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ORIGINAL ARTICLE

Application-based management of perioperative anticoagulant therapy: description of POPACTApp

Michael Thomaschewski[1] · Florens Beyer[2] · Martin Thomaschewski[3] · David Ellebrecht[1] · Markus Jonczyk[4] · Matthias Schneider[4] · Tobias Keck[1] · Tilo Mentler[2] · Richard Hummel[1]

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Abstract

Purpose Perioperative management of oral anticoagulation (OAC) is a constant challenge in interventional and surgical procedures. When deciding to discontinue OAC, the risk of thromboembolic events must be balanced against the risk of bleeding during and after the planned procedure. These risks differ across patients and must be considered individually.

Methods POPACTApp, an application for the perioperative or peri-interventional management of oral anticoagulants, was developed using a human-centered design process (ISO 9241-210:2010). The treatment concept developed here can be adapted to a patient's individual risk profile. POPACTApp provides recommendations based on guidelines, consensus statements, and study data. After entering patient-specific risk factors, the attending physician using POPACTApp receives a clear and direct presentation of a periprocedural treatment concept, which should enable the efficient use of the program in everyday clinical practice. The perioperative treatment concept is presented via a timeline, including (1) the decision on whether to interrupt OAC, (2) the timing of the last preoperative administration of OAC in cases of interruption, (3) the decision on whether and how to bridge with heparins, and (4) the decision about when to reinitiate anticoagulation.

Results A task-based survey to evaluate POPACTApp's usability conducted with 20 surgeons showed that all clinicians correctly interpreted the recommendations provided by the app. Further, a questionnaire using a 7-point Likert scale from − 3 (negative) to + 3 (positive) revealed the following results to three specific questions: (1) satisfaction with the current standard procedure in the respective unit of the participant (0.15; SD = 1.57), (2) individual satisfaction with the POPACTApp application (2.7; SD = 0.47), and (3) estimation of the usefulness of POPACTApp for clinical practice (2.7; SD = 0.47).

Conclusions POPACTApp provides clinicians with an individual risk-optimized treatment concept for the perioperative or peri-interventional management of OAC based on current guidelines, consensus statements, and study data, enabling the standardized perioperative handling of OAC in daily clinical practice.

Keywords Medical application · Perioperative bridging · Perioperative management of oral anticoagulation · Perioperative anticoagulant therapy · Usability

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✉ Michael Thomaschewski
Michael.Thomaschewski@uksh.de

[1] Department of Surgery, University Medical Center Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany

[2] Institute for Multimedia and Interactive Systems, University of Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany

[3] Center for Nano Optics, University of Southern Denmark, Campusvej 55, 5230 Odense, Denmark

[4] Department of Vascular Surgery, Academic Teaching Hospital St. Adolf-Stift, University of Hamburg, Hamburger Straße 41, 21465 Reinbek, Germany

Introduction

Increasing numbers of patients receive prophylactic or therapeutic oral anticoagulation (OAC) for thromboembolic events/diseases [1]. Currently, roughly one in 10 surgical patients in the USA receives OAC [2, 3].

For most major surgical and interventional procedures, OAC should be stopped—at least temporarily—to prevent serious bleeding complications. However, the interruption of anticoagulation potentially increases the risk of perioperative thromboembolic events, thus requiring the stringent selection of patients, and the interval without anticoagulation should be minimized [2]. Currently, atrial fibrillation (AF) is the most common reason for OAC therapy, with the intention of reducing the risk of stroke and other systemic embolism [4], followed by other indications such as mechanical heart valves and venous thromboembolism. However, the risk of thromboembolic events in patients with AF varies among patients. Risk factors include heart failure, hypertension, older age, diabetes, previous stroke or transient ischemic attack, vascular disease, and female sex, and scoring systems such as the CHADS2 and CHA2DS2-VASc are used to determine patients' individual risk [5–8]. For bleeding complications, the risk is influenced by patient-specific risk factors and the invasiveness or extent of the planned procedure [9–13].

Until a few years ago, mainly vitamin K antagonists were used for OAC. In recent years, "new oral anticoagulants" or "direct-acting anticoagulants" (DOACs) such as apixaban, dabigatran, edoxaban, and rivaroxaban have been developed and are now increasingly used for OAC. DOACs differ from vitamin K antagonists in their pharmacokinetics: The elimination of DOACs is primarily renal (excretion through the kidneys). There is also significant variation among DOACs in their pharmacokinetics [3, 14].

The abundance of anticoagulants available and the variable risks of different surgical or interventional procedures often complicate decision-making regarding the perioperative management of OAC. In this regard, new technologies and (mobile) applications (mobile apps) summarized under the term "mobile Health" (mHealth) [15] could support individual clinical decision-making by processing procedure- and patient-related data in structured (algorithmic) ways. However, users' abilities, goals, tasks, needs, and work conditions need to be carefully considered in order to develop computer-based solutions that are both usable and accepted.

The aim of our work was to develop a mobile app that provides assistance with the perioperative and periinterventional management of OAC therapy for individual patients. Based on guidelines, consensus statements, and study data, we created a mobile app to support clinical decision-making around four key questions: (1) Should the patient's anticoagulation be interrupted? (2) When and how should the patient's anticoagulation be interrupted? (3) Is bridging necessary? (4) When should the patient's anticoagulation be resumed? In short, the purpose of the application is to provide a clear and evidence-based treatment concept for individual patients, minimizing risk of both bleeding and thromboembolic complications.

Material and methods

Human-centered design process

An application for perioperative anticoagulation therapy (POPACTApp) was developed using a human-centered design process—"an approach to interactive systems development that aims to make systems usable and useful by focusing on the users, their needs and requirements, and by applying human factors/ergonomics, and usability knowledge and techniques" [16]. This approach is characterized by an iterative design process driven by insights from formative and summative evaluations with respect to users, tasks, and environmental conditions (e.g., stressors, work area layout).

