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PhD THESIS
**OPTIMISATION POSSIBILITIES
IN THE MANAGEMENT OF CHRONIC
VENOUS DISEASE**

A B S T R A C T

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ABSTRACT

Introduction and. Considering the worldwide literature data, we can say that chronic venous disease (CVD) is a frequent pathology, condition affecting millions of individuals globally. It is precisely in this context that the therapeutic methods have advanced, leading to innovations in the field. Progress has also been made in the methods of assessment and follow-up of these patients. In this doctoral thesis I have described the results of studies conducted in the 1st Surgical Clinic, “Pius Brînzeu” University Clinical Hospital Timișoara, interpreting them in terms of in terms of improvement possibilities in phlebological patients management.

Aim. This paper aims to assess the potential possibilities for improving the management of patients with CVD, both in terms of diagnosis and prognosis, and in terms of establishing optimal therapeutic conduct, the following objectives being evaluated: a. effects of statin treatment on venous wall morphology in patients with chronic venous disease; their implications in the therapeutic approach and postoperative course of these patients; b. minimally invasive therapeutic methods used in CVD treatment; c. morphological changes associated with comorbidities with impact on diagnosis and therapy of chronic venous disease; d. reassessment of the usefulness of certain clinical laboratory parameters in the prognosis and management of patients with chronic venous disease

Methods. a. 102 operated patients with chronic venous disease in the CEAP C2-C3 stage were included in the first study. 215 venous fragments, collected from 50 patients within the study group and 179 venous fragments collected from 52 patients within the control group were microscopically analysed, evaluating a series of morpho-anatomical parameters. b. This retrospective study presents the results of 1087 operated patients, including follow-ups. As surgical treatment, cryostripping was practiced in all mentioned cases. Patient follow-up was made at one week, one month, and six months postoperatively by clinical examination, duplex ultrasonography, CIVIQ-20 and r-VCSS questionnaires. Outcomes, complications, surgery and hospitalisation

period, and benefits of the method were analysed. *c.* This study presents and discusses the case of a great saphenous vein giant aneurysm, diagnosed in an obese female patient with other associated pathologies. *d.* This retrospective study evaluated the laboratory results of 256 patients diagnosed with CVD. According to the CEAP classification, depending on the CVD stage, three groups were formed: Group 1 (C2-C3– mild disease), Group 2 (C4 – moderate to severe disease) and Group 3 (C5-C6– severe disease). The considered parameters were: age, RBC, WBC, and platelet counts, percentage of neutrophils and lymphocytes, neutrophil-to-lymphocyte percentage ratio, ESR, CRP, fibrinogen, prothrombin time (in percentages and seconds), INR, aPTT, CK, CK-MB, glycaemia, ALT, AST, total bilirubin, and urea.

Results. *a.* In the study group, it was found that, venous reflux predominantly affects small veins, and also, a significant increase in collagen deposits in the adventitia and media tunics, proportional to the thickening of the venous wall. *b.* Generally, good functional and aesthetic outcomes defined by clinical symptoms remission, absence of insufficient veins on Doppler ultrasonography, QoL and r-VCSS improvement ($p < .001$) were obtained. Complications included bruising $\varnothing < 2$ centimetres (32.38%), haematoma (8.92%), saphenous nerve injury (3.49%), deep vein thrombosis (0.18%). Recurrence was noted in 2.94% cases. Mean duration of procedure was 42 ± 12.5 minutes, mean duration of hospitalization was 1.29 days. Compared to high ligation and conventional stripping, the postoperative pain was reduced; compared to other minimally invasive procedures, the costs were reduced. *c.* we did not notice fragmentation of the elastic fibers or changes in the adventicea; we did not notice any thrombus inside the parts of apparently healthy great saphenous vein; we consider that the deposition of fibrous tissue between the smooth muscle layers that explained the degeneration of the media can be considered the main aspect that led to the enlargement of the aneurysm. *d.* Analysing RBC, WBC, PLT and coagulation factors, no significant differences were noticed; on the other hand, inflammatory markers revealed differences among the groups. Several alterations were observed in hepatic, metabolic and muscle tissue markers analyses.

Conclusions. Statin treatment has a potential role and influences the morphological changes occurred in the venous wall in chronic venous disease. Clinically, these results suggest that in the case of patients with chronic venous disease who associate outpatient chronic statin medication for the treatment of other diseases, when the venous reflux is not objectified through Doppler ultrasound in the trunks of the saphenous veins, the minimally invasive approach, targeting the varicose veins/veins with reflux, can be considered, preserving the saphenous veins and establishing subsequent prophylactic measures – compressive stockings, phlebotonic medication, and avoiding risk factors.

Therapeutically, in case of the radical treatment of venous reflux, cryostripping has proven to be an efficient, accessible, and feasible method. According to the medium- and long-term proven results, as a surgery, cryostripping makes its mark as a gold standard in the treatment of chronic venous disease, starting with the CEAP C2 stage. It combines the advantages of minimally invasive procedures with the principles of classical surgery, leading to very good results from a clinical and functional, as well as an aesthetic point of view. Economically, the method is significantly cheaper compared to other minimally invasive endovenous procedures, being perfectly adaptable to in-hospital conditions, even in countries with low- and middle-income countries. At the same time, the method can be successfully practiced as day-case surgery.

The primary venous aneurysm is a relatively rare pathological entity. Even though the case presented in this study seems to be one of the largest ones described to this day, in comparison to similar studies, it did not pose any particular problems from a therapeutic point of view. Correctly instituted prophylactic measures for complications have led to their absence, despite the potential risks. In case of large primary venous aneurysms, endophlebohypertrophy and endophleboscclerosis plead as a hypothesis of aetiology.

Some parameters of routine laboratory tests can be correlated with the disease progression towards higher severity stages. The neutrophil-to-lymphocytepercentage ratio, ESR, CRP, fibrinogen could be considered useful markers in the evaluation of CVD progression. Intraluminal thrombus formation in case of varicose veins (thrombophlebitis) is due to conditions of turbulent

flow, stasis, and endothelial inflammation, rather than hypercoagulability. Inflammatory factors follow the CVD progression, being involved in pathophysiological modifications as that of the thickening of venous walls, valvular modification, the appearance of intraluminal thrombi, and trophic lesions.

Therapeutical management of CVD can be improved through: minimally invasive approach and the adaptation of therapeutic measures according to the particularities of certain patient categories; full imaging assessment and prompt implementation of complications prevention methods concurrently with surgery, in case of the presence of certain morphological particularities of the disease; CVD severity/progression monitoring with the help of routine blood tests.