Perioperative Management of Direct Oral Anticoagulants (DOACs) in Elective Surgery Candidates: A Drug Utilization Evaluation (DUE) Study

Negar Kariznoee[1], Reza Mollazadeh[2], Soha Namazi[3,4], Shakila Yaribash[1, 5], Ramin Ansari[3], Keyhan Mohammadi[3, 6*]

[1] School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

[2] Department of Cardiology, School of Medicine, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

[3] Department of Clinical Pharmacy, School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

[4] Research Center for Rational Use of Drugs, Tehran University of Medical Sciences, Tehran, Iran.

[5] Iran Network of Immunity in Infection, Malignancy & Autoimmunity (NIIMA), Universal Scientific Education & Research Network (USERN), Tehran, Iran.

[6] Research Center for Antibiotic Stewardship and Antimicrobial Resistance, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

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Abstract

Background: This study aimed to evaluate physicians' practice regarding perioperative Direct Oral Anticoagulants (DOACs) management in patients undergoing elective procedures and compare it to established institutional standard protocols and the most recent guidelines.

Methods: Over seven months, a cross-sectional descriptive-analytical study was conducted at Imam Khomeini Hospital Complex, affiliated with Tehran University of Medical Sciences. Patients receiving DOACs and undergoing elective procedures/surgery were enrolled.

Results: In total, 170 patients who underwent 200 procedures while taking DOACs were included, with a total mean age (SD) of 62.2 (16.5) years. DOAC therapy was primarily prescribed for atrial fibrillation (75%) and deep vein thrombosis (25%), with 97% taking Apixaban. Approximately 125 (62.5%) of the performed procedures were categorized as high risk for bleeding, among which only 16.8% adhered to preoperative management guidelines. The mean (SD) time to reintroduce DOACs after procedures was 57.7 (45.3) hours. Bridge therapy was used in 66% of cases before and 74% after procedures. Blood products were administered in 36 cases of high-risk procedures. The average overall perioperative management score calculated was 3.3, representing less than 50% of the maximum possible score of 7. In only 8.5% (N=17) of the procedures, the total pre- and postoperative management of DOACs was concordant with the guideline.

Conclusion: The study showed poor perioperative adherence to international DOAC management guidelines. Expert collaboration is crucial for DOAC patients undergoing surgery. More research is needed to understand the reasons for low adherence.

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Keywords: Direct Oral Anticoagulant; Surgery; Atrial Fibrillation; Deep Vein Thrombosis ; DUE; Drug Utilization Evaluation

Introduction

Direct oral anticoagulants (DOACs) are widely used as the anticoagulant of choice for preventing stroke and systemic embolism in patients with atrial fibrillation (AF), compared to vitamin K antagonists (1). DOACs offer several advantages, including more convenient dosing, fewer dietary restrictions, a lower risk of drug-drug interactions, and a predictable anticoagulation profile compared to vitamin K antagonists (2, 3).

The proper utilization of DOACs in specific populations,

*** Corresponding Author:** Keyhan Mohammadi
Address: Department of Clinical pharmacy, School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran. Tel: +982164122208
E-mail: keyhanmohammadi72@yahoo.com

such as patients who need surgery, requires careful consideration (4, 5). These considerations include renal and liver function, bleeding risk, age, weight, risk of thromboembolic events, comorbidities, and concurrent medications (6-9).

As the population ages, there is a growth in the prevalence of AF patients receiving DOACs (10, 11). The use of DOACs presents several challenges within the treated population (12), particularly for older patients who may face an increased likelihood of requiring surgical procedures due to their age and the risks associated with anticoagulant therapy (13-16). DOAC-treated patients frequently encounter elevated risks of bleeding, leading to the frequent interruption of their anticoagulant treatment (17). Appropriate management of these interruptions is crucial for preventing perioperative bleeding or ischemic events.

