

Preoperative Management of Patients Receiving Anticoagulants: Systematic Literature Review

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Abstract

This review is aiming to discuss the preoperative management of patients receiving anticoagulants, the presented review was conducted by searching in Medline, Embase, Web of Science, Science Direct, BMJ journal and Google Scholar for, researches, review articles and reports, published over the past years. were searched up to May 2020 for published and unpublished studies and without language restrictions, if several studies had similar findings, we randomly selected one or two to avoid repetitive results. On the basis of findings and results this review found the preoperative management were interruption of Aspirin and Warfarin before ophthalmological operations and refer patients to cardiologist or a GP prior to surgery, enoxaparin bridging anticoagulation, DOAC-specific interruption and resumption intervals.

Keywords: Preoperative; Management; Anticoagulants

Introduction

Anticoagulation is a very important as a prophylaxis to prevent stroke, coronary ischemia and peripheral arterial obstruction. These drugs used to safe millions of cardiac patients after implanting a stent yearly [1,2].

Although it is well known that anticoagulated patients are exposed to more risk of hemorrhages when submitted to incisional surgeries, but in ophthalmological surgeries, there are some data postulating the safety in maintaining anticoagulants before cataract surgery.

However, there is little data available to offer definitive guidance in glaucoma surgery and retina surgery [3-6].

One approach to maintain a degree of functional anticoagulation is to administer short-acting parenteral anticoagulants such as heparin while oral anticoagulant therapy is sub-therapeutic, a strategy known as bridging therapy [7].

However, bridging anticoagulation can expose patients to serious bleeding complications [8]. Low-molecular-weight heparin (LMWH) can be administered subcutaneously, in a fixed-weight-based dose without the need for laboratory monitoring, thereby obviating the need

for hospitalization to administer anticoagulants [9]. Although the safety and efficacy of LMWH for the prophylaxis and treatment of deep vein thrombosis and treatment of acute coronary syndromes have been well described in clinical trial settings, there is little evidence to support its efficacy and safety as a bridging anticoagulant [10,11].

In dental operation, the risk of mortal bleeding is low and the site of procedure is easy to access, and that's the reason for some researches recommend a continuation of VKA therapy.

The risk of thrombolytic events after cessation or bridging of oral anticoagulation is reported to be 0.8%, including 0.2% fatal events [12-14]. However, discontinuation is still frequently practiced and many patients interrupt their therapy without consulting their medical professionals [15].

In large systematic studies it has been reported that dabigatran, rivaroxaban, apixaban or edoxaban show comparable, or even less hemorrhagic side-effects than VKAs and are regarded as a feasible alternative for oral anticoagulation [16,17]. Advantageous is the short half-life of these drugs (dabigatran: 12 - 17 hours; rivaroxaban: 5 - 13 hours; apixaban: 12 - 18 hours) [18]. However, there are different recommendations regarding the perioperative management of DOAC therapy in dental surgery, such as either pausing DOAC intake for 24 hours prior to surgery with low bleeding risk and continuing 24 to 48 hours afterwards, or waiting for 4 to 6 hours after the last intake when conducting surgery or no pause of intake at all. Empirical-based practical guidelines of how to handle DOAC therapy in dental surgery are non-existent and large clinical studies are still lacking [19-23].

Pragmatic approach to manage new oral anticoagulants in patients undergoing) Which is why the clinical pathway tends to be different for each institution. A representative opinion poll regarding empirical knowledge could be helpful at this point. Therefore, the aim of this multicentric questionnaire survey was to gain insight into the current perioperative management of patients treated with DOACs at different clinical institutions and medical practices located in Germany, Austria and Switzerland.

Once DOAC regimens became available for clinical use in AF, starting in 2010, there are no studies had been conducted to notify the good time for DOACs therapy interruption before surgery and their resumption after it, when heparin bridging should be given, and when coagulation function testing was needed prior surgery [24].

