Thrombotic complications with interruption of direct oral anticoagulants in dermatologic surgery

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Background: Direct oral anticoagulants (DOACs), such as apixaban, rivaroxaban, and dabigatran, are increasingly being used to provide prophylaxis and treatment for arterial and venous thromboembolism. Multiple procedural subspecialties have implemented guidelines detailing time frames for perioperative DOAC interruption; however, the impact of perioperative DOAC interruption in patients undergoing dermatologic surgery is currently unknown, and evidence-based guidelines are lacking.

Objective: To assess the 30-day postoperative rate of thrombotic complications (ischemic stroke, transient ischemic attack, systemic embolism, deep vein thrombosis [DVT] and pulmonary embolism) in patients with nonvalvular atrial fibrillation (AF) or a history of DVT who underwent perioperative DOAC interruption during dermatologic surgery.

Methods: A retrospective medical record review was performed of all patients with AF or a history of DVT who underwent perioperative DOAC interruption during dermatologic surgery at Advanced Dermatologic Surgery and the University of Kansas Medical Center between January 1, 2016, and August 31, 2020.

Results: Among 806 operations, comprising 750 Mohs micrographic operations (93.1%) and 56 excisions (6.9%), 1 patient (0.14% of patients with AF) sustained a transient ischemic attack and 2 patients (0.25% of all patients) sustained minor bleeding complications during the 30-day postoperative period.

Conclusion: Perioperative DOAC interruption appears to be safe and efficacious in dermatologic surgery. (J Am Acad Dermatol 2021;84:425-31.)

Key words: anticoagulation; atrial fibrillation; cutaneous surgery; dermatologic surgery; direct oral anticoagulation; DOAC; Mohs micrographic surgery; venous thromboembolism.

Perioperative management of oral anticoagulation has become increasingly complex in recent years. Nearly 38% of patients who undergo dermatologic surgery are taking an antithrombotic agent that places them at a slightly higher risk for bleeding.[1] Direct oral anticoagulants (DOACs) are an increasing presence in the dermatologist's office and have largely replaced warfarin as a first-line anticoagulant.[2,3] Unlike warfarin, DOACs act independently of the vitamin K pathway and directly inhibit specific clotting factors.[3] Widespread use of DOACs is mainly due to their improved efficacy, more predictable pharmacokinetics, superior safety profile, and ease of use.[4] Starting in 2010, the first 3 DOACs to be approved in the United States were dabigatran, rivaroxaban, and apixaban. Currently, DOACs are indicated for stroke prevention in nonvalvular atrial fibrillation (AF),[5-7] treatment of venous thromboembolism (VTE),[8-10] and deep vein thrombosis (DVT) prophylaxis.[11-13]

Dermatologists treating patients using DOACs must be aware of their perioperative management. Incorrect management in the perioperative setting may lead to complications ranging from increased

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intraoperative bleeding to postoperative hematoma formation or skin graft compromise.[14,15] Perioperative interruption of DOACs is increasingly common among multiple procedural subspecialties, and time frames regarding DOAC interruption have been included in their working guidelines.[16-20] However, the impact of perioperative DOAC interruption in patients undergoing dermatologic surgery is currently unknown, and evidence-based guidelines are lacking. To our knowledge, no studies to date have investigated the risk of thrombotic events in patients who interrupt their DOAC regimen during dermatologic surgery. Therefore, the aim of the present study was to assess the rate of thrombotic complications associated with perioperative DOAC interruption in patients undergoing dermatologic surgery.

CAPSULE SUMMARY

- The impact of interrupting direct oral anticoagulants in patients undergoing dermatologic surgery is currently unknown. Perioperative interruption time frames are included in the working guidelines among nondermatologic procedural subspecialties.
- This retrospective analysis suggests that perioperative interruption of direct oral anticoagulants appears to be safe and efficacious in dermatologic surgery.