The lack of validated protocols for the preoperative management of patients receiving DOACs can indeed lead to potentially harmful results (18). The risk assessment for preoperative management of patients on DOACs encompasses various aspects, including patient-related factors, thromboembolic risk, drug-specific considerations, and procedure-related factors. It is crucial to take these elements into account when deciding the appropriate timing for discontinuing and resuming a DOAC (9, 18, 19). The overall guideline-based recommendation for the perioperative management strategy of DOACs is illustrated in Figure 1 (20). Generally, for low-risk surgeries, interrupting DOAC therapy for one or two days is acceptable (8). In general, patients with severe renal dysfunction require a longer interruption duration before surgery (21-23). In patients with a high risk of thromboembolism, prolonged interruption of DOACs can increase the risk of thromboembolic events. Conversely, shorter interruption intervals, particularly before procedures with a higher risk of bleeding, are associated with an increased likelihood of surgery-related bleeding (20).

Many guidelines' recommendations stem from the findings of the Perioperative Anticoagulation Use for Surgery Evaluation (PAUSE) study, given its low incidence of thromboembolic and hemorrhagic complications. Major bleeding occurred in fewer than 2% of patients, while ischemic stroke was observed in less than 0.5%, underscoring the safety of this approach (24); however, adherence to this protocol in clinical practice may be challenging (17). Despite clear and relatively easy-to-use guidance, many clinicians find the management of DOACs in the pre- and post-operative phases challenging. The primary objective of the present study was to evaluate physicians' practice regarding the preoperative and postoperative management of DOACs in patients undergoing elective procedures in a referral hospital and compare it to established institutional standard protocols guided by the most recent guidelines.

Methods

Study design

During a period of seven months, a cross-sectional descriptive-analytical Drug Utilization Evaluation (DUE) study using a standardized data extraction sheet in DUE form was carried out at Imam Khomeini Hospital Complex, which is associated with Tehran University of Medical Sciences. Initially, an extensive search was conducted in libraries such as PubMed using keywords related to DOACs, anticoagulants, bridge therapy, preoperative, postoperative, surgery, procedure, and guidelines. Thereafter, to facilitate the study, a specific internal protocol aligned with the latest guidelines from the American College of Clinical Pharmacy (ACCP) (8) and the European Heart Rhythm Association (9) on perioperative DOAC management was developed after collaboration with an electrophysiologist and a clinical pharmacist.

The study enrolled participants aged 18 years and above who provided consent and received one of the DOACs for any duration necessitating an elective procedure during their hospitalization. Exclusion criteria involved individuals who lacked essential data. All hospital departments were included, and informed consent was obtained from the patient or a legally authorized representative. Patient medical records were monitored six days pre-procedure, on the day of the procedure, and six days post-procedure.

Data collected from each patient included demographics, indication for DOAC use, DOAC administration details, comorbidities, medication history, bleeding history, need for blood products during the procedure, perioperative injectable anticoagulant use, laboratory results, procedure types and durations, bleeding risk assessment based on surgical type, DOAC dose and timing pre- and post-procedure, and any short-term drug-related adverse events (Supplementary file). Based on most international guidelines and standardized DUE forms, a scoring system was defined in line with the guideline-directed perioperative DOAC management approach. In this system, seven items were listed for every patient. Each item was designed and provided to compare physicians' practice to guidelines through expert panel discussions. In concordance with the guidelines' recommendations, a score of 1 was given for each item if the corresponding action was conducted, with a maximum score of 7. On the other hand, a score of 0 was assigned if the action was not performed. Subsequently, the average of the seven scores was calculated for each case, awarding a score of 1 for compliant actions (with a maximum total score of 7) and a score of 0 for non-compliant actions (the lowest possible score is 0), and the discrepancies before and after the procedure were evaluated via comparison with guidelines (8, 9)

Ethical considerations

The research protocol obtained approval from the Research Ethics Committees at the Institute of Pharmaceutical Sciences, Tehran University of Medical Sciences (ethics code: IR.TUMS.TIPS.REC.1401.085). Participants were assured that their data would remain confidential and would not be shared with external parties.

Statistical analysis

The sample size was determined to be 200 procedures, guided by the hospital bed capacity and the utilization trends of DOACs within the hospital's electronic health records, aiming to achieve a 95% confidence level with a maximum permissible error of 0.05. Quantitative variables were presented as mean ± standard deviation (SD) or median (interquartile range (IQR)), and qualitative variables were presented as frequency (percentage). Data analysis was conducted using SPSS 26.0.

