THE UNIVERSITY OF MEDICINE AND PHARMACY
"CAROL DAVILA" BUCHAREST
DOCTORAL SCHOOL

Assessment of the risk of bleeding in patients receiving new oral anticoagulants

PHD THESIS SUMMARY

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Cuprins

Introduction

The doctoral thesis "Assessment of hemorrhagic risk in patients treated with new oral anticoagulants" is a research paper specific to the field of medical sciences, which includes research data conducted at the Clinic of Oro-Maxillofacial Surgery - University of Medicine and Pharmacy "Carol Davila ”Bucharest, in the period 2018-2022, in compliance with the current standards and the institutional protocol.

The motivation for conducting this study started from the fact that until now, no specific data are known on the risk of perioperative bleeding in patients receiving new oral anticoagulants, being known that the other categories of antithrombotic drugs traditionally used are associated with bleeding events, leading to a significant increase in morbidity.

Researching data from the literature, for a thorough understanding of the relationship between treatment with new oral anticoagulants and the risk of bleeding associated with their administration, I found that although it has been more than a decade since the first non-coumarin oral anticoagulant (dabigatran) was introduced in cardiac medication, so far the relationship between this category of antithrombotic and the risk of perioperative bleeding in patients with surgical pathology has been studied very little.

Based on literature data, I believe that perioperative hemorrhage may pose a problem with a multidisciplinary therapeutic approach and that a systematic approach to early recognition, risk assessment, and appropriate treatment may reduce the morbidity associated with bleeding surgery in anticoagulated patients.

The main objectives of this paper are to establish possible associations and statistically significant correlations between perioperative hemorrhagic risk in oral anticoagulated patients and other clinical-biological parameters, the ultimate goal being to establish a preoperative evaluation algorithm for patients requiring surgery.

This paper is structured in two parts. The general part contains general considerations about hemostasis disorders and the current state of research in current antithrombotic therapy.

The personal contributions, constituted in the second part of the paper, will follow the detailed description and analysis of the research, followed in the end by the conclusions obtained from the statistical analysis of the data.

The information and partial results of this paper have been published in specialized journals, indexed in international databases.

The realization of this research would not have been possible without the permanent support of the staff of the OMF Surgery Clinic from the University of Medicine and Pharmacy "Carol Davila" Bucharest, for which I am deeply grateful.

CURRENT STATE OF KNOWLEDGE

Chapter 1. General considerations on hemostatic balance disorders in the patient with Oro-Maxillo-Facial surgical pathology

Disorders of hemostatic balance are a major concern in oro-maxillo-facial surgery, given that they are highly complex in terms of the pathophysiological mechanisms that determine them, but also in terms of clinical symptoms and therapeutic algorithm to be taken in these situations.

Chapter 2. Antithrombotic drugs

According to the action mechanism, antithrombotic medication is divided into three groups, as follows:

- anticoagulant medication;
- antiplatelet drugs;
- fibrinolytic drugs

There are currently two categories of new oral anticoagulants widely used in practice:

1. Direct thrombin inhibitors:
    - Dabigatran exexilated (Pradaxa).
2. Direct inhibitors of factor Xa:
    - Rivaroxabanul (Xarelto);
    - Apixaban (Eliquis).

PERSONAL CONTRIBUTION

Chapter 3. Working hypothesis and general objectives

In oro-maxillofacial surgery, the appearance of a postoperative hemorrhage can cause the consumption and rapid depletion of coagulation factors.

Failure to restore hemostasis and the occurrence of postoperative bleeding increase the risk of reoperation, the need for blood transfusion, translated in practice by increasing the overall duration of treatment and of course short and medium term morbidity.

The prospect of identifying risk factors with an impact on the haemostatic system would therefore allow the practical establishment of the categories of patients with a predisposition to postoperative haemorrhage and the adoption of an appropriate therapeutic attitude for a favorable course of progress in patients who have undergone surgery in the oral-maxillofacial field.

