

## COMPARISON OF BLEEDING RISKS WITH NEW ORAL ANTICOAGULANTS VERSUS ACENOCUMAROLUM – part 1

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### ABSTRACT

**Aim of the study** Oral anticoagulants are effective therapies for reduction of stroke risk in patients with atrial fibrillation. However, blocking elements of the clotting cascade carries an inherent risk of bleeding. Also, anticoagulated patients sometimes require tooth extractions and other invasive procedures. The purpose of the present study was to compare the relationship between the risk factors and postoperative hemorrhage among dental patients with atrial fibrillation receiving acenocumarolum versus new oral anticoagulants users.

**Material and methods** A sample of consecutive patients exposed to oral anticoagulants who required tooth extraction at our institution were retrospectively reviewed. Categorical data are summarized as percentages, and differences between groups were tested using Stata/IC 16 software (StataCorp). Ethical approval from the local institutional ethics comitee was obtained for this study.

**Results** The overall bleeding rate was higher in new anticoagulant users than in acenocumarolum users (26.72% vs 12%,  $p = 0.03$ ) and similar (17.8% vs 14.1%,  $p = 0.129$ ) between the two groups. There were no significant differences between atrial fibrillation patients and non-atrial fibrillation patients regarding bleeding rate. The highest rates were observed in patients with congestive cardiac failure exposed to new oral anticoagulants.

**Conclusions** According to the results of our study, patients exposed to new oral anticoagulants had higher rates of overall bleeding events than chronic acenocumarolum users.

**Keywords:** Bleeding rate. Acenocumarolum. New oral anticoagulants

### INTRODUCTION

Since their approval for stroke prevention, prescription rates for new oral anticoagulants have risen among patients with atrial fibrillation [1-3].

While new oral anticoagulants are being increasingly used, there is a paucity of information on the outcomes of patients with atrial fibrillation who are treated with anticoagulants who subsequently undergo tooth extraction.

Accordingly, we examined the postoperative outcomes of patients with and without atrial fibrillation in the Clinic of Oral and Maxillofacial Surgery, Carol Davila University Bucharest - Hospital of Oral and Maxillofacial Surgery between 2019 and 2020, who subsequently underwent tooth extraction as elective procedures.

We hypothesized that outcomes among patients with atrial fibrillation would be

influenced by the specific type of anticoagulant prescribed.

## MATERIAL AND METHODS

We included all patients exposed to oral anticoagulants who underwent an elective tooth extraction in the Clinic of Oral and Maxillofacial Surgery, Carol Davila University Bucharest - Hospital of Oral and Maxillofacial Surgery between 2019 and 2020. Medical comorbidities were identified by examining secondary diagnosis codes from admission. We excluded from the study cohort patients with valve replacements and patients who were prescribed both acenocumarolol and new oral anticoagulants within 30 days.

Patients were further classified based on their anticoagulation regimen as acenocumarolol users or new oral anticoagulants (dabigatran, apixaban or rivaroxaban) users. All patients needed to have at least one tooth extracted according to an oral examination and panoramic radiography.

Postoperative hemorrhage was defined as oozing after the use of gauze pressure. Patients were instructed to visit our Clinic if postoperative hemorrhage occurred at a later date. The follow-up period was 3 days postoperatively.

The study was approved by the Committee of the Ethics of the Hospital of Oral and Maxillofacial Surgery, Bucharest. Informed consent was obtained from each patient.

Categorical data were summarized as percentages, and differences between comparison groups were tested with the chi-square test. All propensity-weighted analyses accounted for the following covariates: age, sex, comorbidities (congestive heart failure, hypertension, valvulopathies) and use of bleeding-relevant drugs (antiplatelet agents, nonsteroidal anti-inflammatory drugs). Statistical significance was defined by a 2-sided  $p \leq 0.05$ . Analyses were performed with Stata/IC 16 software (StataCorp).

## RESULTS AND DISCUSSIONS

A total of 181 patients exposed to oral anticoagulants underwent tooth extraction during the study period, with a mean age of 70.82 years ( $\pm 9.74$ ). 85 cases (46.96%) were females and 96 cases (53.04%) were males.

The acenocumarolol users group consisted of 50 patients - mean age of 68.5 years ( $\pm 9.45$ ). Of these, 29 cases (58%) were females and 21 cases (42%) were males.

The new oral anticoagulants users group consisted of 131 patients - mean age of 71.71 years ( $\pm 9.75$ ). Of these, 56 cases (42.75%) were females and 75 cases (57.25%) were males.

There was a significant difference between new oral anticoagulant users and acenocumarolol users regarding the overall bleeding rate (26.72% vs 12%,  $p = 0.03$ , chi-square test).

No significant differences were observed between the ages or genders of the patients in whom postoperative hemorrhage had occurred.

Many investigators reported on postoperative hemorrhage after tooth extraction in patients receiving anticoagulants [4-6]. The risk of bleeding is dominated by medical comorbidities and medications that affect hemostasis [7].

The most common indication in both groups was atrial fibrillation - 132 (72.93%) patients; of these, 36 (72%) patients received acenocumarolol and 96 (73.28%) received new oral anticoagulants. The atrial fibrillation was not associated with an increased risk of overall bleeding events in none of the two groups.

Congestive cardiac failure was reported in 74 (40.88%) patients. Of these, 23 (46%) patients received acenocumarolol and 51 (38.93%) received new oral anticoagulants. The rate of postoperative hemorrhage in the

patients with congestive cardiac failure who received anticoagulants was significantly

higher (32.43% vs 15.89%,  $p=0,009$ , chi-square test) (Table 1)

Table 1 – Postoperative hemorrhage in congestive cardiac failure patients

Congestive cardiac failure	Hemorrhage following extractions	
	Yes	No
Yes	90 (84.11%)	17 (15.89%)
No	50 (67.57%)	24 (32.43%)

New oral anticoagulants administration and concomitant congestive cardiac failure were found to be significant factors related to postoperative hemorrhage (37.25% vs 20%,  $p=0,03$ , chi-square test).

There were no significant differences between valvulopathies and postoperative hemorrhage (23.33% vs 22.52%,  $p \geq 0.05$ ).

Although conclusive associations cannot be made given the small sample size, the hypertension was found to be a significant predictor of postoperative hemorrhage (26.43% vs 9.76%,  $p = 0.032$ , Fisher's exact test) (Table 2).

Table 2 – Postoperative hemorrhage in valvulopathies patients

Hypertension	Hemorrhage following extractions	
	Yes	No
Yes	37 (90.24%)	4 (9.76%)
No	103 (73.57%)	37 (26.43%)

We recognize that this study has a number of limitations. Thus, the sample size of each cohort was limited to the eligible patients who presented to our Clinic and provided informed consent, sample size calculations were not performed. In addition, the number of patients was relatively small, particularly for those on acenocumarolum. Also, given that this study was not randomized, results may have been affected by residual confounding.

## CONCLUSIONS

Among patients who underwent tooth extraction, patients with preoperative atrial fibrillation who were treated with new oral anticoagulation had higher bleeding rates when compared with acenocumarolum users. In addition, we found that patients with valvulopathies who were treated with new oral anticoagulants or acenocumarolum had similar bleeding outcomes after elective teeth extraction. Further investigations are needed to understand the mechanisms underlying the postoperative bleeding risk associated with common comorbidities in oral anticoagulants users.

### **Conflict of interest**

The authors declare that they have no conflict of interest.

### **Acknowledgment**

In this article, all authors have an equal contribution as the first author.

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