Digestive complications in patients with cardiovascular disorders under anticoagulant treatment

PhD candidate: IONELA (COZLEA) SILIVASTRU

PhD coordinator: PROF. DR. DANIELA ECATERINA DOBRU

The cardiovascular disorders within which it can be included also the congestive cardiac failure, atrial fibrillation, deep vein thrombosis, valvulopathies, have an increased prevalence among the elderly patients, with an increasing incidence due to the aging of the population and are the main cause of death at the world level.

Due to several common physio-pathological mechanisms, the cardiac failure and the atrial fibrillation coexist up to 30 % of the patients with congestive cardiac failure, when the structural causes of the atrial fibrillation, such as the myocardia heart attack, are absent, it is difficult to prove in patients present both disorders, which is the primary pathology. The annual incidence of the atrial fibrillation is of 5 % in patients with compensated congestive cardiac failure, while among those with decompensated congestive cardiac failure it is of 40 %.

The main issue of the clinicians who face these pathologies is the systemic thromboembolism. In order to prevent this complication, these patients are administered anticoagulant therapy. The worst complication of the anticoagulant treatment is the intra-cerebral bleeding, which has a reserved prognostic, mainly due to the extension risk.
The gastro-intestinal bleedings are more frequent than the intra-cerebral bleeding events, especially in patients who use the anticoagulant treatment associated with the antiplatelet therapy, association which determines an increase by 13 times of the haemorrhagic risk, especially in the elderly.

The selection of the present research theme is fully justified because in the last years studies were carried out which tracked the apparition and recurrence of the haemorrhages in patients with cardiovascular disorders which require anticoagulation, but among the Romanian patients, these studies are few and also at the world level there are very few studies analysing the haemorrhagic digestive disorders which appear among the patients with compensated congestive cardiac failure placed under anticoagulant treatment compared to the patients with decompensated congestive cardiac failure with anticoagulants. Due to these reasons, in this paper we proposed to study the secondary digestive disorders of the anticoagulant treatment which appeared among the patients with cardio-vascular disorders, taking into account also the comorbidities, developing risk profiles for the patient under treatment with anti-vitamin K and for the patient which follows a direct anticoagulant treatment.

Main objectives: 1. Evaluation of the haemorrhagic digestive events in patients with associated cardiovascular disorders and pathologies which predispose to bleeding, with direct anti-coagulant comparated to those using the anti-vitamin K. treatment **2.** Study of the rates for the digestive haemorrhages according to the associated pathologies which rise the level of bleeding: hepatopathy, Diabetes Mellitus, chronic kidney disease; **3.** Evaluation with the help of the digestive superior endoscopy of the digestive haemorrhages disorders which appear in patients with compensated congestive cardiac failure **(NYHA** I or II) versus decompensated congestive cardiac failure (NYHA III or IV) placed under anticoagulant treatment and the emphasis of the associated pathologies which raise the bleeding risk.

Secondary objectives: 1. Influence of the toxic behaviours: chronic alcoholism, chronic smoking, of the platelet anti-aggregate medication and of the body mass index upon the frequency of the digestive haemorrhages in anti-coagulated patients. **2.** The evaluation of the rate

of extra-digestive haemorrhages in patients which follow an anti-coagulant therapy.

In the general part it is presented the current stage of knowledge regarding the cardio-vascular disorders which requite an anticoagulant treatment, the action mechanism of the anti-coagulant therapy and the associated pathologies which raise the bleeding risk.

The first study which had as main object the evaluation of the haemorrhagic events in patients with cardiovascular disorders and associated pathologies which predispose to bleeding, under the treatment with D.O.A.C: dabigatran, rivaroxaban, apixaban, compared to patients which followed a drug therapy with A.V.K - acenocumarol. 289 patients were included during the period July 1st 2013 – June 30th 2016, the study being a retrospective, observational, analytical one, over a period of 30 months (July 1st 2016 – December 31st 2018), the data was collected from the medical computer system and from the medical sheets. 146 (50.5 %) received the anticoagulant AVK treatment, and 143 (49.5 %) the direct anticoagulant therapy, 52.6 % females, 47.4 % males, average age 69 years+/-10.95 SD, 34.9 % of the patients having the age past 75 years.

The treatment with AVK (O.R= 1.40), congestive cardiac insufficiency and treatment with AVK (O.R: 1.4), hepatopathy and treatment with AVK (p: 0.041, O.R: 2.77) are associated with minor haemorrhages. The Diabetes Mellitus and treatment with AVK (p- 0.035), BCR and treatment with AVK (O.R= 1.35), Diabetes Mellitus (O.R de 2.712), hepatopathy (O.R de 2.463) are associated with major haemorrhages. The risk of appearing a superior digestive haemorrhage is higher in diabetic patients under treatment with AVK(O.R= 4.722), in patients with hepatopathy (O.R= 4.762). Diabetes Mellitus and the treatment with AVK increase the risk of HDI, O.R: 1.115 namely O.R: 1.371. The asthenic patients under treatment with AVK presented more cases of haemoptysis (l8.2 %) compared to those with direct anticoagulant (p- 0.036), among them being registered statistically significant more cases of inferior digestive haemorrhages (p- 0.054).

In the second study, the main objective was evaluated with the help of the superior digestive endoscopy in patients with ICC NYHA I, II versus ICC NYHA III, IV placed under anticoagulant treatment. In the retrospective analytical study it was included 123 patients, aged between 50 and 94 years, average age: 72 ani +/ -8 .84 SD, 77 patients with anticoagulant treatment (AVK and DOAC), of which: 32 with ICC NYHA I, II, 45 with ICC NYHA III, IV. The control lot (without anticoagulant therapy): 46 patients with ICC: 31 NYHA I, II, 15 stage NYHA III, IV. The lesions noticed during the superior digestive endoscopy were: congestive gastritis, erosive gastritis and gastro/duodenal ulcer. Patients with ICC **NYHA** III, IV anticoagulated have statistically significant more cases of congestive gastritis (p- 0.0001) and gastric/duodenal ulcer, both with anticoagulant (p- 0.0001), as well as without p- 0.002. Patients with hepatopathy and anticoagulant treatment (p- 0.01), as well as intoxicated persons (p- 0.007) showed congestive gastritis. The platelet antiaggregant treatment increases the apparition risk of the gastro/duodenal ulcer (O.R= 1.889), but without statistical significance (p- 0.95) due to the therapy with proton pump inhibitors followed by patients.

Via the two studies, we managed to achieve the risk profiles of the patients who follow an anticoagulant therapy with anti-vitamin K or direct anticoagulant therapy, for the digestive bleedings, useful in the medical practice:

AVK: diabetic patients, with hepatopathy, chronic renal disease, ICC NYHA III, IV, antiaggregant platelet associated treatment, asthenic, chronic intoxicated persons.

DOAC: patients with ICC NYHA III, IV, asthenic, chronic intoxicated persons.