Results

Patients' characteristics

Overall, 200 medical procedures were documented among the 170 included patients. The demographic data, drug history, medical history, and results of routine laboratory tests are presented in Table 1.

Table 1. Demographic, clinical, and laboratory characteristics of the patients at baseline(N=170)

Characteristic			Statistics parameters
Sex, N (%)		Male	87 (51.2)
		Female	83 (48.8)
Age (year)		Mean (SD)	62.2 (16.5)
		Range	19-97
BMI (kg/m^2)		Mean (SD)	26.5 (3.5)
Past drug class history, N (%)		Vitamins	163 (96)
		Cardiovascular medications	159 (94)
		Herbal medications	147 (86)
		Lipid-lowering agents	144 (85)
		Aspirin	123 (72)
		NSAIDs	12 (7)
		Oral antidiabetic agents	92 (54)
		Sedative, Hypnotic	58 (34)
		Antibiotics	31 (18)
		Ear, Nasal, and Ophthalmic drops	29 (17)
		Insulin	28 (16)
		Inhalations	9 (5)
		Others	72 (42)
Past medical history, N (%)		Cardiovascular disorders	166 (98)
		Endocrine disorders	100 (59)
		Gastrointestinal disorders	93 (55)
		Nervous system disorders	32 (19)
		Musculoskeletal disorders	22 (13)
		Respiratory disorders	6 (4)
		Immunological disorders	4 (2)
		Others[1]	21 (12)
Routine laboratory data among included patients	Parameters	Before the procedure, mean (SD)	After the procedure, mean (SD)
	WBC (10^9 /L)	8.9 (3.7)	9.4 (5.3)
	Hb (g/dL)	10.5 (2.4)	10.5 (2.3)
	PLT (10^9 /L)	216.9 (133.7)	205.8 (113.9)
	Cr (mg/dL)	1.6 (2.1)	1.5 (1.6)
	INR	1.4 (0.9)	1.4 (0.8)
	PTT (second)	37.2 (22.1)	36.7 (16.9)
	AST (units/L)	34.6 (21)	38.8 (22.1)
	ALT (units/L)	27.5 (10.5)	37 (23.6)
	Total bilirubin (mg/dL)	1.4 (1.4)	1.6 (1.6)

N: number (percentage), SD: Standard deviation, BMI: Body Mass Index, NSAID: Non-steroidal anti-inflammatory drugs, WBC: White blood count, Hb: Hemoglobin, PLT: Platelet, Cr: Creatinine, INR: International normalized ratio, PTT: Partial thromboplastin time, AST: Aspartate transaminase, ALT: Alanine transaminase
[1]Other diseases included G6PD deficiency, genetic disorders, and Cancers

The main comorbidities observed among the included patients were cardiovascular diseases (97.5%) and gastrointestinal disorders (68.5%). Notably, there were no instances of gastrointestinal bleeding history or documented cases of inherited coagulopathies such as hemophilia, thrombocytopenia, or von Willebrand disease. Within the study group, DOAC therapy was initiated primarily for AF in 128 individuals (75%) and for deep vein thrombosis in 42 patients (25%). Regarding the specific DOACs administered, apixaban was the most frequently used DOAC, given to 165 patients (97%), while rivaroxaban was utilized in the remaining 3% of cases. The distribution of DOACs and dosing specifics can be found in Table 2. In patients who received apixaban, approximately half had a median treatment duration of less than 14 months (IQR: 24, 8), whereas for those on rivaroxaban, the reported duration was 13 months (IQR: 12, 30).