The practical impact of this approach is the possibility of implementing a set of variables valid for assessing the risk of bleeding in anticoagulated patients, who are to undergo oro-maxillofacial surgery, a prerequisite for improving the prognosis and optimizing therapeutic behavior, minimizing bleeding events .

The working hypothesis in the research sample consisted in confirming the existence of statistically significant disproportions, between individuals who benefited from "traditional" anticoagulant therapy with oral administration (acenocoumarol derivatives) on the one hand, and on the other hand people who have received new type anticoagulant medication.

At the same time, we tried to establish the direct relationship between the bleeding risk associated with the type of anticoagulant drug administered to patients with thrombotic risk and the main variables that could theoretically influence this risk.

The main purpose of this research is to evaluate the differentiated predictive value of bleeding risk factors in patients receiving anticoagulant medication.

The main objectives of doctoral research:

a. evaluation of the prognostic prediction relationship of the hemorrhagic risk associated with oral anticoagulant medication in patients with stable heart disease (atrial fibrillation / drug-controlled hypertension);

b. evaluation of the prognostic prediction relationship of the hemorrhagic risk associated with oral anticoagulant medication administered for preventive purposes in patients at risk or with a history of ischemic stroke (including patients with diabetes);

c. evaluation of the prognostic prediction relationship of the hemorrhagic risk associated with oral anticoagulant medication in patients with coronary angioplasty.

Study 1

In the first study, we looked at the differences between postoperative bleeding events in patients on oral anticoagulant medication for the treatment of atrial fibrillation.

We established this first research guideline taking into account that atrial fibrillation is the most common condition associated with cardiac embolic risk and consequently the comorbidity most often indicated for oral anticoagulant drug treatment.

In this regard, we established as objectives the analysis of postoperative hemorrhagic incidents recorded in the study group consisting of patients diagnosed with atrial fibrillation, in relation to "classical" oral anticoagulant therapy (acenocoumarol derivatives), and treatment with new oral anticoagulants such as inhibitors. thrombin or direct factor X inhibitors.

The data obtained were integrated in the complex statistical analysis, which took into account the general variables with the potential to modulate the hemorrhagic risk - demographic factors, associated general conditions, concomitant medication that the patient receives.

Study 2

In the second study, we assessed the risk of bleeding in patients receiving permanent oral anticoagulation for secondary prophylaxis of ischemic strokes, including transient ones (such as those that occur during pregnancy, due to pre-existing thrombophilia).

For this situation, we aimed to establish the risk of bleeding in patients with a history of stroke, treated either with acenocoumarol derivatives or with one of the medicinal products in the category of new oral anticoagulants.

We also analyzed in this case the potential impact of diabetes as a risk factor in favor of hemorrhage, but also of embolic accident, a consequence of microangiopathy.

Study 3

The third study focused on another diagnostic category - that of patients undergoing stent angioplasty interventional cardiology procedures.

For this last investigated category, the comparison of the hemorrhagic risk was made between the patients who received treatment with acenocoumarol, on the one hand, and on the other hand with the subjects who received oral anticoagulant medication of direct thrombin inhibitor type.

I point out that in the case of patients with venous thromboembolism, direct factor X inhibitors are not used in current medical practice and as a result the study did not take this medication into account.

Chapter 4. General research methodology

The study protocol was approved by the Ethics Commission of the Clinical Hospital of Oro-MaxilloFacial Surgery "Prof. Dr. Dan Theodorescu" Bucharest, Romania (no.8128/20.09.2018).

All participants in the clinical trials conducted at the OMF Surgery Clinic of the "Carol Davila" University of Medicine and Pharmacy in Bucharest expressed their agreement and signed their informed consent.

As the author of this paper, I fully assume the anonymization of the data used to write the thesis, all the data of the patients followed in this study respecting the confidentiality.

The data collection was carried out in collaboration with the staff of the OMF Surgery Clinic of the University of Medicine and Pharmacy "Carol Davila" Bucharest, under the coordination of Prof. Univ. Dr. Alexandru Bucur.

