

# The approach of Turkish ophthalmologists concerning anticoagulant/antiaggregant therapy: a questionnaire study

*Türk oftalmologların antikoagülan/antiagregan tedavisi alan hastalara preoperatif yaklaşımı: bir anket çalışması*

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## Abstract

**Purpose:** The aim of the study was to update the information about anticoagulant/antiaggregant drugs for ophthalmologists.

**Materials and methods:** A questionnaire investigating the information about anticoagulant/antiaggregant drugs and perioperative management of these agents was answered by 106 ophthalmologists.

**Results:** The participants included residents by 19 (17.9%), specialists by 69 (65.1%), academic members by 18 (17%); 47.2% of the participants have been serving in ophthalmology field for  $\geq 10$  years.

It was detected that 58 (54.7%) participants were trained about these drugs; and 78 (73.5%) participants have knowledge on terms as well as differentiation of anticoagulant/antiaggregant agents. There was not any difference between the physicians in terms of training and drug differentiation ( $p=0.970$ ,  $p=0.948$ , respectively). Six or more preparations were known by 10.4% of the participants whereas 4 to 6 preparations were known by 48.1% of the participants and 1 to 3 preparations were known by 41.5% of the participants.

In consideration of perioperative drug management, it was determined that 52 (49.1%) physicians recommend discontinuation of the medications whereas 24 (22.6%) physicians suggest continuation of drug use. The rates for drug discontinuation were found higher in university hospitals as well as training and research hospitals when compared with public hospitals and private hospitals ( $p=0.03$ ).

**Conclusion:** Information on anticoagulant/antiaggregant agents as well as perioperative management is essential to prevent complications. Therefore, training in ophthalmology clinics where the patients who are treated with aforesaid drugs may increase the awareness on this issue.

**Keywords:** Ophthalmologist, anticoagulant/antiaggregant, hemorrhagic complication, preoperative management.

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## Özet

**Amaç:** Bu çalışmanın amacı, oftalmologların antikoagülan/antiagregan ilaçlar hakkındaki bilgilerini güncellemektir.

**Gereç ve yöntem:** Antikoagülan/antiagregan ilaçlar ve bu ajanların perioperatif yönetimi hakkındaki bilgileri araştıran bir anket 106 oftalmolog tarafından cevaplandı.

**Bulgular:** Katılımcıların 19'u (%17,9) asistan, 69'u (%65,1) uzman, 18'i (%17) akademisyen olup; %47.2'si 10 yıldan beri oftalmoloji alanında hizmet vermektedir.

Elli sekiz (%54.7) katılımcının bu ilaçlar hakkında bir eğitim aldığı, 78 (%73,5) katılımcının antikoagülan/antiagregan ajanların ayırt edilebilmesinin yanı sıra; konuyla ilgili terimler hakkında da bilgi sahibi olduğu görüldü. Hekimler arasında eğitim alma ve ilaçların tanınması açısından fark yoktu (sırasıyla,  $p=0.970$ ,  $p=0.948$ ). Katılımcıların %10.4'ü 6 veya daha fazla ilacı, %48.1'i 4-6 arası ilacı, %41.5'i 1-3 arası ilacı biliyordu.

Perioperatif ilaç yönetimi göz önüne alındığında, 52 (%49,1) hekimin ilaç tedavisinin kesilmesini, 24 (%22,6) hekimin ise ilaç kullanımının devamını önerdiği görüldü. İlaç kesilme oranları; üniversite hastaneleri ve eğitim ve araştırma hastanelerinde, kamu hastaneleri ve özel hastanelere kıyasla daha yüksek bulundu ( $p=0,03$ ).

**Sonuç:** Antikoagülan/antiagregan ilaçlar ve bu ajanların perioperatif yönetimleri hakkındaki bilgilerin bilinmesi komplikasyonların önlenmesi açısından esastır. Bu nedenle; bu ilaçlar ve ilaçlarla tedavi edilen hastalarla ilgili oftalmoloji kliniklerinde uygulanacak düzenli eğitim, bu konudaki farkındalığı artırabilir.

**Anahtar Kelimeler:** Oftalmolojist, antikoagülan/antiagregan, hemorajik komplikasyon, preoperatif yönetim.

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## Introduction

According to US Department of Health and Human Services data, the 49.2 million people 65 years of age and older in 2016 are expected to increase to 98.2 million by 2060 [1]. Prolongation of life expectancy increases the incidence of cardiovascular and cerebrovascular diseases progressing to thromboembolic events.

