

RESEARCH ARTICLE

The Complication Rates of Oral Anticoagulation Therapy in Deep Venous Thrombosis

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The **objective** of the current study is to evaluate the complication rates (embolic and hemorrhagic events) in deep venous thrombosis (DVT) patients on different types of oral anticoagulation therapy (OAC): direct oral anticoagulant therapy and vitamin K antagonist therapy. **Methods:** A number of 62 DVT patients were included and divided in two groups, depending on the type of oral anticoagulation therapy administered. The first group was composed of patients treated with direct oral anticoagulant treatment (Dabigatran, Rivaroxaban) and the second group was composed of patients treated with vitamin K antagonist (Acenocumarol). General data, including BMI and comorbidities were noted. Embolic and hemorrhagic events were noticed. **Results:** in the first group of patients (DOAC therapy), a number of 34 patients were included (14 of them with BMI higher than 25 kg/m² and 14 with concomitant atrial fibrillation), while the second group comprised of 28 patients treated with VKA (21 of them with a high BMI and only 3 of them with atrial fibrillation). After a mean period of 36 months of anticoagulant therapy, complications were present in 17 patients, hematuria (8 episodes) and pulmonary embolism (4 cases) were the most frequent, with no difference regarding the treatment applied. **Conclusion:** No statistically significant difference was encountered regarding embolic and hemorrhagic event rates in our deep vein thrombosis patients.

Keywords: deep venous thrombosis, direct oral anticoagulants, Acenocumarol, obesity

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Introduction

Deep venous thrombosis (DVT), along with pulmonary embolism (PE) are parts of venous thromboembolic (VTE) disorder with an incidence of nearly 1.6 per 1000 inhabitants a year, affecting especially the lower limbs [1].

DVT is rare if no risk factors are present; the most important risk factors are a history of DVT or pulmonary embolism (PE), severe infection, heart failure, obesity, oral contraceptive treatment, cancer, surgery. More than half of all cases of DVT present with no clinical symptoms. When present, signs and symptoms include local pain and swelling, superficial venous system dilatation [2].

WELLS or modified WELLS score guide the clinician on diagnosing DVT, with a high negative predictive value [3, 4]. Also, D-dimer test and venous ultrasonography of the lower limb are highly accurate in diagnosis.

A frequent and life-threatening complication of DVT is PE, after embolization of a thrombus into the pulmonary arteries. To prevent this important complication, anticoagulant treatment is recommended. Therapies may vary, from parenteral anticoagulation with low molecular weight heparin (LMWH) or unfractionated heparin (UFH) switching to vitamin K antagonist (VKA - Acenocumarol) or to the direct oral anticoagulants (DOAC), such as Dabigatran, Rivaroxaban or Apixaban.

The aim of this study is to evaluate the complication rate (embolic and hemorrhagic events) in DVT patients on oral anticoagulation therapy.

The protocol of this study was approved by the Ethics Committee of the University of Medicine and Pharmacy of Targu Mures, Romania, number: 171/28.12.2016 in accordance with standards of 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Methods

A retrospective observational study was performed on 62 adult patients with confirmed deep venous thrombosis diagnosis, treated with OAC.

Patients were admitted between 2013, July, 1 – 2016, June, 30, irrespectively of the time when anticoagulation was started or interrupted by various reasons.

Main exclusion criteria were: cancer patients, history of bleeding, major head trauma.

Other comorbidities included the presence of heart failure, systemic hypertension, atrial fibrillation, diabetes mellitus, chronic kidney disease, documented alcohol abuse.

Patients were divided in two groups: group I: 28 patients receiving DOAC's, group II composed of 34 patients with VKA therapy.

We considered the approved regime for the DOAC: Dabigatran 150 mg twice daily (BID) or Rivaroxaban 20 mg once daily (OD). The anticoagulant treatment was applied as recommended.

In group II, Acenocumarol dose was given so that the patients were in time therapeutic range.

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All included patients had serum creatinine levels clearance over 30mL/min/1.73m² (MDRD formula).

For hemorrhagic events four class classification of bleeding provided by American College of Surgeons' advanced trauma life support (ATLS) was used [5].

Bleeding events occurred during the 36 months of treatment were divided in:

- minor events including hospitalization for haematuria, epistaxis, hemoptysis;
- major events including hospitalization for intracranial bleeding, gastrointestinal (GI) bleeding (superior or inferior), and blood transfusion after hemorrhagic events linked to OAC treatment.

The statistical analysis was performed using Microsoft Office Excel 2010 and EpiInfo software. The chi-square statistical analysis was performed. Continuous variables are reported as mean \pm standard deviation (SD) and categorical variables as observed number of patients.

In the period 2013 July, 1 – 2016, June, 30, the electronic registries were consulted and each patient was checked for the occurrence of embolic or hemorrhagic events.