METHODS

Study design and population

A retrospective medical record review was performed on all patients who underwent dermatologic surgery, consisting of Mohs micrographic surgery (MMS) and traditional excision, at Advanced Dermatologic Surgery—ADS Ambulatory Surgery Center and the University of Kansas Medical Center between January 1, 2016, and August 31, 2020. The following additional patient characteristics were assessed for study eligibility: adults (aged ≥18 years) with nonvalvular AF or prior VTE who were receiving apixaban, dabigatran, or rivaroxaban and who adhered to the present study's perioperative DOAC interruption protocol. Thromboembolic risk, based on the CHA_2DS_2-VASc score (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, previous Stroke [transient ischemic attack {TIA}or thromboembolism], Vascular disease [previous myocardial infarction or peripheral artery disease or aortic plaque], Age 65-74 years; and Sex category) was recorded for patients with nonvalvular AF. However, the CHA_2DS_2-VASc score did not affect perioperative DOAC management because this risk score is used in a perioperative setting to assess the need for heparin bridging,[17] which was not performed.

Procedures

All patients in this study omitted their DOAC regimens 1 day before dermatologic surgery and resumed their DOAC regimen 1 day after. All dermatologic operations were performed under local anesthesia with 1% lidocaine with 1:100,000 epinephrine. Clinical characteristics included tumor location, tumor type, postoperative defect size, surgical repair type, and surgical repair dimensions. The postoperative defect sizes were recorded as 2 orthogonal dimensions (x and y axis) by the surgeon as postoperative size X and Y. Smaller orthogonal length of the defect size was recorded as size X, and longer length was recorded as size Y. Surgical repair types included linear closure, second intention (no closure), flap (including advancements, rotations, transpositions, and interpolations), full-thickness skin graft, or a combination of the above (linear + graft, or flap + graft).

Tumor location was defined using zones corresponding to H, M, and L areas consistent with the 2020 National Comprehensive Cancer Network Guidelines,[12] and the American Academy of Dermatology's appropriate use criteria on MMS.[13] Zone 1 was defined as the "mask areas" of the face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermillion], chin, mandible, preauricular, and postauricular skin/sulci, temple, and ear), genitalia, hands, and feet. Zone 2 was defined as the cheeks, forehead, scalp, neck, and pretibial surface. Zone 3 was defined as the trunk and extremities, excluding hands, nail units, pretibial, ankles, and feet.

Study outcomes

Study outcomes were assessed from the time the first DOAC dose was interrupted until 30 days after surgery. Primary outcomes were arterial thromboembolism (ischemic stroke, TIA, and arterial systemic embolism), recurrent DVT or pulmonary embolism (PE), and bleeding complications. Secondary outcomes were death and myocardial infarction. Outcomes were assessed by reviewing patient electronic medical records and by contacting patients via telephone. Outcomes were defined according to standardized criteria (Supplemental Appendix 1 available via Mendeley at https://data.mendeley.com/datasets/nmg9kh33sv/3).[21,22]

Abbreviations used:

ACC:	American College of Cardiology
AF:	atrial fibrillation
CHA_2DS_2-VASc:	Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus. previous Stroke, transient ischemic attack, or thromboembolism, V, vascular disease (previous myocardial infarction or peripheral artery disease or aortic plaque), A, age 65-74 years, and Sc, sex category
CI:	confidence interval
DVT:	deep vein thrombosis
DOAC:	direct oral anticoagulant
PE:	pulmonary embolism
TIA:	transient ischemic attack
VTE:	venous thromboembolism

Analysis

Outcomes were analyzed per patient. Patient characteristics were analyzed using calculations of mean values and SDs. Proportions with 95% confidence intervals (CIs) were calculated for outcomes using the Wilson method without continuity correction. Statistics calculations were conducted using SAS 9.4 software (SAS Institute Inc, Cary, NC). The study was approved by the University of Kansas Medical Center Institutional Review Board.