Anticoagulant and antithrombotic drugs are used in a wide range of conditions, including acute and chronic disorders, such as deep vein thrombosis (DVT), embolism, myocardial infarction, and stroke [2, 3]. Patient management becomes difficult due to diversity of concepts that may cause incomprehensibility, like anticoagulant and antiplatelet agents [4]. Underlying comorbid conditions that require continuous use of such drugs and possible hemorrhagic complications during perioperative use of these drugs create a risk/benefit contradiction for physicians and require individualized management of each patient [3, 5].

Although there is a wide range of patients who undergo operations due to ophthalmologic conditions, anticoagulant and antiaggregant drugs are frequently used due to advanced age and comorbid cardiovascular and cerebrovascular diseases [6-8]. An increase in perioperative ischemic or hemorrhagic complications due to preoperative discontinuation and/or uncontrolled continuation of these drugs may occur.

The aim of the present questionnaire study was to obtain updated information and increase the awareness of ophthalmologists, who had different training and experience levels and worked in different hospitals, on anticoagulant and antiaggregant drugs and perioperative management of patients using such drugs.

## Materials and methods

The study was initiated after receiving approval from the Clinical Researches Ethical Committee (CREC) of the medical faculty within Kahramanmaraş Sutcu Imam University (protocol number/date; 74/14.02.2018) and verbal consent from the ophthalmologists following explanation of the study objective and content. The questionnaire was prepared by

revising the questions created by Akturk et al. [9] to determine the approaches of dentists on anticoagulant treatment in patients undergoing coronary stent procedures.

A power analysis performed prior to the study (G\*Power 3.1 Statistical Power Analyses program) revealed that the number of ophthalmologists to be included in the study should be 96 according to a power of 85%. Accordingly, 106 ophthalmologists working in different hospitals under different titles (e.g., resident, specialist, academic member) were asked to complete a questionnaire consisting of 14 questions about demographic information, anticoagulant and antiaggregant drugs, and perioperative management through an in-person interview, telephone call, or e-mail.

## Statistical analysis

Statistical evaluation was performed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA) software. Descriptive statistical data were used as follows: categorical data were expressed as frequency (n) and percentage (%), whereas numerical data were expressed as mean  $\pm$  standard deviation (SD). Conformity of numerical data to a normal distribution was assessed through Kolmogorov-Smirnov and Shapiro-Wilk tests. An independent chi-square test was used to evaluate the association between categorical data, but the likelihood ratio or Fisher's exact test was preferred according to a minimum expectancy ratio. The statistical significance level was accepted as  $p < 0.05$  for all evaluations.

## Results

For the demographic data, 46.2% (n=49) of the participating ophthalmologists were female, and 53.8% of them were male, with an average age of  $36.48 \pm 5.59$  years (range 24-51 years) for all participants. Nineteen (17.9%) participants were residents; sixty-nine (65.1%) participants were specialists; and eighteen (17%) participants were academic members. The participation from university hospitals was highest with 35 (33%) physicians. This group was followed by 31 (29.2%) physicians from training and research hospitals and 24 (22.7%) and 16 (15.1%) physicians from public hospitals and private hospitals, respectively. Most participants (47.2%) had served in the

ophthalmology department for 10 years or more. Demographic data for the ophthalmologists are presented in Table 1.

All the participating ophthalmologists answered all questions adequately. Fifty-eight (54.7%) participants expressed that they were trained on anticoagulant and antiaggregant drugs once during their residency training; and 78 (73.5%) participants knew anticoagulant and antiaggregant drug concepts and how to differentiate the corresponding drugs. There was no statistically significant difference in terms of training and the ability to differentiate these drugs among the physicians of each title ( $p=0.970$  and  $p=0.948$ , respectively). Among the drugs classified in these groups, 6 or more drugs were known by 11 (10.4%) physicians, whereas 4 to 6 drugs were known by 51 (48.1%) physicians and 1 to 3 drugs were known by 44 (41.5%) physicians. When the groups were compared, drug recognition of 4 or more drugs by specialists was significantly lower than by residents and academic members ( $p=0.013$ ) (Table 2).