POPACTApp was programmed using Java, allowing the program to be used as a mobile app on devices such as smartphones, tablets, and other mobile devices or as a browser-based web application. POPACTApp was designed for use with Windows, Android, and iOS.

User interface design

When POPACTApp starts up, the user is asked to select the indication for OAC: (1) AF, (2) mechanical heart valve (MHV), or (3) venous thromboembolism (VTE). The POPACTApp user is then asked to enter several pieces of clinical information that are known patient-related risk factors for calculating the risk of both thromboembolic events and bleeding complications (Fig. 1). Specifically, the clinical information requested includes renal or hepatic function/failure, history of bleeding, labile international normalized ratio (INR), use of antiplatelet or nonsteroidal anti-inflammatory medication, abnormality in platelet quality and quantity, and active cancer disease and (1) in cases of AF details on heart failure, hypertension, age, diabetes, previous stroke or transient ischemic attack, vascular disease, and sex; (2) in cases of MHV, the type of MHV, prior embolic event, severe left ventricular dysfunction, and hypercoagulable state; and (3) in cases of VTE thrombophilia, protein C deficiency, protein S deficiency, antithrombin deficiency, antiphospholipid antibodies, recurrent VTE, time of onset of thrombosis, and active cancer disease.

In addition, POPACTApp requests details on the bleeding risk of the planned invasive procedure; users are asked to choose from three categories: clinically insignificant, minor surgery/intervention, and major surgery/intervention. By

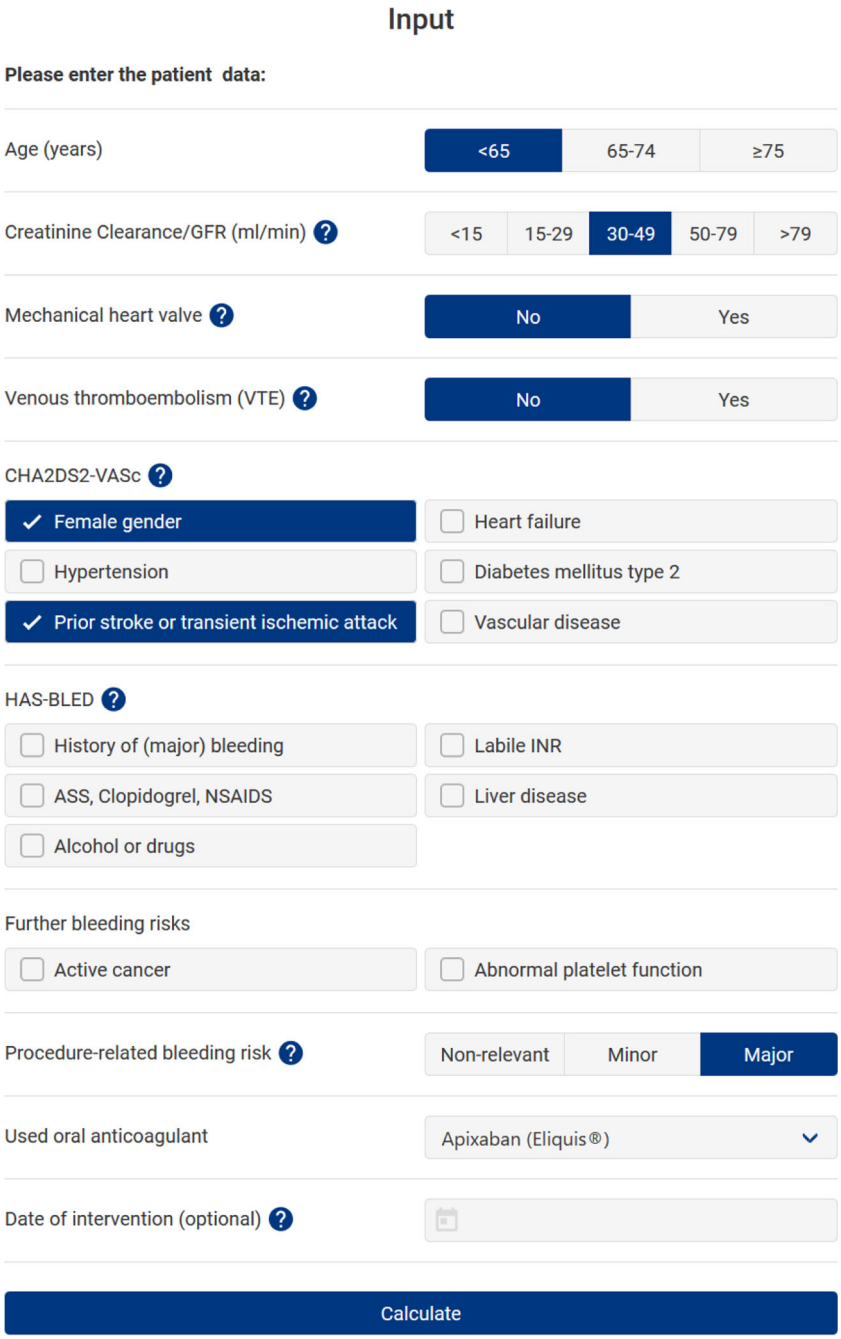

Fig. 1 POPACTApp: a mobile (e.g., smartphones or tablets) or browser-based web application

pressing an "info" button, POPACTApp users can access a catalog of sample procedures for each of the three categories. Finally, the user selects the oral anticoagulant used by the patient. In the current version of the program, three different vitamin K antagonists (acenocoumarol, warfarin, and phenprocoumon) and the four most commonly used DOACs (apixaban, rivaroxaban, edoxaban, and dabigatran) are listed as options.