General characteristics of the patients included in the study

181 patients were included, with a mean age of 70.82 years (+/- 9.74).

Of these, 50 patients (68.5 +/- 9.45 years) were treated with oral coumarin-type anticoagulants (ACO), and 131 patients (71.71 +/- 9.75 years) were treated with the new oral anticoagulant (NACO).

Antithrombotic medication used in patients included in the study

Patients included in the study received the following types of anticoagulant medication:

• ACO: acenocoumarol (Syndrome 4 mg tablets or Thrombostop 2 mg tablets)

• NACO:

o a direct thrombin inhibitor (factor II): dabigatran etexilate (Pradaxa) - 110 mg tablets

o Direct X-factor inhibitors:

 rivaroxaban (Xarelto) - 15 mg tablets;

 apixaban (Eliquis) - 5 mg tablet.

Characteristics of the patient group

The sex distribution of the patients included in the study group was as follows:

• 85 (46.96%) women;

• 96 (53.04%) men.

In the group of patients receiving ACO, 29 (58%) were female and 21 (42%) were male.

In the patients receiving NACO, 56 (42.75%) were women and 75 (57.25%) were men.

Regarding the area of origin, a number of 41 patients (22.65%) came from rural areas and 140 (77.35%) from urban areas.

Chapter 5. Study on the risk of post-extraction hemorrhage in patients with atrial fibrillation

Introduction

As I stated in the general part of this paper, atrial fibrillation is a cardiac arrhythmia with a major embolic risk for the cerebrovascular sphere, benefiting as a first-line therapy from oral anticoagulant medication.

The objective of the study

The aim of this first study within the doctoral research was the assesment of the risk of perioperative hemorrhage in a sample of patients with atrial fibrillation, who received antithrombotic therapy.

Material and method

The study was monocentric, prospective, analytical, conducted during 2018-2022 at the Oro-Maxillo-Facial Surgery Clinic of the University of Medicine and Pharmacy "Carol Davila" in Bucharest.

After applying the inclusion and exclusion criteria, a number of 132 consecutive patients were enrolled in the study.

Statistical analysis

The data were processed and statistically analyzed using the Stata / IC 16 program (StataCorp), which specializes in scientific statistical calculations.

Comparative analyzes for continuous variables were performed using the Student test (t-test).

The Student test (t-test) was used to compare the averages of the corresponding quantitative variables of two independent groups if the variables were normally distributed.

The Fisher Exact test was used to compare qualitative variables.

The accepted error threshold considered was 0.05.

Result

In the group of patients receiving oral coumarin-type anticoagulant medication, non-valvular atrial fibrillation was previously identified in 36 patients (72%).

In the second group, which included patients receiving new type of anticoagulant medication, non-valvular atrial fibrillation was present in 96 patients (73.28%).

In the sample of patients diagnosed with non-valvular atrial fibrillation, treated with oral anticoagulants, we did not find a statistically significant association between the presence of heart rhythm disorder and the occurrence of late post-extraction hemorrhage.

This finding is in the category of subjects who received coumarin anticoagulants.

Similar results were established for patients in the category of subjects who received new generation anticoagulants.

There were no significant associations between oral anticoagulant monotherapy and late post-extraction haemorrhage in patients with non-valvular atrial fibrillation.

The highest prevalence of postoperative bleeding was recorded for Eliquis, which is close to that seen with ticagrelor (Brilique).

In patients with a history of a diagnosis of non-valvular atrial fibrillation established in the past but with congestive heart failure as a complication of heart rhythm disturbance, we observed late postextraction bleeding in 74 patients (40.88%).

In the sample of patients receiving coumarin-type oral anticoagulant medication, congestive heart failure was previously diagnosed in 23 patients (46%).

In the sample of patients receiving new oral anticoagulant medication, congestive heart failure was previously diagnosed in 51 patients (38.93%).