Table 2. Doses of Direct oral anticoagulants (DOACs) administered in included patients (N= 170)

Type of DOAC	Strength	Dosing	N (%)
Apixaban	2.5 mg	Twice daily	95 (57.5)
	2.5 mg	Once daily	4 (2.4)
	5 mg	Twice daily	60 (36.6)
	5 mg	Once daily	2 (1.2)
	10 mg	Twice daily	4 (2.3)
Rivaroxaban	20 mg	Twice daily	1 (20)
	20 mg	Once daily	4 (80)

N: Number

Characteristics of procedures/surgeries among included populations

Of the 200 procedures performed, 62.5% (N=125) occurred in surgical wards, and 37.5% (N=75) were carried out in medical wards. The average duration of these procedures was 123.3 (79.2) minutes, ranging from 30 to 480 minutes. A total of 125 cases were classified as high risk, 15 as low risk, and 60 as minor risk for bleeding associated with the procedures, as illustrated in Tables 3 and 4. Regarding the need for blood product administration during the operation, packed red blood cells were administered in 23 high-risk surgical procedures and one minor- and low-risk procedure. Furthermore, 13 patients undergoing high-risk procedures received platelet transfusions.

Table 3. Distribution of various procedures and risk of bleeding among included procedures (N=200)

	Risk of bleeding based on EHRA guidelines & type of procedure/surgery	N (%)	Number of procedures that required blood products during the operation
Risk of bleeding, N (%)	Minor	60 (30)	1 (pRBCs)
	Endoscopy (without biopsy)	36 (60)	
	Coronary/ Peripheral Angiography	15 (25)	
	Superficial procedures	9 (15)	
	Low	15 (7.5)	1 (pRBCs)
	Endoscopy (with biopsy)	10 (66.7)	
	Non-major orthopedic surgery	5 (33.3)	
	High	125 (62.5)	23 (pRBCs)
	Abdominal surgery	40 (32)	13 (platelet)
	Major urological surgery	27 (21.7)	
	Major orthopedic surgery	25 (25)	
	Peripheral vascular reconstruction surgery	19 (15.2)	
	Major Thoracic surgery	11 (8.8)	
	Major Cardiac surgery	3 (2.3)	

N: Number

Table 4. Distribution of procedures among included patients and rate of concordance with guidelines

Parameters		Number of procedures; N (%)	Concordance with guidelines in both pre-and post-operative phases, N (%)
Inpatient Ward	Surgical	125 (62.5)	12 (9.6)
	Medical	75 (37.5)	5 (6.7)
The specialty of physicians who treat cohort patients on DOACs	Plastic and Reconstructive Surgery Specialist	13 (6.5)	2 (15.4)
	Orthopedic Specialist	20 (10)	3 (15)
	Fellowship in Cancer Surgery	7 (3.5)	1 (14.3)
	Obstetrics and Gynecology Specialist	19 (9.5)	2 (10.5)
	General Surgery Specialist	39 (19.5)	4 (10.3)
	Gastroenterologist	51 (25.5)	4 (7.8)
	Urology Specialist	19 (9.5)	1 (5.3)
	Neurosurgery Specialist	8 (4)	0 (0)
	Vascular Surgery Specialist	24 (12)	0 (0)

N: Number

The management of DOAC in the pre-operative phase

Among the included patients in the study, the strategies employed for managing DOACs in the preoperative phase are delineated in Table 5. As presented, in 36 cases of high-risk surgeries, DOACs were discontinued four days before the procedure, which was not in accordance with the guidelines' recommendations. Furthermore, among these high-risk procedures, 22 patients had their DOACs discontinued three days before surgery. In contrast, in 21 procedures, DOACs were withheld two days before the procedure, which was in line with guideline recommendations. Among low- and minor-risk procedures, DOACs were held for 48 hours in four and eight procedures, respectively. Although continuing DOAC therapy and performing the procedure at the trough level was possible for minor-risk procedures based on guidelines, among 33 minor-risk procedures (55% of minor-risk and 16.5% of total procedures), DOACs were discontinued at least 24 hours before procedures (ranging from 24 to more than 145 hours), which was not recommended by guidelines. In 19 and five cases of minor- and low-risk procedures, DOACs were continued on the day of surgery with a minimal interruption period of six hours. Guidelines recommend that for patients receiving DOACs who require elective surgery, DOACs should be interrupted for two days in high-risk procedures (8); however, in our report, in 10 cases of high-risk surgeries, DOACs were continued on the day of surgery with an interruption time of less than 24 hours. In addition, in four procedures with a high-risk profile for bleeding, DOACs were only held for one to less than two days (24–48 hours) before surgery. Among all patients for whom DOACs were interrupted before surgery, the mean (SD) duration of DOAC interruption was 68.2 (49.3) hours.