Results

The mean age of the entire group was 64 \pm 13 years, with no statistical difference between the 2 groups of patients (Table I).

Body mass index (BMI) difference between the 2 studied groups was statistically significant, 21 patients on VKA therapy were overweight, while only 14 patients on DOAC treatment had a BMI over 25 kg/m², p value (chi square Yates corrected) = 0.015, OR = 4.285 (1.434-12.806).

Also, atrial fibrillation was present more often in the first group compared to the VKA regimen group, p value (Fisher exact test) = 0.047, OR = 0.269 (0.076-0.953).

The mean period of oral anticoagulant treatment of the 62 patients was 32 months.

At the time of the electronic register check of all patients, a total of 17 (27.43%) patients presented with com-

plications, in some patients, more than one complication occurred. The statistical analysis revealed no significant difference between the treatment applied and the complication rate, p = 0.637 (Figure 1).

Out of the 17 patients with one or more complications, 8 (47.1%) of them were in group 1 and 9 (52.9%) were in the second group treated with VKA therapy, with no statistically significant difference between the two groups.

The mean age of the 17 patients, cross tabled with the therapy applied, was similar, with no significant differences (Table II).

Regarding a possible association between the BMI and complication rate, 9 of the 17 patients were overweight, with no significant role of the BMI in complication occurrence, p = 0.955.

Also, the BMI showed no significant role in complication occurrence in the two groups taken separately, depending on the type of OAC therapy applied.

Regarding the associated diseases in the 17 patients with complications, chronic kidney disease occurred most often (Figure 2).

Discussions

A high body mass index (obesity) was proven to have an important role in thrombosis, due to chronic inflammation and impaired fibrinolysis, more and more obese people presenting DVT and the complications that come with it [6]. In our study, high BMI was not proven to have an important role in the occurrence of embolic or hemorrhagic complications in DVT patients.

Studies show that patients with chronic kidney disease have altered the pharmacokinetics of drugs. [7]. Administered in the therapeutic dose direct anticoagulants do not produce more complications compared to acenocoumarol in patients with chronic kidney disease [8].

In the current study, we wanted to determine the benefit of the prophylactic OAC treatment applied to prevent the mentioned complications, using to different classes of OAC. The classic vitamin K antagonist (Acenocoumarol) compared to the new class of OAC (Dabigatran, Rivaroxaban).

The results revealed no difference between the two groups regarding the rate of embolic or hemorrhagic complication.

Table I. Group characteristics

Baseline group characteristics	Entire group	Group I -NOAC	Group II- VKA	P value
	(nr. of patients/percentage)			
Number of patients	62 (100%)	34 (54.8%)	28 (45.2%)	
Male gender	33 (51.6%)	15 (45.5%)	18 (54.5%)	0.133
Rural area	33 (51.6%)	16 (48.5%)	17 (51.5%)	0.283
BMI - overweight	35 (61.3%)	14 (40%)	21 (60%)	0.015
Associated Diseases				
Heart failure	46 (74.2%)	25 (54.3%)	21 (45.7%)	1
Arterial Hypertension	44 (70.9%)	24 (54.5%)	20 (45.5%)	1
Diabetes mellitus	10 (16.1%)	4 (40%)	6 (60%)	0.494
Chronic kidney disease	43 (69.4%)	24 (55.8%)	19 (44.2%)	1
Alcohol abuse	0	0	0	NA
Atrial fibrillation	17 (27.4%)	14 (82.4%)	3 (17.6%)	0.047

Table II. Complications occurred in the 2 groups

Complications	Group 1	Group 2		P value
		Dabigatran	Rivaroxaban	
Pulmonary embolism	1	1	2	0.619
Stroke/TIA	2	1	0	0.584
Hematuria	8	3	3	0.472
Epistaxis	0	1	0	1
Haemoptysis	0	0	0	-
GI bleeding	0	1	0	1
Blood transfusion	0	0	2	0.496