The responses of the participant physicians on the subject of patients with anticoagulant and antiaggregant drug history whose surgery was planned to include local anesthesia (LA) are given in Table 3. Accordingly, 89 (84%) physicians personally investigated the medication histories of their patients. The investigation rates were high at each title level; and there was no statistically significant difference ( $p=0.265$ ). It was observed that 80 (75.5%) physicians knew 5 of the blood tests used to analyze drug levels. However, only 63 (59.4%) ordered blood tests for these patients; 20 (18.9%) physicians rarely ordered these tests; and 23 (21.7%) physicians never ordered any of these tests. When the participants were compared, the rates for ordering tests were substantially higher for residents and academic members than for specialists ( $p=0.009$ ). A preoperative consultation order for patients with medication histories from departments such as anesthesia, cardiology, and neurosurgery was not ordered by 20 (18.9%) physicians; 55 (51.9%) physicians requested a consultation; and the remaining 31 (29.2%) physicians rarely requested a consultation. When the

consultation requests were compared among participants, requests by the academic members were significantly higher than those by other participants ( $p=0.04$ ). An assessment performed based on the institutions where the physicians provided services revealed that the rates of blood test and consultation orders were significantly higher in training institutions, such as university hospitals and training and research hospitals, than public and private hospitals where no residency training was provided ( $p=0.00$  and  $p=0.02$ , respectively).

Possible complications in case of interruption in or continuation of anticoagulant and antiaggregant drugs were well known by 88 (83%) physicians, whereas 52 (49.1%) physicians suggested absolute interruption and 24 (22.6%) physicians recommended continuation of the drugs. The academic members mostly preferred interruption; however, specialists preferred to continue the drugs, but statistical significance was not reached ( $p=0.284$ ). In line with these outcomes, the rates for drug discontinuation were significantly higher in university hospitals and training and research hospitals when compared with those in public hospitals and private hospitals ( $p=0.03$ ).

## Discussion

The present study is the first questionnaire study on anticoagulant and antiaggregant drugs and perioperative management of these drugs by ophthalmologists in our country. The study showed that ophthalmologists have an opinion on anticoagulant and antiaggregant concepts and drugs; however, such information is prone to be forgotten by specialists during their services, although almost half of the participants mentioned receiving training on this topic. Physicians usually know about perioperative management of patients using such drugs and the process to be followed; however, tests and consultations are not ordered as much as required, and the members of hospitals providing residency training are more careful about this issue. The present study detected that there was no consensus on the continuation or discontinuation of drugs during the perioperative period; academic members especially express their opinion about discontinuation in university hospitals.

**Table 1.** Demographic data of ophthalmologists.

<b>Mean±SD</b>	
<b>Age (year)</b>	36.48±5.59
<b>Sex</b>	<b>n (%)</b>
Female	49 (46.2)
Male	57 (53.8)
<b>Place of employment</b>	<b>n (%)</b>
University hospital	35 (33.0)
Training and Research hospital	31 (29.2)
State hospital	24 (22.7)
Private hospital	16 (15.1)
<b>Professional experience (year)</b>	<b>n (%)</b>
0-3	16 (15.1)
4-6	15 (14.1)
7-10	25 (23.6)
>10	50 (47.2)
<b>Training title</b>	<b>n (%)</b>
Research assistant	19 (17.9)
Specialist	69 (65.1)
Lecturer	18 (17.0)

**Table 2.** General questions about anticoagulant/antiaggregant drugs.

	<b>n (%)</b>
<b>† Have you received any training about anticoagulant/antiaggregant drugs?</b>	
Yes	58 (54.7)
No	35 (33.0)
I Cannot recall	13 (12.3)
<b>ª Do you know the anticoagulant / antiaggregant concepts and / or the distinction of drugs?</b>	
Yes	78 (73.5)
No	13 (12.3)
I Cannot recall	15 (14.2)
<b>§ How many anticoagulant / antiaggregant drugs do you know?</b>	
I don't know	0 (0)
1-3	44 (41.5)
4-6	51 (48.1)
>6	11 (10.4)

Independent chi-square test; minimum expect ratio: Likelihood ratio or Fisher's Exact test;

$p < 0.05$  was accepted as statistically significant;

†, ª, §: When the answers given to the questionnaire were compared between all physicians;

†:  $p = 0.970$ , ª:  $p = 0.948$ , §:  $p = 0.013$

**Table 3.** Questions about the use of anticoagulant/antiaggregant drugs and general approach in patients who will be operated.