The evaluation of the whole group of patients included in the study (n = 181 patients) showed a significant association between the occurrence of late post-extraction hemorrhage and the history of congestive heart failure (regardless of cause) in anticoagulated subjects - (32.43% vs 15.89 %, p = 0.009, chi square test).

In the evaluated group, there was a statistically significant association between late post-extraction haemorrhage and a history of congestive heart failure in subjects treated with the new oral anticoagulants (37.25% vs 20%, p = 0.03, test chi square).

In the study group we did not observe a significant association between the presence of late post-extraction hemorrhage and oral anticoagulant monotherapy in patients with congestive heart failure.

In the case of antiplatelet monotherapy with ticagrelor (Brilique) there is a strong association with this type of medication (72.73% vs. 21.74% Sintrom and 20% Pradaxa, p = 0.049, Fisher test).

In patients with hypertension associated with atrial fibrillation, we found a significant association with late post-extraction hemorrhage (26.43% vs. 9.76%, p = 0.032, Fisher test).

In the study group we did not observe a significant association between oral anticoagulant monotherapy and the occurrence of late post-extraction hemorrhage in patients with hypertension.

In the case of antiplatelet monotherapy with ticagrelor (Brilique) there is a strong association with this type of medication (50% vs 14.63% Sintrom, $p = 0.048$, Fisher test).

The presence of atrial valvular fibrillation increased the percentage of post-extraction bleeding, but did not have a significant impact (23.33% vs. 22.52%, $p > 0.05$).

Chapter 6. Study on the risk of post-extraction bleeding in patients with the risk of a stroke

Introduction

Modern scientific data on the administration of antithrombotic treatment in ischemic stroke have been summarized in practice guidelines in recent years, as shown in the general part of this thesis.

The objective of the study

The aim of this second study within the doctoral research was to assess the risk of post-extraction bleeding in a sample of patients receiving antithrombotic medication for the prophylaxis of ischemic strokes.

Material and method

The study was monocentric, prospective, analytical, conducted during 2018-2022 at the Oro-Maxillo-Facial Surgery Clinic of the University of Medicine and Pharmacy "Carol Davila" in Bucharest.

After applying the inclusion and exclusion criteria, a number of 28 patients (15.47%) had a ischemic stroke in their personal history, and one patient (0.55%) was registered with stroke sequelae.

Result

For the whole study group (n = 181), although the prevalence was higher among patients with a history of ischemic stroke, there were no significant associations between the presence of late postextractional haemorrhage and a history of stroke (32,14 % vs 20.92%, p> 0.05, chi square test).

In the study group, the expression of late post-extraction hemorrhage was not influenced by the category of oral anticoagulant used (35% NACO vs 25% ACO, p> 0.05, Fisher’s test exactly).

In the study group we did not observe a significant association between the association of the presence of a history of stroke and the occurrence of late post-extraction hemorrhage in the case of oral anticoagulant or antiplatelet therapy (p> 0.05).

The highest prevalence of bleeding was recorded for Pradaxa, close to that recorded for Brilique.

Of the 181 patients, a total of 50 patients (27.62%) had associated diabetes mellitus, 2 patients (1.1%) with type I diabetes and 48 patients (26.52%) with type II diabetes.

For the whole study group (n = 181), there were significant associations between the presence of diabetes and late post-extraction hemorrhage (36% vs 17.56%, p = 0.008, chi-square test).

In diabetics, late post-extraction bleeding was statistically significant associated with the type of anticoagulant used (47.06% NACO vs 12.5% ACO, p = 0.026, Fisher's test exactly).

In the study group we did not observe a significant association between the association of the history of diabetes mellitus and the occurrence of late post-extraction hemorrhage in the case of oral anticoagulant or antiplatelet therapy (p> 0.05).

The highest prevalence of bleeding was recorded for Eliquis, close to that recorded for Brilique.