After entering this clinical information, the user presses the "calculate" button and receives an individualized treatment concept and recommendation for the periprocedural management of the specific patient (Fig. 2). For this output, POPACTApp creates a periprocedural timeline providing information about the need for the temporary interruption of OAC, the timing of last administration of OAC, and postoperative reinitiation of anticoagulant therapy/bridging treatment if OAC is temporarily interrupted and whether and how to bridge OAC with heparins. POPACTApp also provides recommendations on how to control coagulation in specific cases such as patients with chronic renal failure. Moreover, calculated risk scores for both thromboembolic events and bleeding complications are displayed. To find out more about the

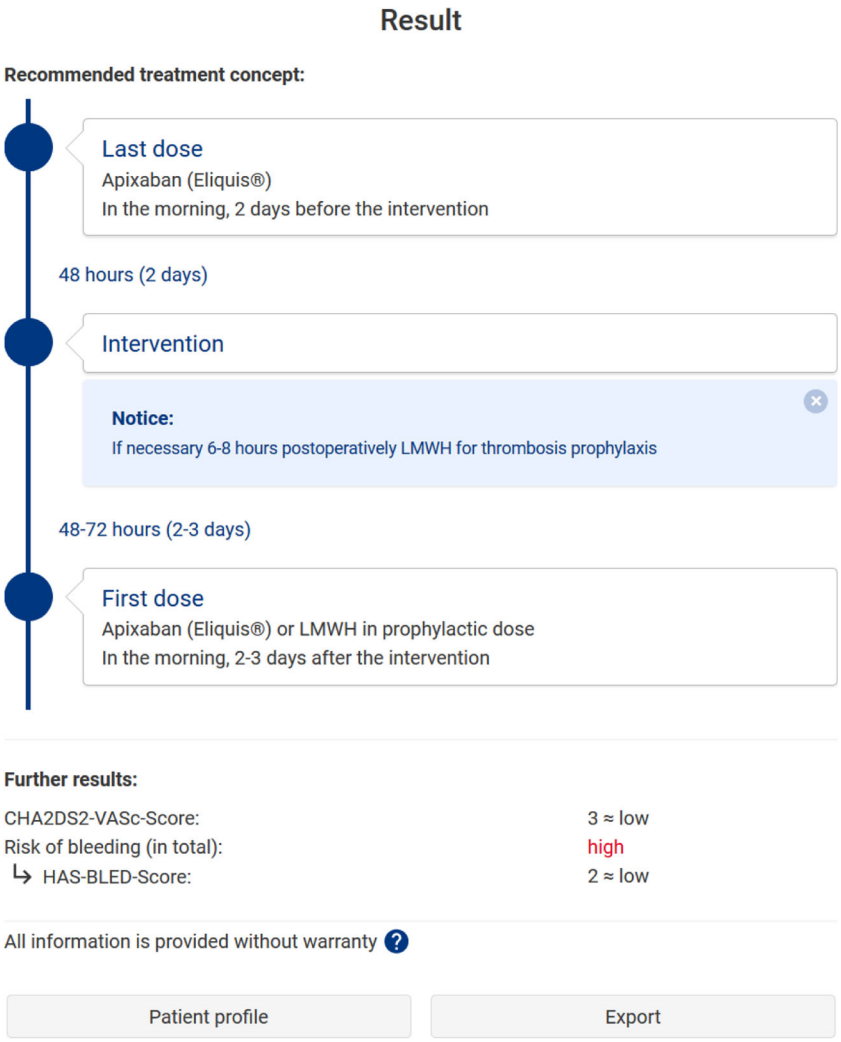

Fig. 2 POPACTApp: example of a perioperative treatment concept for a patient with atrial fibrillation, chronic renal insufficiency (CrCl 40 ml/min), and oral anticoagulation with apixaban undergoing major surgery *Note:* CrCl: creatinine clearance

evidence on which the suggestions are based and about current study data and guidelines, users can select POPACTApp's "info" buttons to access information, diagrams, and a source directory.

Medical background: establishment of treatment algorithms for recommendations

The algorithms used in POPACTApp were established based on data published in the *British Guidelines on Oral Anticoagulation with Warfarin (4th Edition)*, the *American College of Chest Physicians Evidence-based Clinical Practice Guidelines (9th Edition)*, and the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation* [2, 13, 17]. Relevant results from recent clinical studies were also taken into account to generate pathways as indicated [2, 9–12, 14, 18–25].

Definitions and limitations of the use of POPACTApp

1. POPACTApp was designed for patients with nonvalvular AF, MHV, or VTE—the most common indications for OAC.
2. In the establishment of the algorithms, we assumed that the indication for OAC for the selected patient was correct and that there were no contraindications to the current medication.
3. In the establishment of the algorithms, we assumed that the current OAC dosage was consistent with clinical guidelines and prescribing information/instructions.
4. POPACTApp was designed for elective procedures only. For emergency procedures, a number of additional aspects such as altered hemostasis or hemodynamic shock require critical consideration [26]. These aspects are not addressed in POPACTApp. This also includes patients receiving chemotherapy who often have severe thrombocytopenia.

5. POPACTApp does not analyze or comment on the potential interference of anticoagulants with the patient's other medications. For example, antiplatelet agents are associated with an increased risk of bleeding and should be considered separately by the treating physician.
6. POPACTApp is predominantly designed for standard surgical or interventional procedures. Highly invasive procedures such as extensive tumor resections or major vascular surgery were underrepresented in current trials, and evidence for the perioperative management of patients undergoing these procedures is lacking [2, 11, 17, 18, 27]. Therefore, POPACTApp's recommendations have to be considered with caution when applied to these patients, although POPACTApp's output might provide a framework for individual and interdisciplinary clinical decision-making in these cases.
7. POPACTApp does not replace interdisciplinary discussion and consensus on the optimal treatment path for individual patients.