Ambiguity about the perioperative management of DOACs may be associated with unsubstantiated practices and increased damage to patients. Therefore, a too short DOAC therapy interruption interval may lead to thromboembolism, where a sa too short interval may lead to bleeding risk [25].

We designed the Perioperative Anticoagulation Use for Surgery Evaluation (PAUSE) study to assess the safety of a standardized perioperative management strategy for a DOAC regimen. We hypothesized that a simple management approach, which is based on DOAC-specific interruption and resumption intervals, for goes perioperative heparin bridging, and does not require preoperative coagulation function testing, is safe to use for patient care. For each DOAC cohort that received DOAC-specific perioperative management, we defined safety as excluding 30-day perioperative rates of major bleeding of 2% and arterial thromboembolism of 1.5%, according to expected outcome rates (1% for major bleeding and 0.5% for arterial thromboembolism) observed with optimal perioperative management of warfarin sodium [26,27] and with a proof-of concept prospective study of standardized perioperative dabigatran management [28]. We also postulated that this management would yield a high proportion of patients (> 90%) with an undetectable or minimal residual anticoagulant level at the time of the procedure.

Materials and Methods

The present review was conducted May 2020 in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) declaration standards for systematic reviews. We reviewed all the topics on Preoperative management of patients receiving

anticoagulants. such as Interruption of aspirin and warfarin before operating on Anticoagulant patients, discontinuation of Warfarin and administration of enoxaparin, interrupt the DOAC therapy and apply suture, and DOAC therapy discontinuation with no heparin bridging and no coagulation function testing.

To achieve this goal, we searched Medline, Embase, Web of Science, Science Direct, and Google Scholar for, researches, review articles and reports, published over the past 15 years.

Our search was completed without language restrictions. Then we extracted data on study year, study design, and key outcome on diabetes. The selected studies were summarized and unreproducible studies were excluded. Selected data is shown in the table 1.

Author and Year	Sample	Preoperative Management	Key Point
Marcos Bal Bino 2013 [29]	A questionnaire submitted by 52 participants submitted.	Interruption of aspirin and warfarin before operating on anticoagulated patients. Refer patients to cardiologist or a GP prior to surgery	Currently there is no specific recommendation scheduled for the management of anticoagulated patients prior glaucoma surgery.
Hwang H-G2017 [30]	between August 2009 and July 2011 A total of 49 patients were involved in the study	Withdrawal of Warfarin prior to surgery, and administration of enoxaparin. (bridging therapy)	The results demonstrate that a therapeutic-dose of enoxaparin as bridging therapy is feasible and associated with a less incidence of major bleeding and no thromboembolic complications.
Clarissa Prech2019 [31]	A questionnaire with 13 topics was designed and sent to 120 Departments of Oral and Maxillofacial Surgery in Austria, Switzerland and Germany, as well as to 85 oral and maxillofacial/oral surgeons in medical offices in Hamburg, Germany.	Interrupt the DOAC therapy.	The postoperative bleeding risk seems to be equivalent comparing VKAs and the new DOACs, but surgeons are still more cautious conducting dental surgery in patients undergoing DOAC therapy. Empirical-based practical guidelines for dental surgery in patients treated with DOACs are still lacking, but the need is obvious.
James. D 2019 [32]	Patients from August 1,2014, through July31, 2018.Participants (n = 3007) had AF.	DOAC therapy discontinuation with no heparin bridging, And no Coagulation function testing	A perioperative management strategy without heparin bridging or coagulation function testing was associated with low rates of major bleeding and arterial thromboembolism.

Table 1: Results from sequencing studies.

Inclusion criteria

Inclusion criteria were preoperative management of patients receiving anticoagulants.

Exclusion criteria

Irrelevant articles [not related to the aim of this review and articles that did not meet the inclusion criteria in this review.