RESULTS

Between January 1, 2016, and August 31, 2020, 806 dermatologic operations, comprising 750 MMS procedures (93.1%) and 56 excisions (6.9%), were performed on patients who adhered to the perioperative DOAC interruption protocol. Patients were a mean age of 76.8 ± 9.1 years, and 659 (81.8%) were men. A total of 719 patients (89.2%) had nonvalvular AF, and 87 (10.8%) had a history of a prior DVT (Table I). Distribution of DOAC type among patients was 459 (56.9%) on apixaban, 265 (32.9%) on rivaroxaban, and 82 (10.2%) on dabigatran. Overall, 1 patient (0.14% of patients with nonvalvular AF) reported a TIA, and 2 patients (0.25% of all patients) reported bleeding complications during the 30-day postoperative period (Table II). The TIA occurred 25 days postoperatively in a male patient with nonvalvular AF on apixaban and aspirin who had a CHA_2DS_2-VASc score of 5 (indicating a 6.7% annual risk of ischemic stroke) and underwent a full-thickness skin graft on the nose. He fully recovered from the TIA with no lasting sequelae.

The only bleeding complication that required evacuation of a hematoma occurred 24 hours postoperatively in a patient on rivaroxaban who underwent a large 66 cm^2 advancement flap on the cheek.

Table I. Baseline characteristics

Characteristic	Result (N = 806)
Age at procedure, mean (SD), y	76.8 (9.1)
Sex, No. (%)	
Female	147 (18.2)
Male	659 (81.8)
Direct oral anticoagulation	
Indication, No. (%)	
Atrial fibrillation	719 (89.2)
Prior VTE	87 (10.8)
Agent	
Apixaban	459 (56.9)
Rivaroxaban	265 (32.9)
Dabigatran	82 (10.2)
CHA_2DS_2-VASc score,* mean (SD)	2.9 (1.2)
Dermatologic surgery	
Mohs micrographic surgery	750 (93.1)
Excision	56 (6.9)
Location, No. (% of surgical sites)†	
Zone 1	408 (50.6)
Zone 2	302 (37.5)
Zone 3	96 (11.9)
Postoperative size X, cm	
Mean (SD)	2.01 (1.02)
Median (range)	1.8 (7.6)
Postoperative size Y, cm	
Mean (SD)	1.69 (0.80)
Median (range)	1.5 (5.0)
Repair, No. (% of surgical sites)	
Linear closure	366 (45.4)
Second intention	86 (10.7)
Flap	188 (23.3)
Graft	138 (17.1)
Other	28 (3.5)

No., Number; *VTE*, venous thromboembolism.

*Applies to patients with nonvalvular atrial fibrillation only. CHA_2DS_2-VASc score: C = Congestive heart failure (or left ventricular systolic dysfunction), 1 point; H = Hypertension: blood pressure consistently >140/90 mm Hg (or treated hypertension on medication), 1 point; A_2 = Age ≥75 years, 2 points; D = Diabetes mellitus, 1 point; S_2: prior stroke or transient ischemic attack or thromboembolism, 2 points; V = Vascular disease (previous myocardial infarction, peripheral arterial disease or aortic plaque), 1 point; A = Age 65-74 years, 1 point; Sc = Sex category (female sex) 1 point.

†National Comprehensive Cancer Network Guidelines version 2.2020 of cutaneous squamous cell carcinoma. Zone 1, "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, and ear), genitalia, hands, and feet; zone 2, cheeks, forehead, scalp, neck, and pretibia; zone 3, trunk and extremities (excluding hands, nail units, pretibia, ankles, and feet).

The other mild bleeding complication required reapplication of a pressure dressing and occurred 48 hours postoperatively in a patient on rivaroxaban who underwent a 7.0-cm linear closure on the cheek. No cases of recurrent DVT, PE, myocardial infarction,

Table II. Characteristics of patients taking direct anticoagulants (*DOACs*) who experienced postoperative thromboembolic or bleeding complications

Patient	Age/sex	DOAC	Indication	Tumor/ location	Postop size, cm	Repair	Complication	Management
1	68/M	Apixaban	AF	BCC/nose	1.0 × 1.0	FTSG	TIA at 25 days	Full recovery
2	90/M	Rivaroxaban	AF	BCC/cheek	3.8 × 2.6	Flap	Acute hematoma at 24 hours	Hematoma evacuation
3	78/M	Rivaroxaban	AF	Lentigo maligna/ neck	2.0 × 2.3	Linear	Bleeding at 48 hours	Pressure dressing reapplication

AF, Atrial fibrillation; *BCC*, basal cell carcinoma; *FTSG*, full thickness skin graft; *M*, male; *TIA*, transient ischemic attack.

or death within the 30-day perioperative period were reported.