Establishment of algorithms for patients with AF

Calculation of thromboembolic risk

To determine a patient's risk of periprocedural thromboembolic events, POPACTApp uses the CHA2DS2-VASc score, which allocates patients into three risk groups, following the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation* [8, 13, 28]: low risk, moderate risk, and high risk (Table 1). In addition, in line with the *British Guidelines on Oral Anticoagulation with Warfarin (4th Edition)*, all patients who have had a thromboembolic event in the past are classified as high-risk patients by POPACTApp, even if their CHA2DS2-VASc score indicates a low or moderate risk [17].

Patient-related bleeding risk

To determine overall bleeding risk, both patient-related risk factors (HAS-BLED and additional factors) and procedure-related bleeding risk are considered (Table 2). The HAS-BLED score was initially developed to evaluate the risk of spontaneous bleeding with OAC [10] and has been confirmed as appropriate for the assessment of the risk of periprocedural bleeding [9–11]. A HAS-BLED score of ≥ 3 points is highly predictive of bleeding events; patients with such a scoring are designated as having a high risk of periprocedural bleeding in POPACTApp. Additional factors such as prior bleeding events, abnormality in platelet quality and quantity, and active cancer disease have also been found to be associated with a high risk of periprocedural bleeding [11, 12]. In POPACTApp, these factors are used to classify a patient as having a high risk of periprocedural bleeding.

Table 1 POPACTApp classification of three risk categories for perioperative risk of thrombotic events according to CHA2DS2-VASc score

Thromboembolic risk	CHA2DS2-VASc score	
Low (< 5%/year)	0–4	
Moderate (5–10%/year)	5–6	
High (> 10%/year)	> 6	Thromboembolic events in the past

Procedure-related bleeding risk

Procedure-related bleeding risk is determined by the extent and the invasiveness of the planned procedure, also taking into account the clinical effect and relevance of bleeding complications. Here, three procedure-related bleeding risk categories were established for POPACTApp, based on the BRIDGE trial, the *ACC Expert Consensus Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation*, and the *Updated Guidelines from the French Working Group on Perioperative Haemostasis (GIHP)* [13, 18, 26]: clinically insignificant, minor surgery/intervention, and major surgery/intervention (Supplementary Table 1).

Recommendation I: interruption of anticoagulation

POPACTApp recommends continuing OAC with vitamin K antagonists for procedures with clinically insignificant procedure-related bleeding risk when the individual patient has a low risk profile for periprocedural bleeding. According to the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation*, there is no general need for the temporary interruption of OAC for procedures with clinically insignificant procedure-related bleeding risk [13]. This recommendation is based on prospective randomized trials demonstrating that, in cases of pacemaker or cardioverter/defibrillator implantation, continuing OAC with vitamin K antagonists without interruption is associated with a significantly lower bleeding risk, compared with temporarily interrupting OAC and bridging with heparins [19, 20].

However, data on uninterrupted periprocedural OAC with DOACs are rare. There is very limited evidence suggesting that uninterrupted DOACs might not lead to a higher bleeding risk in low-risk procedures [21]. However, because of the lack

Table 2 POPACTApp classification of overall bleeding risk based on patient-related risk factors and procedure-related bleeding risk

Bleeding risk (overall)	Patient-related risk factors	Procedure-related bleeding risk
Low	HES-BLED score < 3	Clinically insignificant, minor surgery/intervention
High	HES-BLED score ≥ 3, prior bleed event, quantitative or qualitative platelet abnormality, active cancer disease	Major surgery/intervention

of relevant evidence, POPACTApp recommends temporarily interrupting DOACs, even for procedures with clinically insignificant procedure-related bleeding risk.

For procedures categorized as minor or major surgeries and for patients with a high-risk profile for periprocedural bleeding, POPACTApp recommends the interruption of OAC.

Recommendation II: last administration of OAC before the procedure

In cases of DOAC therapy, POPACTApp considers the specific pharmacokinetic properties of the medication, depending on renal function for example, and adjusts the timing of the

