more focused study about NOACs<sup>3</sup> and bleeding is recommended. Dental surgeons had different levels of training and skill sets; thus, extractions were conducted according to dental training and learned techniques. These variations may affect the incidence of bleeding complications. Furthermore, a history of herbal or food supplements may have an adverse effect on bleeding, and this information was not collected.

## 5. Conclusions

Dental extractions of single and multiple teeth were conducted safely with minimal or no interruption to antithrombotic therapy. The risk of bleeding complications was extremely low and well-managed using standard hemostatic agents in approximately half of the extraction cases. Routine use of hemostatic agents could easily be conducted in general practice by non-oral surgery specialists. The greater risk of a bleeding complication in women was notable, and dental professionals should be more cautious when conducting dental extractions on women, especially those receiving anticoagulation medications. Dental professionals may consider using local hemostatic agents preemptively. Well-designed clinical studies are needed to further elucidate female-specific bleeding risks in oral surgery. Establishing standard guidelines for the management of patients on new oral anticoagulant medications, together with professional education encouraging general dental and medical practitioners to adhere to these guidelines, will likely reduce the risk of bleeding complications associated with dental extractions.

## Ethical considerations

The study was approved by the Institutional Review Board of King Fahad Medical City, Riyadh, Saudi Arabia (Protocol # RC17-267). The study was conducted by recommendations of the International Conference on Harmonization for Good Clinical Practice (ICH-GCP).

## CRedit authorship contribution statement

**Mohammed AlSheef:** Conceptualization, Methodology, Writing - review & editing, Visualization, Supervision, Project administration. **Jenny Gray:** Validation, Formal analysis, Data curation, Writing - original draft, Funding acquisition. **Abdul-Salam AlShammari:** Investigation, Resources.

<sup>5</sup> NOAC new oral anticoagulants.

## Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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