Table 5. Comprehensive data on the timing of Direct oral anticoagulants (DOAC) discontinuation before and re-initiation after procedures/ surgery across included cases, categorized by bleeding risk (N=200)

Duration/time of DOAC management before and after procedures		Category of procedures based on bleeding risk, N(% of total procedures)			Total number in the overall cohort
Days	**Hours**	**Minor, N (%)**	**Low, N (%)**	**High, N (%)**	**All procedures', N (%)**
Duration of DOAC discontinuation *before* procedure/surgery					
> 6	**>145**	1 (0.5)	-	22 (11)	23 (11.5)
6	**121-144**	1 (0.5)	-	2 (1)	3 (1.5)
5	**97-120**	4 (2)	-	10 (5)	14 (7)
4	**73-96**	3 (1.5)	-	36 (18)	39 (10.5)
3	**49-72**	3 (1.5)	-	22 (11)	25 (12.5)
2	**48**	8 (4)	4 (2)	21 (10.5)	33 (16.5)
1	**24-48**	13 (6.5)		4 (2)	21 (10.5)
<1	**12-23**	8 (4)	-	4 (2)	12 (6)
	<12	19 (9.5)	5 (2.5)	6 (3)	29 (14.5)
Time for DOACs re-initiation *after* procedure/surgery					
<1	**<12**	11 (5.5)	4 (2)	1 (0.5)	16 (8)
	12-23	7 (3.5)	-	4 (2)	11 (5.5)
1	**24 - <48**	11 (5.5)	3 (1.5)	22 (11)	36 (18)
2	**48**	10 (5)	2 (1)	45 (22.5)	57 (28.5)
3	**49-72**	5 (2.5)	3 (1.5)	11 (5.5)	19 (9.5)
4	**73-96**	5 (2.5)	-	14 (7)	19 (9.5)
5	**97-120**	1 (0.5)	-	7 (3.5)	8 (4)
6	**121-144**	-	-	2 (1)	2 (1)
>6 days	**145-240**	4 (2)	1 (0.5)	7 (3.5)	12 (6)
Not re-initiated	**-**	6 (3)	-	14 (7)	20 (10)

N: Number

The management of DOAC in the post-operative phase

In nine procedures with moderate to high bleeding risk and 18 procedures with minor bleeding risk, DOACs were reinitiated on the day of surgery within 24 hours of the operation, which was not in concordance with the guidelines (8). On the other hand, in five procedures with low bleeding risk, DOACs were restarted 1 to 2 days after the operation, which seems to be an acceptable strategy. These data are presented in Table 5. In the context of 22 procedures with a high risk of bleeding, it was observed that patients restarted DOACs within 24–48 hours post-operation, indicating an earlier reintroduction of the medication compared to the recommended guideline timeline. In 28% of the total procedures, the reintroduction of DOACs occurred 48–72 hours post-operation in cases involving a high risk of bleeding. This approach adheres to guideline recommendations. As shown, in 20 procedures, DOAC therapy was not resumed post-operation. The mean (SD) time to reintroduce DOACs after surgery was 57.7 (45.3) hours.

Use of bridge therapy in the perioperative setting

In our report, bridge therapy for at least one dose with a therapeutic or prophylactic dose of unfractionated heparin (UFH) was utilized in 132 procedures (66%). In the pre-procedural setting, a prophylactic dose of UFH was administered in 65 procedures (32.5%), while a therapeutic dose was utilized in 67 procedures (33.5%). The frequent use of UFH as bridge therapy may be attributed to the extended interruption period of DOACs and concerns regarding thromboembolic occurrences.