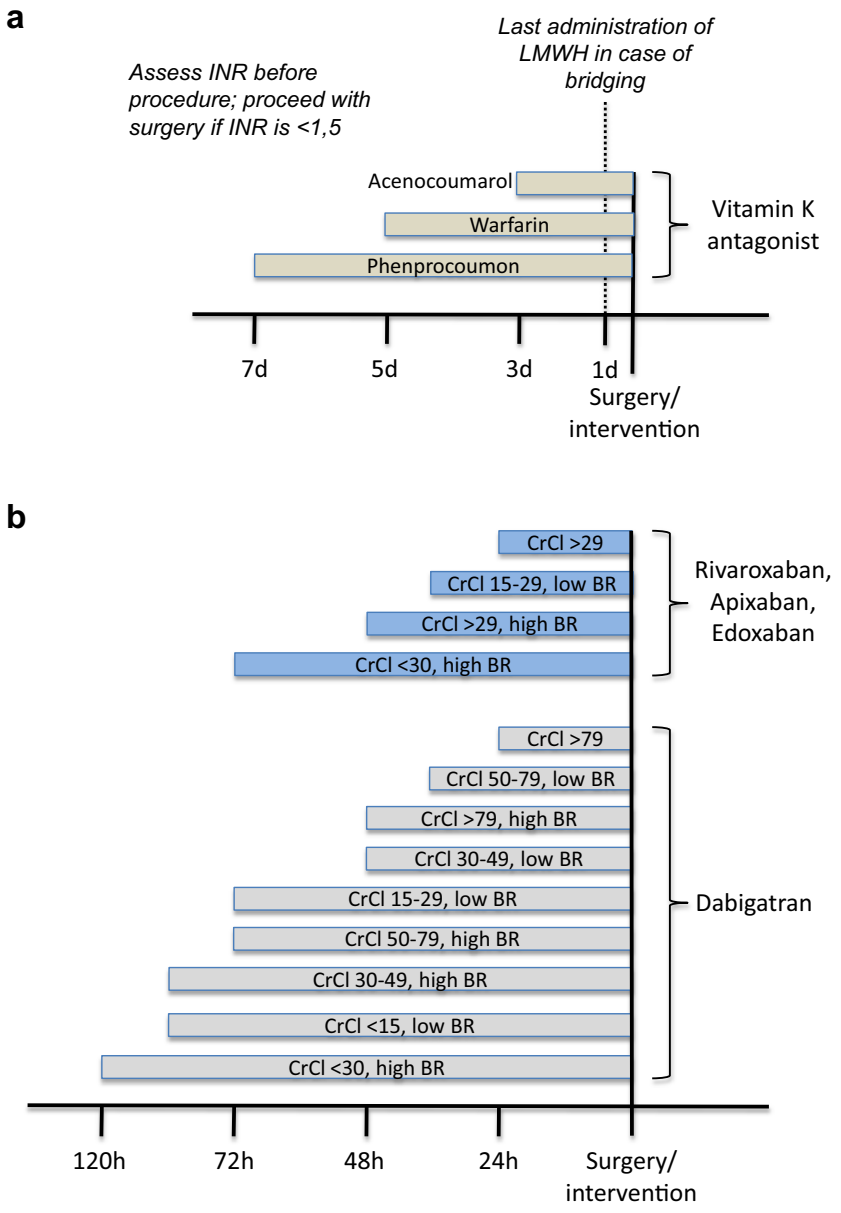

Fig. 3 Preoperative interruption of vitamin K antagonists (**a**) and direct-acting anticoagulants (**b**). *Note:* CrCl: creatinine clearance; BR: bleeding risk; LMWH: low-molecular weight heparin

last preoperative dose (Fig. 3). Generally, the excretion or half-life of DOACs depends on renal function and can vary strongly in cases of decreased renal function, which is determined by creatinine clearance in POPACTApp. POPACTApp also takes into account that DOACs should be paused for a longer time before interventions or surgeries with high bleeding risk (major surgery/intervention).

Recommendations for discontinuing vitamin K antagonists follow published recommendations (Fig. 3) [3, 13, 29]. Monitoring OAC with vitamin K antagonists includes controlling thromboplastin time (INR value). POPACTApp recommends that the user check the INR directly before the intervention or surgery to ensure proper hemostasis for the planned procedure. In cases where bridging with low molecular weight heparin (LMWH) is started preoperatively, the last dose of LMWH should be administrated 24 h before the planned surgery or intervention [2, 13, 17].

Recommendation III: bridging

POPACTApp suggests using only LMWH for bridging OAC. For bridging of oral anticoagulants, most published protocols use LMWH because they are more cost-effective, easier to control, and easier to handle, compared with unfractionated heparins [14, 17, 22, 23]. Furthermore, a register study has found evidence that LMWH and unfractionated heparins have similar results with regard to thromboembolic events and bleeding complications [30]. However, comparative prospective randomized data are not available. In addition, the anticoagulant effect of LMWH can be dangerously prolonged in cases of decreased renal function, and "overdosing" may increase the risk of bleeding complications. POPACTApp refers to this issue and recommends measuring anti-factor Xa activity to monitor the anticoagulant effect if CrCl is < 50 ml/min. This might lead to the adjustment of the dose of LMWH. When CrCl < 30 ml/min, POPACTApp recommends halving the dose of LMWH for bridging or using unfractionated heparins instead.

In general, bridging with heparins is only necessary in patients with MHV and in patients with high risk of embolism (see Tables 1 and 3) using vitamin K antagonists for anticoagulation (Fig. 4). Because of their pharmacokinetics, vitamin K antagonists are difficult to control and are therefore temporarily replaced by bridging with heparins, which present a shorter half-life and a rapid onset of action. In cases of DOAC treatment, bridging with heparins is not necessary in most periprocedural settings because DOACs and LMWH have similar pharmacokinetics, with short half-lives and rapid onset of action. Bridging is therefore generally not recommended when DOACs are used for OAC [13] (Fig. 4). However, when renal function is decreased or there is questionable enteral resorption (e.g., after gastrointestinal interventions), the effect of DOACs may vary significantly and is difficult to monitor [24]. Therefore, POPACTApp recommends postoperative anticoagulant therapy with heparins instead of DOACs if renal function is heavily impaired. POPACTApp offers two postoperative options for procedures categorized as major surgeries/interventions in cases of questionable enteral resorption: (1) restarting DOACs directly or (2) bridging with heparins. The treating physician must make the final decision about which option fits best in the case of the individual patient.

POPACTApp's recommendations about whether to bridge and how to bridge with heparins depend on the risk of thromboembolic events, as determined by the CHA2DS2-VASc score and patient's risk of bleeding (Fig. 4): For patients with a low risk profile (CHA2DS2-VASc score of 0–4 points) and no prior stroke or thromboembolic events, bridging is not recommended. In these cases, POPACTApp directs the user to consider the need for standard postoperative thrombosis prophylaxis. For patients with a moderate risk of a thromboembolic event (CHA2DS2-VASc score of 5 or 6 points) and no prior thromboembolic events, bridging does not appear to be beneficial in a therapeutic dose but rather increases the risk of bleeding complications [13, 18]. This recommendation is mainly based on the recently published BRIDGE trial, which showed no significant difference in the risk of thromboembolic events between patients with or without bridging. Furthermore, patients with perioperative bridging with LMWH showed a significantly increased risk of minor and major bleeding complications [18]. For patients at high risk of a thromboembolic event (CHA2DS2-VASc score > 6 points), POPACTApp recommends bridging with a therapeutic dose of LMWH [2, 13, 17, 27].