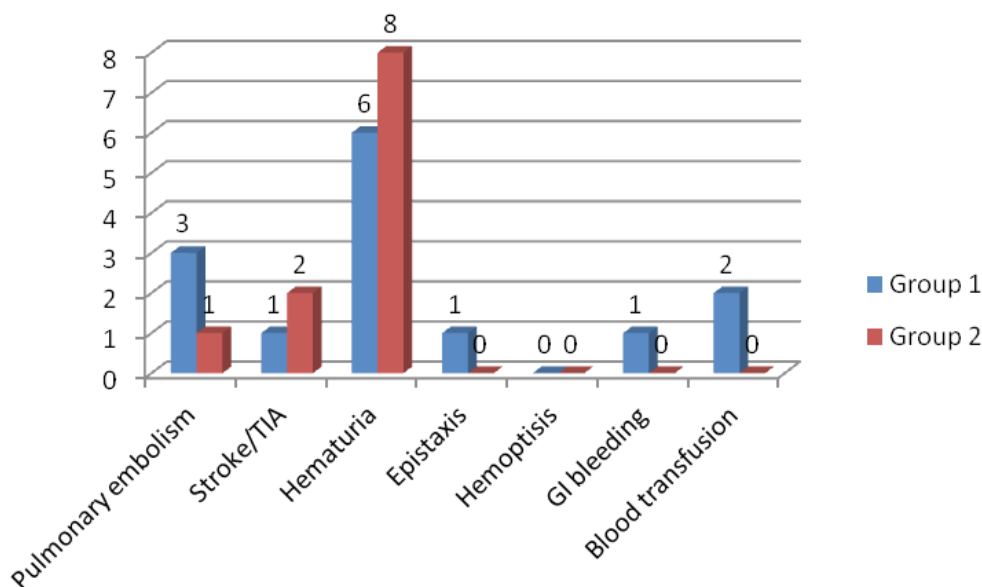


Fig. 1. Complications occurrence rate

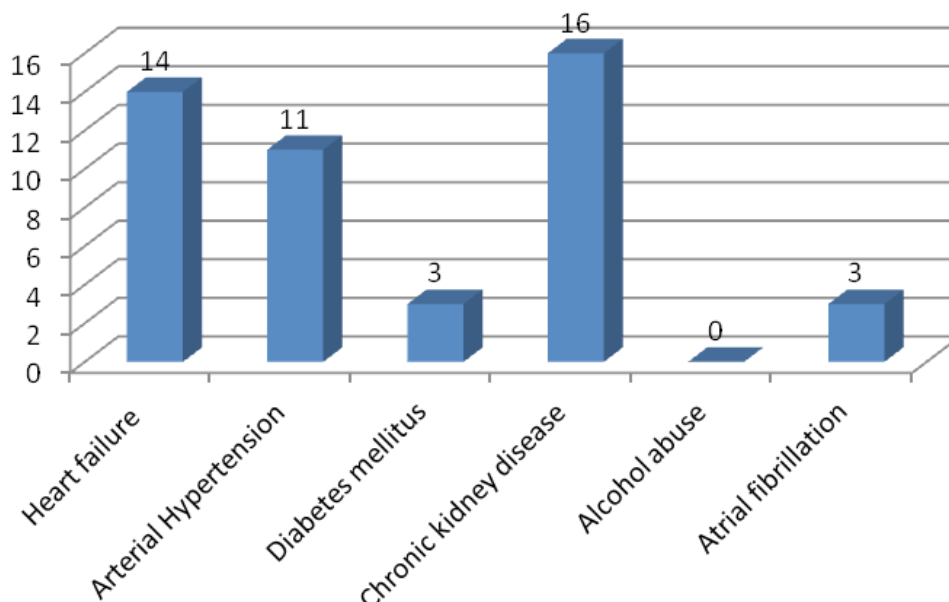


Fig. 2. Associated pathology in patients with complications

Other studies confirm our findings, the DOAC's non inferiority to VKA regarding embolic episodes with lower bleeding risk [9,10].

Conclusions

No statistically significant difference was encountered between the applied class of oral anticoagulation treatment and the embolic or hemorrhagic event rate in our studied deep vein thrombosis patients.

Hematuria and pulmonary embolism were the most frequent complications occurred, with no statistically significant difference between the treatments applied.

High body mass index did no prove to have a significant role in complication occurrence in the two studied groups.

Chronic kidney disease, heart failure, arterial hypertension, atrial fibrillation and diabetes mellitus were the most

associated pathologies at baseline, while chronic kidney disease highest encountered at patients with complications.

Authors' contribution

Ionela Silivastru (Cozlea) (Conceptualization; Methodology; Project administration; Writing – original draft)
 Arthur-Atilla Keresztesi, (Formal analysis; Software)
 Asofie (Keresztesi) Gabriela (Data curation; Investigation; Software)
 Daniel Cozlea, (Supervision; Writing – review & editing)
 Daniela Ecaterina Dobru (Supervision; Validation)

Abbreviation list

DVT: deep venous thrombosis, OAC: oral anticoagulation, BMI: body mass index, DOAC: direct oral anticoagulation, VKA: vitamin K antagonist, PE: pulmonary

embolism, VTE: venous thromboembolic, LMWH: low molecular weight heparin, UFH: unfractionated heparin, BID: twice daily, OD: once daily, ESC/EHRA: European Society of Cardiology/European Heart Rhythm Association, MDRD: modification of diet in renal disease, ATLS: American College of Surgeons' advanced trauma life support, GI: gastrointestinal, SD: standard deviation, OR: odds ratio.

Conflict of interest

The authors declare there are no conflicts of interest regarding this paper.

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