Among the included procedures, the injectable anticoagulant was used in 144 procedures (72%) in the post-operative setting. A prophylactic low dose of UFH was used in 109 procedures (54.5%), and a therapeutic dose of UFH was used in 39 procedures (19.5%)

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Concordance rate with guidelines for perioperative management of DOACs

The study also evaluated the level of concordance with guideline recommendations (7, 19). As shown in Table 4, most of the procedures were conducted by a gastroenterologist (25.5%). About 62.5% (N=125) and 37.5% (N=75) of the total procedures were performed in surgical and medical wards, respectively. Regarding concordance with guideline recommendations in pre-operative timing of DOAC discontinuation, the DOACs were discontinued in 27 minor risk procedures (13.5%) within 24 hours before the procedures and discontinued in high-risk procedures (10.5%) 48 hours before surgery, which was concordant with the guidelines, with a rate of concordance of 24%.

Overall results showed that, among the 200 included surgeries/procedures, 17 cases (8.5%) conformed to the guidelines in preoperative, intraoperative, and postoperative settings. As detailed in the methodology section, a seven-item, seven-point scoring system was implemented to evaluate the adherence of our medical center's practices to the guidelines for each patient undergoing a procedure. The items utilized for scoring are outlined in Table 6. A score of 7 indicates complete adherence to the guidelines. After scoring each procedure, the average overall score was computed, resulting in a mean score of 3.3, corresponding to less than 50% of the maximum achievable score of 7.

Table 6. Scoring system for evaluation of guideline-directed perioperative DOAC management undergoing elective procedure and the results of the mean score among included cohort (Procedure number = 200 among 170 patients)

Mean score in our study	Score	Concordant with Guideline?	Item
0.9	1	Yes	Correct decision for DOAC interruption before the surgery
	0	No	
0.1	1	Yes	Correct Timing of DOAC interruption before the surgery according to the risk of bleeding
	0	No	
0.9	1	Yes	Indication for DOACs reinitiating after surgery
	0	No	
0.3	1	Yes	Timing of reinitiating DOACs after surgery according to the risk of bleeding
	0	No	
0.2	1	Yes	No need for routine preoperative bridge therapy
	0	No	
0.3	1	Yes	Correct dosing of injectable anticoagulant before the surgery
	0	No	
0.6	1	Yes	Correct dosing of injectable anticoagulant after the surgery
	0	No	
3.3	7	Calculated score	

Discussion

DUE is a critical program aimed at ascertaining the rational usage of drugs, leading to patient safety and reducing the economic burden associated with irrational drug usage (25, 26). The peri-procedural discontinuation

of DOACs was confusing for physicians when introducing these agents. Personal experience was the sole resource for decision-making. Consequently, a balance should be achieved between bleeding and thromboembolic event risk factors in this field (27).

Very few prospective studies have assessed the perioperative management approach for DOAC-treated patients requiring surgery. A standard approach has been introduced based on the PAUSE study (24). A summary of perioperative DOAC management is presented in Figure 1.