Data extraction and analysis

Information relating to each of the systematic review question elements was extracted from the studies and collated in qualitative tables. Direct analysis of the studies of Preoperative management of patients receiving anticoagulants

Results and Discussion

A total of fifty-two participants submitted a complete questionnaire. Warfarin or aspirin was routinely interrupted before the glaucoma surgery by 82.7% of the participants. The majority of the surgeons who discontinued these medications stated doing so a week prior to surgery and resumed their use the day after the operation. Nearly half of our respondents reported hemorrhagic complications that could be related to anticoagulant therapy. A great number of the surgeons (86.5%) preferred a particular surgical technique for anticoagulated patients, still, most of them (88.5%) do not change the anesthetic planning in such patients. Lastly, the majority of the respondents (90.4%) refer their patients to an appointment with a cardiologist or a GP prior to surgery [29].

This was a retrospective, single-center study that evaluated the efficacy and safety of therapeutic-dose enoxaparin for bridging therapy in patients on long-term warfarin at Soonchunhyang University Hospital in Korea in the period between August 2009 and July 2011. Warfarin was discontinued 5 days' prior surgery, and enoxaparin was administered two times daily subcutaneously at a dose of 1 mg/kg from 3 days before the surgery to the last dose 24 hours' prior the procedure. Anticoagulation was resumed when proper hemostasis had been confirmed. A total of 49 patients, of whom 25 (51%) were men, and the mean age was 63 years. Thirty-four (69%) received warfarin therapy for VTE, and 9 (18%) for atrial fibrillation. Twenty-nine patients (59%) underwent major surgery and 20 (41%) minor surgery. The mean postoperative duration of enoxaparin was 4 days. No patients had thromboembolic complications through 30 days after the procedure. The overall 30-day mortality rate was 0%. However, the results validate that bridging therapy with therapeutic-dose enoxaparin is feasible and associated with the decreased incidence of major bleeding and no thromboembolic complications. Still, the optimal approach to managing patients preoperatively is uncertain and needs more evaluation [30].

About 56% of the surgeons specified that fewer than 5% of their patients receiving VKAs needed inpatient treatment after surgery. A similar proportion (54%) reported the same for LMWH-treated patients and even 71.6% for dual anticoagulation therapy with ASA/clopidogrel ($p < 0.001$; $p = 0.001$). DOAC therapy was also in this range: 68.4% of the surgeons stated that fewer than 5% of their patients receiving DOACs needed inpatient treatment. Significantly fewer patients needed inpatient treatment after surgery in medical practices than in hospitals ($p < 0.001$), clopidogrel (78%, $p = 0.801$) and DOACs (67%; $p = 0.806$). 21% supposed that tests should be performed for patients treated with DOACs before surgery and 10% directly at the time of surgery. In contrast to ASA/clopidogrel and DOACs, the conducting of laboratory tests was rated as more important for those treated with VKA. Forty-four percent stated they would perform tests in patients who received VKAs before surgery and 29% directly at the time of surgery; only 4% deemed laboratory tests unnecessary ($p = 0.505$). For LMWH, 32% said they would perform laboratory tests before an operation and 23% directly at the time of operation, but 30% did not see a need for laboratory tests ($p = 0.117$) [31].

The 3007 patients with AF (mean [SD] age of 72.5 [9.39] years; 1988 men [66.1%]) comprised 1257 (41.8%) in the apixaban cohort, 668 (22.2%) in the dabigatran cohort, and 1082 (36.0%) in the rivaroxaban cohort; 1007 patients (33.5%) had a high-bleeding-risk

procedure. The 30 - day postoperative rate of major bleeding was 1.35% (95%CI, 0% - 2.00%) in the apixaban cohort, 0.90% (95%CI, 0% - 1.73%) in the dabigatran cohort, and 1.85% (95%CI, 0% - 2.65%) in the rivaroxaban cohort. The rate of arterial thromboembolism was 0.16% (95%CI, 0% - 0.48%) in the apixaban cohort, 0.60% (95%CI, 0% - 1.33%) in the dabigatran cohort, and 0.37% (95%CI, 0% - 0.82%) in the rivaroxaban cohort. Inpatients with a high-bleeding-risk procedure, the rates of major bleeding were 2.96% (95%CI, 0% - 4.68%) in the apixaban cohort and 2.95% (95%CI, 0% - 4.76%) in the rivaroxaban cohort [32].