DISCUSSION

We found that in patients with nonvalvular AF or a history of VTE who were receiving a DOAC and underwent perioperative interruption of their DOAC regimen for dermatologic surgery, a simple standardized perioperative management strategy, was associated with low 30-day rates of arterial thromboembolism (0.14%; 95% CI, 0.04%-0.78%) in patients with AF, no occurrences of recurrent VTE or PE, or both (0.0%; 95% CI, 0.0%-4.2%) in patients with prior VTE, and low rates of bleeding complications (0.25%; 95% CI, 0.07%-0.90%) in all patients.

Our results are consistent with those from multiple recent studies on periprocedural DOAC interruption in the nondermatologic literature. Similar to our study, these studies have found that routine periprocedural DOAC interruption is not associated with an increased rate of stroke, TIA, or recurrent DVT/PE relative to DOAC continuation throughout the entire periprocedural window.

A large meta-analysis that included 19,353 patients with nonvalvular AF who underwent perioperative DOAC interruption or DOAC continuation demonstrated no increase in the 30-day rates of arterial thromboembolism (0.4% with DOAC interruption vs 0.6% with DOAC continuation) or major bleeding with DOAC interruption.[23] Importantly, this large meta-analysis demonstrated that there is a 0.6% (95% CI, 0.4%-0.8%) "baseline risk" for arterial thromboembolism in this patient population even when DOACs are continued throughout the perioperative period.

Similarly, the randomized controlled continued vs. interrupted direct oral anticoagulants at the time of device surgery, in patients with moderate to high risk of arterial thromboembolic events (BRUISE CONTROL-2) trial conducted on 662 patients with AF undergoing periprocedural DOAC interruption or continuation during electrophysiology procedures demonstrated no significant differences in the rates of ischemic stroke (0.3% with DOAC interruption vs 0.3% with DOAC continuation) or hematoma formation (2.1% with DOAC interruption vs 2.1% with DOAC continuation).[24]

Additionally, a recent prospective study by Nakamura et al[25] examined 846 patients with nonvalvular AF who randomly underwent periprocedural DOAC interruption or continuation during catheter ablation of AF. They found no significant differences in the rates of systemic thromboembolism (0.2% with DOAC interruption vs 0.2% with DOAC continuation) or bleeding (0.9% with DOAC interruption vs 0.5% with DOAC continuation).[25]

More recently, results from the large, prospective Perioperative Anticoagulation Use for Surgery Evaluation (PAUSE) study demonstrated low 30-day rates of arterial thromboembolism (0.33%) and major bleeding (1.43%) in 3007 patients with AF who underwent standardized perioperative interruption of their DOAC regimens.[17]

Finally, a recent retrospective study by Shaw et al[26] examined 190 patients with a history of prior VTE who interrupted their DOAC regimens periprocedurally. The authors reported low 30-day postoperative rates of recurrent VTE (1.05%) and major bleeding (0.53%).[26]

Our results compare favorably with the outcomes in these studies and suggest that perioperative DOAC interruption in the setting of nonvalvular AF and prior VTE appears to be both safe and effective in dermatologic surgery.

To our knowledge, no prior studies have investigated the risk of thrombotic complications with perioperative DOAC interruption in dermatologic surgery. Rather, previous studies have focused on bleeding complications in dermatologic surgery when DOACs were continued perioperatively. A retrospective analysis of 76 MMS procedures involved 51 patients taking a DOAC and demonstrated a postoperative bleeding rate of 1.3% when DOACs were continued perioperatively.[27] A more

Table III. Perioperative direct oral anticoagulation interruption and resumption protocol for dermatologic surgery

Present study protocol	Creatinine clearance (mL/min)	Interruption any bleed risk		Resumption any bleed risk	
Apixaban Rivaroxaban Dabigatran	Any	24 h		24 h	
ACC guidelines		**Low**	**High**	**Low**	**High**
Apixaban	≥30	≥24 h	≥48 h	24 h	48-72 h
Rivaroxaban Dabigatran	≥80	≥24 h	≥48 h	24 h	48-72 h
	30-79	≥36-48 h	≥72-96 h		
	15-29	≥72 h	≥120 h		