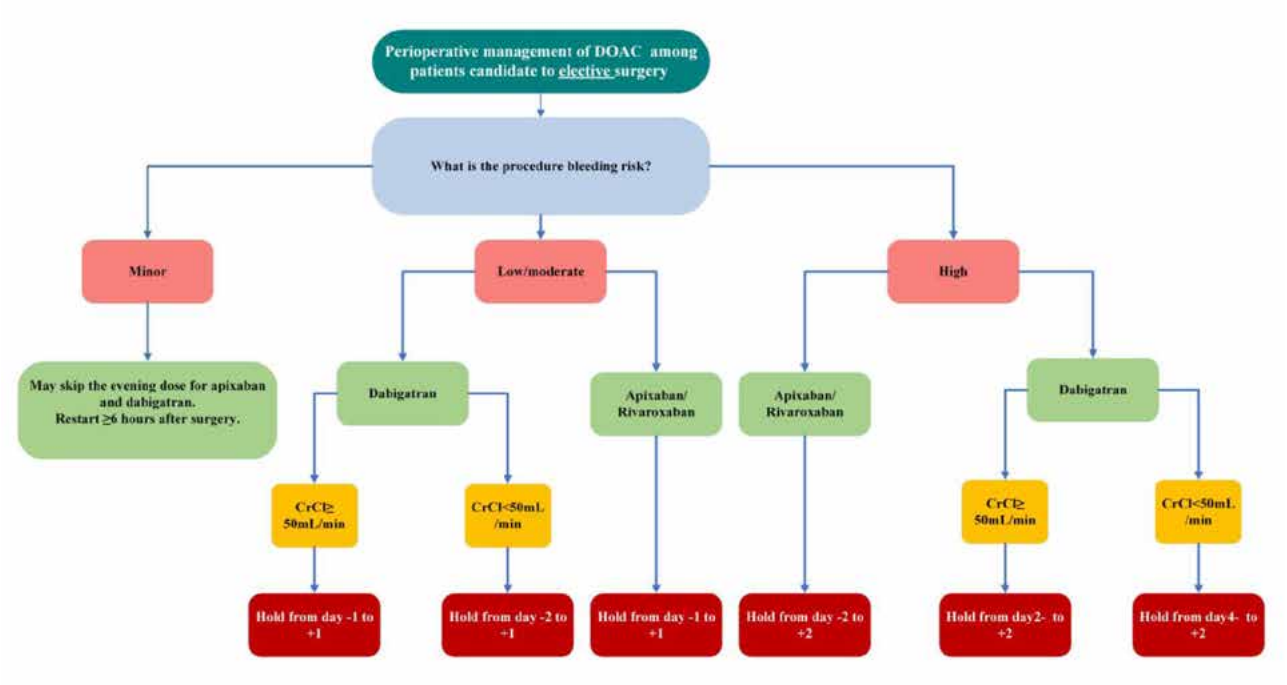

Figure 1. Perioperative management of direct oral anticoagulants (DOACs) (20). CrCl: Creatinine Clearance

Based on the current study, the continuation/discontinuation pattern of DOACs pre/post-procedure does not fully match the current guidelines. This may cause serious complications, although patients in this study did not experience DOAC-related complications during hospitalization; however, post-discharge complications were not evaluated. This is the first published DUE prospective investigation regarding the DOAC administration pattern pre/post-procedure.

The 2022 CHEST guideline (8) suggested that DOAC resumption post-operatively should be considered at least 24 hours after low-to-moderate-bleed-risk and 48-72 hours after high-bleed-risk procedures. Based on the results of this study, in most of the procedures, the DOAC was discontinued earlier and restarted later than the guidelines recommended. This might be due to physicians' concerns regarding DOAC-induced bleeding (especially in neurosurgeries) and the unavailability of a proper antidote in our region.

Generally, pre-operative bridging using low-molecular-weight heparin (LMWH) or UFH is not needed for patients on DOACs due to the anticipated decline in anticoagulant activity (8, 9). In a post-procedural setting, the administration of a low dose of UFH or LMWH could be considered in specific scenarios, including patients for whom resuming DOACs may be delayed for ≥48–72 hours following surgery or in patients for whom oral drug intake is not possible (9). Moreover, it could be considered in cases of concern regarding thromboembolic events (9). This may pose an economic burden to patients without clinical benefit. The Clinical Practice Guideline issued by the ACCP discourages the utilization of heparin bridging in the preoperative management of this population (8). However, as mentioned, there are suggestions that heparin bridging could potentially be considered in post-operative settings for selected patients (9). Some studies suggest that replacing oral anticoagulation therapy with UFH or LMWH may increase the risk of myocardial infarction, stroke, systemic embolism, hospitalization, and/or death within 30 days (28). Additionally, it has been suggested that heparin bridging may increase the incidence of bleeding (29). In this study, the most prevalent anticoagulant used to substitute DOACs pre/post-procedure is the therapeutic dose of UFH and a prophylactic dose of UFH.

In this study, 24% of pre-procedural administration patterns, 36% of post-procedural administration patterns, and 8.5% of both pre/post-procedural administration patterns were consistent with current guidelines. The total points obtained regarding the consistency with CHEST 2022 (8) and the European Heart Rhythm Association 2021 (9) guidelines were 47.14% lower than those of previous DUE studies regarding other anticoagulants.

Results of a retrospective study on 337 patients receiving DOACs and undergoing elective procedures suggest that 65.6% did not undergo the recommended preoperative anticoagulation management based on CHEST 2022. The study also found that clinicians' lack of adherence to recommendations mainly resulted from delayed or unnecessary interruptions in anticoagulation treatment (26.4%) or inappropriate heparin bridging (16.0%) (30).