Recommendation IV: reinitiation of anticoagulant therapy

In POPACTApp, recommendations for postoperative/postinterventional treatment are based on the recommendations in the *British Guidelines on Oral Anticoagulation with Warfarin (4th Edition)*, the *American College of Chest Physicians Evidence-based Clinical Practice Guidelines (9th Edition)*, and the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation* [2, 13, 17]. In cases where a procedure is categorized as a major surgery/intervention and/or the patient has a high HAS-BLED score (≥ 3 points), POPACTApp recommends reinitiating anticoagulant therapy 48–72 h after surgery. When there is a low bleeding risk profile (minor surgery/intervention and HAS-BLED score < 3 points), anticoagulant therapy can be reinitiated 24 h after the surgery/intervention.

Table 3 Risk for perioperative thromboembolism for patients with mechanical heart valve and venous thromboembolism according to [2, 3, 31]

A		
Mechanical heart valve (MHV)		
Risk for perioperative thromboembolism		
High		Low
Any mechanical mitral valve		Bileaflet aortic valve replacement
Recent (< 6 months) stroke or TIA		Without risk factors for stroke[a]
Bileaflet aortic valve replacement with major risk factors for stroke[a]		
Mechanical heart valve (MHV)—prosthesis thrombogenicity		
High	Intermediate	Low
Lillehei-Kaster	Other bileaflet valves with insufficient data	Carbomedics
Omniscience		Medtronic Hall
Starr-Edwards (ball cage)		ATS
Bjork-Shiley		Medtronic Open-Pivot
Other tilting disc valves		St Jude Medical
		On-X
		Sorin Bicarbon
B		
Venous thromboembolism (VTE)		
Risk for perioperative venous thromboembolism		
High	Intermediate	Low
Recent (< 3 months) VTE	VTE within past 3–12 months	VTE > 12 months ago
Thrombophilia	Recurrent VTE	
Deficiency of protein C, protein S, or antithrombin	Active cancer	

[a] Patient-related major risk factors: prior embolic event, severe left ventricular dysfunction (< 35%), atrial fibrillation, mitral stenosis of any degree, and a hypercoagulable state

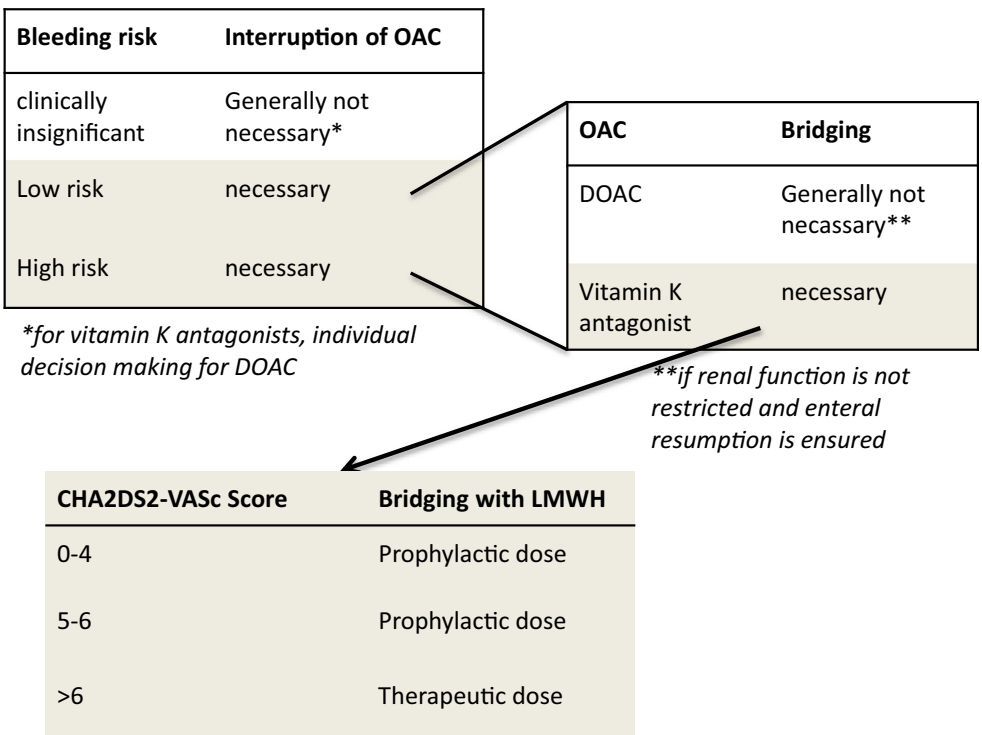

Fig. 4 POPACTApp's algorithm for the decision-making process concerning periprocedural interruption of oral anticoagulants and bridging. *Note:* OAC: oral anticoagulant, DOAC: direct-acting anticoagulant; LMWH: low-molecular weight heparin

Patients with MHV and VTE

The perioperative management recommended in POPACTApp for patients requiring OAC because of MHV or VTE is based on the recommendations in the *British Guidelines on Oral Anticoagulation with Warfarin (4th Edition)* and the *American College of Chest Physicians Evidence-based Clinical Practice Guidelines (9th Edition)* [2, 17]. The categorization of the perioperative risk of thromboembolism for patients with MHV or VTE is described in Table 3 [2, 3]. The algorithm for perioperative management of patients with VTE is analogous to the one for patients with AF, depending on the risk of perioperative thromboembolism (high vs. low risk) and perioperative bleeding (high vs. low vs. clinically insignificant risk). For all patients with MHV undergoing surgery or interventions that mandate interruption of OAC (minor and major surgery according to supplementary Table 1), bridging with heparins is recommended [31]. Although the risk of thromboembolism varies depending on different types of prosthetic valves and patient-related risk factors (Table 3), there is a general recommendation for bridging with heparins during interruption of OAC [31]. In contrast, it is not recommended to interrupt OAC for minor surgical procedures with a clinically insignificant bleeding risk (see Supplementary Table 1).