The majority (80%) of participants are preferred interrupt both drugs, and most of them do it for weepier to surgery, and this could be due to the fact that approximately half of the respondents experienced hemorrhagic complications in their anticoagulated patients during or after a glaucoma surgery. Also majority of the respondents (over 90%) required a cardiologist or a general practitioner opinion when dealing with anticoagulated patients prior to glaucoma surgery, even though there is no approved guideline for this. We found that the majority of BGS members interviewed preferred injectable anesthesia. In this context, a previous report has alerted to the risk of excessive hemorrhage during glaucoma surgery in anticoagulated patients, especially in those taking warfarin [29].

In this study, efficacy was assessed in bridging anticoagulation with therapeutic-dose enoxaparin. There were no thromboembolisms, fourteen patients who had VTE within > 12 months without cancer were deemed low risk and had no embolism 30 days after bridging. The findings demonstrate that bridging therapy with enoxaparin is feasible and associated with a low incidence of thromboembolic complications. Of the 49 patients in this study, 29 (59%) underwent major surgeries or procedures that had high risk of bleeding. The rates of major bleeding for minor and major surgeries or procedures, 0% and 4.1%, respectively, LMWH is the preferred bridging regimen. It has greater bioavailability and a more predictable dose response than unfractionated heparin (UFH). Low-dose LMWH/ UFH may be considered an alternative option during resumption of anticoagulant bridging, particularly after major surgery [30].

Patients who receive therapy with DOACs are becoming more frequent in daily practice. In this study, DOAC therapy was still less common than VKA therapy, but nevertheless 27%of the institutions treated 20 - 50 patients and 37% treated more than 50 patients per year. Most patients treated with DOACs were seen in hospitals, but inpatient treatment was needed less frequently after dental surgery for those undergoing DOAC therapy than those undergoing VKA therapy; 68.4% of the surgeons stated that fewer than 5% of their patients receiving DOACs needed stationary treatment; only 56% did the same for VKA therapy. This was conclusive as the respondents' estimated bleeding risk in comparison with patients not anticoagulant was lower for those on DOACs than for those on VKAs. Interestingly, 34.6% of the participants of our study ranked the bleeding risk of LMWH therapy as very high or high. Also, severe complications were considered rare for VKA, DOAC or antiplatelet therapy. However, studies concerning handling of DOAC treatment in dental surgery are small in number, as well as in size and diversity. Convincing large clinical studies are still lacking [31].

Is a standardized perioperative management approach safe for patients with atrial fibrillation who use a directorial anticoagulant and require elective surgery or procedure? In this cohort study of 3007 patients with atrial fibrillation using apixaban, dabigatran, or rivaroxaban, the direct oral anticoagulant treatment was stopped and resumed before and/or after elective surgery or procedure using standardized protocols without heparin bridging. The 30-daypostoperative rates of major bleeding were less than 2%, and the rates of stroke were less than 1%. In this study, in patients treated with a direct oral anticoagulant, a simple standardized perioperative management approach was associated with low rates of bleeding and stroke [32].

Conclusion

The results of this studies show the preoperative management of patients receiving anticoagulants. On the basis of findings and results this review found interruption of aspirin and warfarin before operating on anticoagulated patients, discontinuation of Warfarin and administration of enoxaparin, interrupt the DOAC therapy and apply suture, and DOAC therapy discontinuation with no heparin bridging and no coagulation function testing.

Conflict of Interest

The authors of this article hasn't receive and support for this work and it was completely self-funded.

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