Results of a cross-sectional, prospective study regarding UFH and LMWH DUE as therapeutic or prophylactic regimens on 400 patients suggest that doses of UFH and LMWH were appropriate in 75% and 79% of the cases of prophylaxis, respectively (31). This study was conducted in four wards, including CCU, cardiology, nephrology, and infectious disease. Better consistency of anticoagulant administration patterns with guidelines might be due to the presence and direct intervention of cardiologists in CCU and cardiology wards (31).

Results of a DUE of enoxaparin in 147 patients in a teaching hospital in Iran suggest that 70.92% of patients received enoxaparin correctly. The most common inconsistency was in the enoxaparin dose, followed by the duration of administration (32).

In our study, the adherence rate to guidelines was lowest in the neurosurgery ward, as the pre- and post-procedure management of DOACs in this ward did not comply with the guidelines in any of the cases. This might be due to concerns regarding cerebral bleeding during or post-surgery. On the other hand, nearly two-thirds of patients undergoing neurosurgical intervention in this study needed semi-urgent interventions; consequently, holding DOACs pre-procedurally was not feasible.

Although the results of the PAUSE study showed satisfactory adherence to the perioperative DOAC management protocol (33), our results showed low adherence to the guideline recommendations for DOAC management in a perioperative setting. Our study described a practical scenario in a real-life setting that cannot be compared to the rate of adherence in the PAUSE study.

There are several reasons for the inconsistency between clinicians' practices and guidelines, including unawareness of the availability of related guidelines, considering guidelines invalid or a threat to the individualized patient-physician relationship, the unavailability of native guidelines, financial problems, and the lack of a driving force to move from traditional habits toward guideline recommendations (34). Moreover, our study focused solely on surgical patients undergoing procedures associated with potential comorbidities and polypharmacy at a specialized referral center. This focus may have influenced physicians' strategies regarding perioperative DOAC management, potentially resulting in discrepancies with established guidelines. As a result, training programs, implementation of existing protocols, and the design of new protocols based on the availability of dosage forms, facilities, and limitations of each region according to international guidelines are needed to improve clinical benefit while reducing unnecessary financial burdens.

This study has some limitations. We have no cases of dabigatran in this study; consequently, the studied population was limited to those using Apixaban and Rivaroxaban. Some patients used over-the-counter products, including herbal medications, vitamins, and minerals. To date, there is little knowledge regarding DOAC-herb interactions. In the case of emergency surgeries, it was impossible to consider the pre-procedural DOAC administration pattern. Another limitation of our study is the absence of post-discharge follow-up data on the rates of thromboembolic and bleeding events following patients' discharge. Delays in the procedure time due to overcrowding in teaching hospitals is another limitation, leading to the earlier discontinuation of DOACs.

As mentioned, following the recommendations from reliable guidelines may reduce the incidence of bleeding/thromboembolic events pre/post-procedures, reduce the administration of unnecessary UFH or LMWH and the associated economic burden, and improve quality of life, safety, and clinical outcomes. This study raises doubts about the generalizability of guidelines in a tertiary hospital setting, where many highly poly-morbid patients are managed. Furthermore, we did not assess clinicians' familiarity, trust, comprehension, and knowledge about recently established guidelines, which could have impacted adherence rates.

More multi-center studies with larger sample sizes and longer durations of follow-up, especially in the post-discharge period, are suggested for future research on both

DUE of DOACs during procedures and the evaluation of the impact of native standardized guidelines prepared by scientific authorities to reduce inconsistency regarding the pre-/post-procedural pattern of DOAC administration between guidelines and physicians' practices.

Conclusions

This study represents a pioneering initiative to assess physicians' clinical practices regarding the perioperative management of DOACs and their concordance with established guidelines. It revealed low compliance and adherence to international guidelines in this context. Enhancing practices requires collaborative consultations with specialized teams proficient in perioperative DOAC management, as well as tailored training and education for the surgical team. Further robust studies are imperative to evaluate the effective management of DOACs in the perioperative setting.

Conflicts of Interest

The authors reported no conflicts of interest.

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