Clinical study part I: evaluation of correctness of the recommendations provided by POPACTApp

Twenty hypothetical cases of patients with AF, MHV, or VTE who received OAC and required surgery were established by the authors MT (surgeon) and MS (vascular surgery) in consultation with our department of hematology (see Supplementary Table 2). Recommendations for the perioperative management of OAC were generated with POPACTApp. These recommendations were compared with those in the *British Guidelines on Oral Anticoagulation with Warfarin (4th Edition)*, the *American College of Chest Physicians Evidence-based Clinical Practice Guidelines (9th Edition)*, and the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation* [2, 13, 17]. The aim of this evaluation was to determine whether POPACTApp's recommendations were in accordance with the published recommendations and guidelines.

Clinical study part II: evaluation of POPACTApp's usability

To analyze POPACTApp's usability, defined as "the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use" [16], 20 surgeons from different departments (including general, orthopedic, and thoracic surgery) at the University Medical Center Schleswig-Holstein, Campus Lübeck, Germany, were selected to participate in this study (Supplementary Table 3). Through a task-based survey, they assessed different usage-related aspects of POPACTApp.

First, the surgeons' perceptions of the standard procedure for perioperative management of OAC in the selected departments were evaluated by asking participants to report their level of satisfaction with the current procedure in the clinic. Second, the participants were given access to POPACTApp and asked to create perioperative management plans for hypothetical patients with AF and OAC requiring surgery. Here, we assessed whether the participants correctly read and interpreted the recommendations provided by POPACTApp. Third, after using POPACTApp, the participants evaluated the app by completing questionnaire items on their satisfaction with the POPACTApp application and on the usefulness of POPACTApp for clinical practice (Supplementary Fig. 1).

The questionnaire items were scored on a 7-point Likert scale, where the most negative answer was scored as − 3, a neutral answer as 0, and the most positive answer as + 3. The values of the survey were summarized for each item as means and standard deviations (SD). We obtained approval for the study from the local ethics board (Ethik-Kommission Universität zu Lübeck, Aktenzeichen 19-105A).

Results

Clinical study part I: evaluation of the correctness of recommendations provided by POPACTApp

The recommendations provided by POPACTApp for 20 hypothetical patients with AF, MHV, or VTE and OAC requiring surgery were reviewed and compared with published recommendations [2, 13, 17]. Here, no deviations or errors could be detected.

Clinical study part II: evaluation of POPACTApp's usability

Twenty surgeons were asked to participate in the task-based survey, with all agreeing to participate. Demographics and qualifications are shown in Supplementary Table 3. The evaluation of POPACTApp by 20 surgeons showed that all of the participants correctly read and interpreted the recommendations provided by the app. To evaluate perceptions of the usefulness of and need for POPACTApp in practice, we created a written questionnaire including three items. The mean response values for the first item (satisfaction with the current procedure in the clinic), the second item (satisfaction with the POPACTApp application), and the third item (usefulness of

POPACTApp for clinical practice) were 0.15 (SD = 1.57), 2.7 (SD = 0.47), and 2.7 (SD = 0.47), respectively.

Discussion

Because of demographic changes in the Western world, surgeons and interventionalists are increasingly exposed to patients receiving OAC therapy [1]. Clinical decision-making about whether or not to interrupt or to bridge OAC is challenging, and decisions need to be based on a large number of patient-specific and procedure-specific risk factors, bleeding, and thromboembolic events. In recent years, the use of mobile technologies (e.g., mobile software/apps) for the delivery of health and health care—known as "mobile health"—has gained increasing attention in clinical practice [15, 32–41], especially for clinical decisions where a large number of clinical parameters have to be taken into account.

Here, we present a software-based solution, POPACTApp, which supports clinicians in the easy assessment of bleeding and thromboembolic risk profiles of individual patients with different comorbidities who are undergoing various surgical or intervention procedures. Most importantly, POPACTApp provides comprehensive and clear recommendations on the individual management of OAC treatment based on existing guidelines, current consensus statements, and study data [2, 9–14, 17–25]. In this context, four major questions are addressed by POPACTApp: (1) Should anticoagulation be interrupted? (2) When and how should anticoagulation be interrupted? (3) Is bridging necessary? (4) When should anticoagulation be resumed? POPACTApp can be used on smartphones, tablets, and other mobile devices or as a browser-based web application.

The recommendations made by POPACTApp are based mainly on the *British Guidelines on Oral Anticoagulation with Warfarin (4th Edition)*, the *American College of Chest Physicians Evidence-based Clinical Practice Guidelines (9th Edition)*, and the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation* [2, 13, 17]. The following sections discuss the evidence behind the recommendations provided by POPACTApp.

Recommendation on whether or not to interrupt OAC

According to the current edition of the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation*, there is no general need for the temporary interruption of OAC for procedures that present no clinically relevant risk of bleeding [19, 20]. This recommendation is mainly based on the COMPARE and the BRUISE trials. Both prospective randomized trials showed significantly increased rates of perioperative bleeding complications in cases where vitamin K antagonists were temporarily interrupted and bridging with heparins was performed, compared with continued anticoagulant therapy with vitamin K antagonists [19, 20]. However, these data include only two procedures: (1) implantation of pacemakers or cardioverter defibrillators and (2) vein catheter ablation. There are very few empirical data available on the safety of uninterrupted OAC with DOACs. Some initial studies have suggested that uninterrupted anticoagulation with DOACs is as safe and efficient as uninterrupted anticoagulation with vitamin K antagonists in the context of procedures without clinically relevant risk of bleeding [21]. Because of this limitation of available data, POPACTApp recommends the temporary interruption of DOACs even for procedures without clinically relevant risk of bleeding [13, 21]. However, one might expect that future trials will confirm that DOACs can also be given without interruption for procedures without clinically relevant risk of bleeding.