Chapter 7. Study on the risk of post-extraction hemorrhage in patients with acute coronary syndrome

Introduction

Assessing the risk of bleeding in patients with a history of acute coronary syndrome and receiving antithrombotic therapy with new drugs implemented in practice is a complex issue, with many unknowns, which I have tried to clarify in this study.

The objective of the study

The aim of this third study within the doctoral research was to assess the risk of post-extraction bleeding in a sample of patients receiving antithrombotic medication for the prophylaxis of acute coronary syndromes.

Material and method

The study was monocentric, prospective, analytical, conducted during 2018-2022 at the Oro-Maxillo-Facial Surgery Clinic of the University of Medicine and Pharmacy "Carol Davila" in Bucharest.

After applying the inclusion and exclusion criteria, a number of 40 patients (22.1%) had an acute coronary syndrome in their personal history.

Result

In the sample of patients with a history of acute coronary syndrome, we identified 3 subjects who received oral anticoagulants of coumarin type, respectively 37 patients who received therapy with the new oral anticoagulants.

The percentage of patients with a history of acute coronary syndrome with a history of new oral anticoagulants was significantly higher compared with those receiving acenocoumarol (28.24% NACO vs. 6% ACO, p = 0.001, Fisher's exact test).

Considering the whole study group (n = 181), it is noted that the prevalence of late postextractional haemorrhage was higher in patients with a history of acute coronary syndrome, but there were no significant associations between the history of acute coronary syndrome and postextractional haemorrhage (30% vs 20.57%, p> 0.05, chi square test).

In subjects with a history of acute coronary syndrome, postextraction hemorrhage was more common in those receiving medication for new oral anticoagulants without statistically significant combinations (32.43% NACO vs. 0% ACO, p> 0.05, test Fisher's exact).

There were no significant associations between the history of acute coronary syndrome and the late post-extraction haemorrhage for any of the anticoagulant / antiplatelet agents administered to patients with a history of coronary heart disease ($p > 0.05$).

The highest prevalence of bleeding was recorded for Xarelto, with values similar to those determined for Brilique.

Chapter 8. Discussions

The present study provides significant insights into the risk of postoperative bleeding complications in patients receiving new oral anticoagulants compared to conventional anticoagulant medication - acenocoumarol derivatives, as shown in previous chapters.

My research is one of the very few studies aimed at the direct assesment of the risk of bleeding in patients with atrial fibrillation, its practical value lies in confirming the safety of new oral anticoagulants, which have now become the therapy of choice in stable heart rhythm disorders.

In the present study, in the category of known subjects with non-valvular atrial fibrillation and oral anticoagulation, there were no statistically significant associations with the risk of late postextractional haemorrhage, if the subjects received coumarin anticoagulants.

We established a similar observation in the case of patients diagnosed with non-valvular atrial fibrillation, who benefited from the oral administration of new anticoagulants.

In my study, we did not identify a significant association between oral anticoagulant monotherapy and late post-extraction haemorrhage in patients with non-valvular atrial fibrillation ($p > 0.05$).

We note that to date we have not identified studies comparing the risk of bleeding of different types of drugs in the class of factor Xa inhibitors, but the conclusions of separate studies are available for the main representatives of this category of oral anticoagulants, which we mention furthermore.

In my study, the highest prevalence of postoperative bleeding was recorded for apixaban, which is close in value to that established for the situation in which patients received a modern antiplatelet agent - ticagrelor (Brilique).

The evaluation of the whole group of patients included in my study (n = 181 patients) showed a significant association between the occurrence of late post-extraction hemorrhage and the history of congestive heart failure (regardless of cause) in anticoagulated subjects - (32.43% vs 15.89 %, $p = 0.009$, chi square test).

In this sample, there was a statistically significant association between late postextraction haemorrhage and a history of congestive heart failure in subjects treated with the new oral anticoagulants (37.25% vs. 20%, $p = 0.03$, test). chi square).

From my results, we could not find a significant association between the presence of late post-extraction hemorrhage and oral anticoagulant monotherapy in patients with congestive heart failure.