ACC, American College of Cardiology.

recent retrospective analysis by Eilers et al[2] investigated 1800 patients taking any form of oral anticoagulation while undergoing dermatologic surgery and demonstrated a 7-times higher likelihood of postoperative bleeding complications in patients taking DOACs compared with all other anticoagulation types combined.[28] Despite the increased risk of bleeding complications with DOAC continuation, the authors of these studies recommended perioperative continuation of DOACs in dermatologic surgery, in accordance with existing dermatologic guidelines regarding other antithrombotic agents such as warfarin, aspirin, and clopidogrel.[27-30]

Historically, the risk of serious thrombotic events associated with perioperative interruption of warfarin or antiplatelet regimens during dermatologic surgery has been thought to outweigh the risk of limited harm (ie, bleeding complications) with their continuation.[31-36] This has led to the broad recommendation in the dermatology literature to continue all antithrombotic agents during dermatologic surgery—a recommendation that has since been extrapolated to include DOACs.[3,27,37] Indeed, the discontinuation of warfarin, aspirin, or clopidogrel during dermatologic surgery has been met with serious thrombotic events.[31,35,36] However, before the present study, the impact of perioperative DOAC interruption in dermatologic surgery was unknown.

DOACs possess several advantages over warfarin that allow for safer and more efficacious perioperative interruption.[23] One major advantage is the much shorter half-life of DOACs as a class (range, 7-14 hours) over warfarin (60 hours) that enables temporary discontinuation much closer to the time of the procedure or surgery (fast offset).[38] Likewise, DOACs will render a patient therapeutically anticoagulated within hours (fast onset) after resumption of the first full DOAC dose, a characteristic that is distinct from warfarin.[38] DOACs also have more predictable pharmacokinetic and pharmacodynamic anticoagulant effects compared with warfarin, which may translate into fewer major bleeding complications in the periprocedural setting.[38]

In 2017, the American College of Cardiology (ACC) issued guidelines recommending that DOACs be withheld ≥24 hours before—and resumed at full dose on the day after—procedures with a low bleeding risk (Table III).[38] Longer periods of DOAC interruption are recommended for procedures with higher bleeding risk, including reconstructive plastic surgery. Given the short half-lives of DOACs, the lack of proven benefit with bridging, and the increased risk of major bleeding with bridging therapy, the ACC also stated that bridging with a parenteral agent (eg, unfractionated heparin) is almost never indicated before procedures.[38]

The perioperative DOAC interruption protocol used in our study is similar to the standardized perioperative DOAC management protocol for procedures with low bleeding risk that was used in the PAUSE study and in the aforementioned recommendations from the ACC. However, one difference is that we did not lengthen our DOAC interruption duration if the patient had diminished creatinine clearance or if the surgery bleeding risk was "moderate," "high," or "uncertain."[17,38] In the setting of diminished creatinine clearance, DOACs are not eliminated as rapidly. As a result, one would anticipate that our study group may have experienced more bleeding complications than if creatinine clearance was assessed before surgery and the DOACs were withheld for longer periods of time in those with renal insufficiency or in those with a surgery that was higher risk for bleeding than standard "low risk" procedures.

Although our findings are reassuring, prospective studies are needed to determine the optimal perioperative DOAC management strategy in patients

undergoing dermatologic surgery. We recommend that dermatologic surgeons counsel patients on the risks and benefits of perioperative DOAC interruption and continuation, particularly when undergoing operations with a higher risk of postoperative bleeding. It is imperative that patients who undergo perioperative DOAC interruption at the time of surgery be thoroughly counseled on the signs and symptoms of thrombotic events.