Recommendation on whether and how to bridge in cases of OAC interruption

In general, bridging with LMWH plays a significant role only in the perioperative management of vitamin K antagonists because of the pharmacokinetics of these drugs. For DOACs, bridging with heparins is generally not recommended [13]. Furthermore, Douketis et al. have demonstrated that perioperative bridging during dabigatran interruption is hazardous [42].

According to the *ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation*, periprocedural bridging with heparins has declined in importance in recent years. Here, POPACTApp's recommendations are based mainly on the recently published BRIDGE trial. Douketis et al. investigated the relevance of perioperative bridging in a large prospective randomized trial and found that bridging leads to significantly increased risk of bleeding complications and does not have any advantage for the risk of thromboembolic events [18]. It should be noted, however, that the average CHADS2 score in the BRIDGE trial was 2.3–2.4. The results from this study can therefore not easily be transferred to patients at high risk of thromboembolism. Furthermore, extremely low proportions of patients (or even no patients) in the BRIDGE trial underwent highly invasive interventions, large tumor operations, or invasive vascular surgery [18]. However, these surgical procedures carry a high risk of both relevant bleeding complications and thromboembolic events. There is extremely little evidence regarding the perioperative treatment of OAC in such cases [2, 11, 17, 27]. In these cases, POPACTApp can provide a basis or framework for clinical

decision-making, quickly providing clinicians with an overview of the guidelines, study data, and expert opinions.

Recommendation on when to reinitiate anticoagulation

The optimal time for reinitiating anticoagulant therapy after surgery for the prophylaxis of thromboembolic events is currently under discussion. Especially in the early postoperative phase, the risk of bleeding must be weighed against the risk of thromboembolic events. Postoperative anticoagulant therapy with heparins significantly increases the risk of bleeding (13% vs. 0.8%) [43]. For example, Dunn et al. reported a risk of bleeding of 20% in cases of postoperative bridging with LMWH for invasive "major surgery" interventions, and 3% of postoperative bleeding events had significant consequences for the patients [27]. In contrast, in their analysis of 31 published reports, Dunn et al. found that only 29 thromboembolic events occurred among 1868 patients receiving long-term anticoagulation in the perioperative setting (1.6%), including seven patients with stroke (0.4%) [44]. However, cerebral infarction occurred in 40% of these cases and was clinically severe in 30% of cases, with severe permanent consequences for the patient [17, 27, 44]. The HAS-BLED score, the categorization of the invasiveness of the planned procedure, and the risk of both perioperative thromboembolic events and bleeding complications can be estimated and considered in decision-making regarding the reinitiation of OAC [2, 13, 17]. However, in terms of patients at high risk of thrombotic events and bleeding, evidence is lacking in the current literature.

Evaluation of POPACTApp

We were able to show that the recommendations provided by POPACTApp were correctly read and interpreted by clinicians. Additionally, using a task-based survey, we demonstrated that the clinicians considered POPACTApp to be helpful and useful in hypothetical test patients, while not being satisfied with the current procedures in the clinics for the perioperative management of OAC. This highlights the need for and usefulness of POPACTApp for everyday clinical use. We plan to conduct additional studies to test POPACTApp in everyday clinical use. The main aim of these future studies is to further investigate whether POPACTApp can help to avoid errors in the handling of OAC and whether the app increases the effectiveness of the management of OAC.

Several limitations of the POPACTApp should be considered. For example, the present version of the app does not take into account additional antiplatelet medications in the generation of recommendations. Especially for patients receiving antiplatelet therapy in addition to OAC, the risk of periprocedural bleeding may be extremely high. Unfortunately, evidence is lacking on this specific topic. Furthermore, the present version of POPACTApp is not designed for urgent or emergency procedures. In these cases, additional aspects such as blood loss, shock, or hypothermia may affect hemostasis [26]. Because these conditions are very complex, it may not be possible to reliably recommend specific treatments for urgent or emergency procedures. In addition, for patients with severe thrombophilias like antiphospholipid syndrome, individual assessment is mandatory. However, future versions of the app might provide framework information in such cases. Finally, POPACTApp clearly cannot replace interdisciplinary clinical decision-making for the individual case. However, POPACTApp can provide evidence-based general recommendations that treating physicians consider before ultimately selecting the optimal treatment for individual patients.

Conclusion

In conclusion, POPACTApp provides clinicians with a tool for individual assessment of patient- and procedure-specific risk profiles for bleeding and thromboembolic complications after surgery, along with a risk-optimized treatment recommendation for the periprocedural management of oral anticoagulants based on current guidelines and research. In clinical practice, POPACTApp may have the potential to provide a unique opportunity for standardizing the handling of oral anticoagulants for surgical patients on the basis of current guidelines. This might lead directly to a significant reduction in errors and problems in the peri-interventional management of patients receiving oral anticoagulants. The subsequent reduction of bleeding and thromboembolic events after surgery could, in turn, improve health care delivery and significantly reduce costs.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Ethik-Kommission Universität zu Lübeck, Aktenzeichen 19-105A) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Abbreviations *OAC*, Oral anticoagulation; *App*, Application; *AF*, Atrial fibrillation; *DOAC*, Direct-acting anticoagulant; *INR*, International normalized ratio; *LMWH*, Low molecular weight heparins; *POPACTApp*, Application for perioperative anticoagulant therapy; *MHV*, Mechanical heart valve; *Mobile app*, Application for mobile devices; *SD*, Standard deviation; *VTE*, Venous thromboembolism

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