In the case of antiplatelet monotherapy with ticagrelor (Brilique) we noticed a strong association with this type of medication (72.73% vs 21.74% Sintrom and 20% Pradaxa, p = 0.049, Fisher test).

In patients with congestive heart failure without a heart rhythm disorder but with a history of acute coronary syndrome, the risk of bleeding with rivaroxaban is higher than with antiplatelet therapy.

In patients with hypertension associated with atrial fibrillation included in my study, we found a significant association with late post-extraction bleeding (26.43% vs. 9.76%, p = 0.032, Fisher test).

In my study group, we did not observe a significant association between oral anticoagulant monotherapy and the occurrence of late post-extraction hemorrhage in patients with hypertension.

In the case of antiplatelet therapy with ticagrelor (Brilique), I established a strong association with this type of medication (50% vs 14.63% Sintrom, p = 0.048, Fisher test) in my study group.

In my study group, the presence of atrial valvular fibrillation increased the percentage of post-extraction bleeding, but did not have a significant impact (23.33% vs. 22.52%, p> 0.05).

For the entire study group analyzed in my doctoral research (n = 181), although the prevalence was higher among patients with a history of ischemic stroke, there were no significant associations between the presence of late post-extraction hemorrhage and a history of seizures. stroke (32.14% vs 20.92%, p> 0.05, chi square test).

In the study group, the manifestation of late post-extraction hemorrhage was not influenced by the category of oral anticoagulant used (35% naco vs 25% aco, p> 0.05, fisher's test exactly).

We also did not observe a significant connection between the association of the presence of a history of stroke and the occurrence of late post-extraction hemorrhage in the case of oral anticoagulant or antiplatelet therapy (p> 0.05), on the analyzed sample.

The highest prevalence of bleeding in my study group was recorded for pradaxa, close to that recorded for brilique.

For the whole study group (n = 181), there were significant associations between the presence of diabetes and late post-extraction hemorrhage (36% vs 17.56%, p = 0.008, chi-square test).

In diabetics, late post-extraction bleeding was statistically significant associated with the type of anticoagulant used (47.06% NACO vs. 12.5% ACO, p = 0.026, Fisher's test exactly) in my study group.

In my study group, I did not notice a significant association between the association of a history of diabetes mellitus and the occurrence of late post-extraction hemorrhage in the case of oral anticoagulant or antiplatelet therapy (p> 0.05).

The highest prevalence of bleeding in the study group was found for Eliquis, which has a prevalence close to that of Brilique.

Considering the whole study group (n = 181), we noticed that the prevalence of late postextractional hemorrhage was higher in patients with a history of acute coronary syndrome, but there were no significant associations between the history of acute coronary syndrome and postextractional hemorrhage (30% vs 20.57%, p> 0.05, chi square test).

In subjects with a history of acute coronary syndrome, postextraction hemorrhage was more common in those receiving medication for new oral anticoagulants without statistically significant combinations (32.43% NACO vs. 0% ACO, p> 0.05, test Fisher's exact).

In the group I studied, there were no significant associations between the existence of a history of acute coronary syndrome, respectively late post-extraction hemorrhage for any of the anticoagulant / antiplatelet drugs administered to patients with a coronary history (p> 0.05).

The highest prevalence of late post-extraction hemorrhage was recorded for Xarelto, with values similar to those determined for Brilique.

Chapter 9. Conclusions and personal contributions

Conclusions

1. Our study showed a significant risk of post-extraction bleeding in patients receiving treatment with new oral anticoagulants, a result consistent with current statistics available in the literature.

2. The statistical correlations showed a lack of a statistically significant association between the bleeding risk and the pathological history of atrial fibrillation with embolic risk, both in the case of administration of coumarin derivatives and in the use of new oral anticoagulants.

3. The presence of congestive heart failure within comorbidities present in oral anticoagulated patients influenced the presence of the risk of late post-extraction hemorrhage.