	n (%)
<b>†Are you questioning the use of preoperative anticoagulant / antiaggregant medication in patients to be operated?</b>	
I'm questioning	89 (84.0)
Asistant medical staff questioning	6 (5.6)
Not questioning	11 (10.4)
<b>ª Do you want any consultation before operating patients receiving anticoagulant/antiaggregant medication?</b>	
Yes	55 (51.9)
No	20 (18.9)
Rarely	31 (29.2)
<b>§ Do you want any blood tests before the patients taking anticoagulant/antiaggregant medication?</b>	
Yes	63 (59.4)
No	23 (21.7)
Rarely	20 (18.9)
<b>How many do you know about the patients who are taking anticoagulant/antiaggregant medication? (PTT, a-PTT, INR, BT, PC)</b>	
I don't know	1 (0.9)
1	0 (0)
2	5 (4.7)
3	9 (8.5)
4	11 (10.4)
5	80 (75.5)
<b>£Do you discontinue these medications before you can operate the patients who receive anticoagulant/antiaggregant drugs?</b>	
Yes	52 (49.1)
No	24 (22.6)
Rarely	30 (28.3)
<b>Do you know that preoperative discontinuation and / or continuation of anticoagulant/antiaggregant medication may cause complications?</b>	
Yes	88 (83.0)
No	1 (0.9)
I know, but I don't recall	17 (16.1)

Independent chi-square test; minimum expect ratio: Likelihood ratio or Fisher's Exact test;  $p < 0.05$  was accepted as statistically significant;

†, ª, §, £: When the answers given to the questionnaire were compared between all physicians;

†:  $p=0.265$ , ª:  $p=0.04$ , §:  $p=0.009$ , £:  $p=0.284$

(PTT: Prothrombin time, a-PTT: activated partial thromboplastin time, INR: International normalized ratio, BT: Bleeding time, PC: Platelet count)

Better knowledge on mortality and risk factors increased because of thromboembolic events which enabled the development of pharmacological precautions. The preference on anticoagulant and antithrombotic drugs was enlarged by the development of agents for target molecules [4]. The number of terms used for these agents are so great that confusion may occur, even among physicians. Anticoagulant drugs act on clot formation and coagulation factors and affect in-vivo and in-vitro coagulation tests. Oral warfarin and parenteral unfractionated heparin (UFH) are basic agents in this drug class. Antithrombotic drugs include UFH, low molecular weight heparins (LMWHs) (e.g., enoxaparin), factor II<sub>a</sub> inhibitors (e.g., dabigatran), factor X<sub>a</sub> inhibitors (e.g., rivaroxaban, fondaparinux), and antiplatelet drugs [4, 5]. Antiplatelet drugs inhibit platelet chemotaxis and aggregation and include non-steroidal anti-inflammatory drugs (NSAIDs) [e.g., aspirin and cyclooxygenase (COX) I and II inhibitors], phosphodiesterase inhibitors (e.g., dipyridamole), thienopyridines (e.g., ticlopidine, ticagrelor, clopidogrel, and prasugrel), and glycoprotein II<sub>b</sub>/III<sub>a</sub> inhibitors (e.g., abciximab, tirofiban, and eptifibatide). In contrast to anticoagulant agents, antiplatelet drugs rarely require monitoring with laboratory tests, since they do not affect in-vitro coagulation tests [4, 10]. Although the majority of the participating ophthalmologists expressed that they were trained during their residency period and they may recognize the concepts and many agents in this drug class, the number of drugs known by specialists was insufficient. This outcome may be explained by the fact that insufficient updates to or rare use of information related to these drugs during practice may be forgotten despite previous training.

Antithrombotic treatment may increase perioperative bleeding risk in ophthalmic surgeries, but the risk during optimal perioperative management has not fully been defined for ophthalmic surgeries, in contrast to other surgical fields [11]. The most significant risk for these drugs, which are used for prophylaxis of pulmonary embolism, acute coronary syndrome, acute treatment of DVT, chronic DVT, and cerebrovascular diseases, is perioperative hemorrhagic complications [3]. Beyond the thromboembolic event requiring use of the drug, surgical trauma and long-term immobilization of the patient after surgery increase the risk for

DVT [10]. Hereby, the decision to discontinue or continue the drug during the perioperative period requires a risk/benefit comparison for thromboembolism and bleeding, and the decision should be made according to the patient's condition.