This study has several limitations, including the single-center retrospective design. We did not assess creatinine clearance, a variable that warrants further investigation in future studies. The high proportion of MMS reconstructive facial procedures may negatively affect the generalizability of bleeding complications, which may be even lower for general dermatologic surgical procedures than was observed in our data set. Assessing patients via telephone for prior thrombotic and bleeding events was subject to recall bias. Importantly, this study did not assess for or interrupt any other antithrombotic agents (eg aspirin or clopidogrel) that patients may have been receiving at the time of surgery. A large prospective study examining a broader array of dermatologic surgical procedures at a variety of anatomic sites would help address these limitations.

CONCLUSION

To our knowledge, this study represents the first investigation of perioperative DOAC interruption in patients undergoing dermatologic surgery. Our study demonstrates that the perioperative interruption of DOACs in patients with nonvalvular AF or a history of DVT/PE during dermatologic surgery appears to be efficacious and safe, from the standpoint of both the thrombotic and bleeding risk. As the use of DOACs continues to increase, dermatologists must possess an awareness and knowledge of perioperative DOAC management. Future studies investigating perioperative DOAC interruption during dermatologic surgery are warranted.

REFERENCES

1. Callahan S, Goldsberry A, Kim G, Yoo S. The management of antithrombotic medication in skin surgery. *Dermatol Surg*. 2012;38:1417-1426.
2. Macle L, Cairns J, Leblanc K, et al. 2016 focused update of the Canadian Cardiovascular Society Guidelines for the management of atrial fibrillation. *Can J Cardiol*. 2016;32:1170-1185.
3. Plovanich M, Mostaghimi A. Novel oral anticoagulants: what dermatologists need to know. *J Am Acad Dermatol*. 2015;72:535-540.
4. Lippi G, Mattiuzzi C, Cervellin G, Favaloro EJ. Direct oral anticoagulants: analysis of worldwide use and popularity using Google trends. *Ann Transl Med*. 2017;5:322.
5. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;361:1139-1151.
6. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2011;365:981-992.
7. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365:883-891.
8. EINSTEIN Investigators, Bauersachs R, Berkowitz SD, et al. Oral rivaroxaban for symptomatic venous thromboembolism. *N Engl J Med*. 2010;363:2499-2510.
9. EINSTEIN—PE Investigators, Büller HR, Prins MH, et al. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. *N Engl J Med*. 2012;366:1287-1297.
10. Schulman S, Kearon C, Kakkar AK, et al. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med*. 2009;361:2342-2352.
11. Agnelli G, Buller HR, Cohen A, et al. Apixaban for extended treatment of venous thromboembolism. *N Engl J Med*. 2013;368:699-708.
12. Cohen AT, Spiro TE, Buller HR, et al. Rivaroxaban for thromboprophylaxis in acutely ill medical patients. *N Engl J Med*. 2013;368:513-523.
13. Lassen MR, Gallus A, Raskob GE, et al. Apixaban versus enoxaparin for thromboprophylaxis after hip replacement. *N Engl J Med*. 2010;363:2487-2498.
14. Kargi E, Babuccu O, Hosnuter M, Babuccu B, Altinyazar C. Complications of minor cutaneous surgery in patients under anticoagulant treatment. *Aesthetic Plast Surg*. 2002;26:483-485.
15. Syed S, Adams BB, Liao W, Pipitone M, Gloster H. A prospective assessment of bleeding and international normalized ratio in warfarin-anticoagulated patients having cutaneous surgery. *J Am Acad Dermatol*. 2004;51:955-957.
16. Dalia AA, Kuo A, Vanneman M, Crowley J, Elhassan A, Lai Y. Anesthesiologists guide to the 2019 AHA/ACC/HRS focused update for the management of patients with atrial fibrillation. *J Cardiothorac Vasc Anesth*. 2020;34:1925-1932.
17. Douketis JD, Spyropoulos AC, Duncan J, et al. Perioperative management of patients with atrial fibrillation receiving a direct oral anticoagulant. *JAMA Intern Med*. 2019;179(11):1469-1478.
18. Ing E, Douketis J. New oral anticoagulants and oculoplastic surgery. *Can J Ophthalmol*. 2014;49:123-127.
19. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2019;74:104-132.
20. Parekh PJ, Merrell J, Clary M, Brush JE, Johnson DA. New anticoagulants and antiplatelet agents: a primer for the clinical gastroenterologist. *Am J Gastroenterol*. 2014;109:9-19.
21. Schulman S, Angeras U, Bergqvist D, et al. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in surgical patients. *J Thromb Haemost*. 2010;8:202-204.
22. Spyropoulos AC, Douketis JD, Gerotziafas G, et al. Periprocedural antithrombotic and bridging therapy: recommendations for standardized reporting in patients with arterial indications for chronic oral anticoagulant therapy. *J Thromb Haemost*. 2012;10:692-694.
23. Nazha B, Pandya B, Cohen J, et al. Periprocedural outcomes of direct oral anticoagulants versus warfarin in nonvalvular atrial fibrillation. *Circulation*. 2018;138:1402-1411.