4. The comparison between the two categories of oral anticoagulants showed significant correlations between the risk of post-extraction hemorrhage and patients with atrial fibrillation and congestive heart failure, treated with the new oral anticoagulants.

5. There is no statistically significant link between valvular insufficiency and the proportion of post-extraction bleeding events in patients with atrial fibrillation undergoing oral anticoagulation, regardless of the category of oral anticoagulant medication administered.

6. Our study found strong evidence of correlations between concomitant hypertension in patients with stable heart rhythm disorders and the risk of late post-extraction bleeding.

7. We did not obtain statistically significant differences between the presence of late post-extraction hemorrhage and the presence of a history of stroke in oral anticoagulated patients in the study population.

8. No significant differences were found in the comparative analysis of the risk of late post-extraction bleeding in patients with a history of stroke who received coumarin anticoagulant medication and, respectively, subjects who were given new oral anticoagulants for the secondary prevention of stroke, no significant statistically differences were determined between the two diagnostic groups.

9. Statistical analysis indicated significant differences between bleeding risk values and a history of diabetes in patients with a history of stroke, oral anticoagulation, compared to subjects without diabetes.

10. Regarding patients with a history of stroke and a history of diabetes, in the sample of subjects who received medication in the category of new oral anticoagulants we found a trend of significant association with the risk of post-extraction hemorrhage, compared to those who benefited from the new oral anticoagulant.

11. Regarding the history of acute coronary syndrome, we have shown that there is no significant association with the presence of post-extraction hemorrhage.

12. We also observed in the sample of patients who received oral anticoagulants following acute coronary syndrome, a higher frequency of post-extraction bleeding events when using new oral anticoagulants, but without this association being statistically significant.

13. The data indicate a higher rate of late post-extraction bleeding in the case of apixaban (Eliquis) in patients with atrial fibrillation, similar to that associated with ticagrelor (Brilique).

14. We found a significant association between the risk of bleeding and the concomitant congestive heart failure in patients with atrial fibrillation, in the case of ticagrelor antiplatelets, compared to subjects receiving oral anticoagulant therapy.

15. We concluded that in the case of concomitant hypertension in patients with atrial fibrillation, there is a significant association with the risk of postextractional hemorrhage only in subjects treated with antiplatelet, not among those with oral anticoagulation.

Personal contributions

This study is unique in the literature because there are no publications on the correlations between the risk of post-extraction bleeding in patients receiving oral anticoagulation compared to the older generation of coumarin anticoagulants and new oral anticoagulants.

The originality consisted in compiling a group of patients with a history of anticoagulant treatment and comparing the risk of late post-extraction hemorrhage with the groups of general conditions indicated for anticoagulation and with the comorbidities that the subjects present.

The originality is also supported by the inclusion in the studied population of similarly numerically sampled subjects who are administered medication from all categories of oral anticoagulants currently available nationally.

The innovative character of the research is given by the obtained results that make it possible to individualize the therapeutic attitude for each category of patients, depending on the class of oral anticoagulant medication they receive, corroborated with the associated comorbidities.

The current work, by clarifying and establishing the risk of late post-stroke hemorrhage in oral anticoagulated patients, is a starting point for reducing the number of postoperative complications in oro-maxillofacial surgery and promotes the practice of medical reasoning in treating patients with complex general pathology, that requires surgery in our area of interest.

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12. Radu R, Dincă O, Pădurariu C, Niță T, Vlădan C, Bucur A. Comparison of bleeding risks with new oral anticoagulants versus acenocumarolum – part 1. Romanian Journal of Oral Rehabilitation, Vol. 14, No. 1, January - March 2022: 97-101

List of published scientific papers

Scientific papers published in journals indexed in international databases (BDI)

1. **Radu R**, Dincă O, Pădurariu C, Niță T, Vlădan C, Bucur A. Comparison of bleeding risks with new oral anticoagulants versus acenocumarolum – part 1. Romanian Journal of Oral Rehabilitation, Vol. 14, No. 1, January - March 2022: 74-77
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