Consideration of a discontinuation period of two-times the half-life of the drug starting from the last administration is essential for all oral and parenteral anticoagulant and antiaggregant drugs [12]. Therefore, the discontinuation period may differ for each drug in elective surgical procedures. For example, the recommended preoperative discontinuation periods are 5 days for warfarin, 10 to 48 hours for glycoprotein II<sub>b</sub>/III<sub>a</sub> inhibitors and 4 to 6 hours, 12 hours, and 36 hours for UFH, DMAH, and fondaparinux, respectively. Discontinuation of aspirin and NSAIDs is not suggested; however, a delay in the operation and discontinuation of thienopyridines are preferred for patients with coronary stenting who concurrently use aspirin and thienopyridines. If a delay in surgery is not possible, the continuation of dual aspirin-thienopyridine treatment is recommended [10]. Bridging treatment with DMAHs is suggested for older patients with cardiac problems to prevent thrombotic complications due to 5-day interruptions in warfarin, which are frequently used [5, 10]. Although there was no consensus among ophthalmologists, recent publications state it is appropriate to continue antithrombotic agent treatment, especially in routine cataract surgery with topical or sub-Tenon's anesthesia, and that dual antiplatelet therapy should be avoided if sharp needle anesthesia is planned [13]. It was determined in the present study that the majority of ophthalmologists investigate drug use history in detail; however, they experience difficulty at the decision stage, although they have sufficient knowledge on complications that may occur with discontinuation or continuation of the drug. Academic members and residents in university hospitals usually preferred discontinuation of the drug, since the cases they accepted were complicated and high complication rates may play a role in their preference. Consultation requests from other disciplines, including anesthesia, cardiology, neurology, and neurosurgery, through a multidisciplinary approach is important in this decision. In addition to indications for surgery, consideration of the suggestions for underlying pathologies may support better patient

management. The participating ophthalmologists remained doubtful in requesting consultations from other departments and in drug management; the consultation rates were higher in training institutions, such as university hospitals and training and research hospitals than in other institutions. A multidisciplinary approach and higher consultation request rates in training institutions were considered as a strengthening factor for the physician to decide to discontinue or continue the drug.

There is no consensus on the effect of anticoagulant and antiaggregant agents on spontaneous ocular hemorrhage. Many articles on patients with age-dependent macular degeneration (ADMD) who use such drugs have reported drug-induced spontaneous subretinal and suprachoroidal hemorrhage [14-16], whereas a study conducted by Ying et al. [17] could not determine an association. The incidence of intraocular bleeding is minimal in patients using warfarin who had uncomplicated phacoemulsification surgery, and the drug may be used safely [6], whereas the frequency of bleeding increased when anticoagulant agents continued to be used [7]. The incidence of bleeding was lower in patients who underwent vitreous surgery and intravitreal injections [8,16]. In addition, hemorrhagic complications were reported in most ophthalmic surgical types except corneal surgeries (glaucoma, vitreoretinal, oculoplastic, lacrimal surgery, etc.) according to a review [13]. Despite whether they are performed spontaneously or postoperatively, blood coagulation tests should be performed preoperatively, and the general condition should be determined. For this purpose, the prothrombin time (PT), international normalized ratio (INR), and partial thromboplastin time (a-PTT) should be tested in patients using anticoagulant drugs and antiaggregant drugs; the platelet count and bleeding time should be utilized for antiplatelet drugs [4]. This situation is related to the occurrence of more intraocular hemorrhage in patients with high INR levels using these drugs. [16, 19]. However, there are also studies suggesting that oral anticoagulants can be maintained at INR values in the therapeutic range [13]. Although the majority of the ophthalmologists knew the blood tests required, the rate of laboratory test orders was not high during the preoperative period. These rates were lower among specialists

working in public and private hospitals.

The limitation of the present study was the sample size, although the questionnaire was delivered to a certain number of physicians. The study was performed through an in-person interview, telephone call, or e-mail; however, the performance of such studies via professional societies would provide a better sample size.

In conclusion, anticoagulant and antiaggregant drugs may cause severe complications during the perioperative period. These complications may be prevented by having general information about the drugs and adequate knowledge on perioperative patient management. Therefore, it is considered that the addition of training to the curriculum would increase the awareness in ophthalmology clinics where older patients with concomitant diseases using these drugs undergo operations.

**Conflict of interest:** The authors declare that they have no conflict of interest.

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