24. Birnie DH, Healey JS, Wells GA, et al. Continued vs. interrupted direct oral anticoagulants at the time of device surgery, in patients with moderate to high risk of arterial thromboembolic events (BRUISE CONTROL-2). *Eur Heart J*. 2018;39:3973-3979.
25. Nakamura K, Naito S, Sasaki T, et al. Uninterrupted vs. interrupted periprocedural direct oral anticoagulants for catheter ablation of atrial fibrillation: a prospective randomized single-centre study on post-ablation thrombo-embolic and haemorrhagic events. *Europace*. 2019;21:259-267.
26. Shaw J, de Wit C, Le Gal G, Carrier M. Thrombotic and bleeding outcomes following perioperative interruption of direct oral anticoagulants in patients with venous thromboembolic disease. *J Thromb Haemost*. 2017;15:925-930.
27. Antia C, Hone N, Gloster H. Perioperative complications with new oral anticoagulants dabigatran, apixaban, and rivaroxaban in Mohs micrographic surgery: a retrospective study. *J Am Acad Dermatol*. 2017;77:967-968.
28. Eilers RE Jr, Goldenberg A, Cowan NL, Basu P, Brian Jiang SI. A retrospective assessment of postoperative bleeding complications in anticoagulated patients following Mohs micrographic surgery. *Dermatol Surg*. 2018;44:504-511.
29. Otley CC. Continuation of medically necessary aspirin and warfarin during cutaneous surgery. *Mayo Clin Proc*. 2003;78:1392-1396.
30. Otley CC. Perioperative evaluation and management in dermatologic surgery. *J Am Acad Dermatol*. 2006;54:119-127.
31. Alam M, Goldberg LH. Serious adverse vascular events associated with perioperative interruption of antiplatelet and anticoagulant therapy. *Dermatol Surg*. 2002;28:992-998. discussion 8.
32. Alcalay J. Cutaneous surgery in patients receiving warfarin therapy. *Dermatol Surg*. 2001;27:756-758.
33. Billingsley EM, Maloney ME. Intraoperative and postoperative bleeding problems in patients taking warfarin, aspirin, and nonsteroidal antiinflammatory agents. A prospective study. *Dermatol Surg*. 1997;23:381-383. discussion 4-5.
34. Bordeaux JS, Martires KJ, Goldberg D, Pattee SF, Fu P, Maloney ME. Prospective evaluation of dermatologic surgery complications including patients on multiple antiplatelet and anticoagulant medications. *J Am Acad Dermatol*. 2011;65:576-583.
35. Kovich O, Otley CC. Thrombotic complications related to discontinuation of warfarin and aspirin therapy perioperatively for cutaneous operation. *J Am Acad Dermatol*. 2003;48:233-237.
36. Schanbacher CF, Bennett RG. Postoperative stroke after stopping warfarin for cutaneous surgery. *Dermatol Surg*. 2000;26:785-789.
37. Brown DG, Wilkerson EC, Love WE. A review of traditional and novel oral anticoagulant and antiplatelet therapy for dermatologists and dermatologic surgeons. *J Am Acad Dermatol*. 2015;72:524-534.
38. Doherty JU, Gluckman TJ, Hucker WJ, et al. 2017 ACC expert consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation: a report of the American College of Cardiology Clinical Expert Consensus Document Task Force. *J Am Coll Cardiol*. 2017;69:871-898.