

CHRONIC VENOUS DISEASE – A RISK FACTOR FOR CARDIOVASCULAR DISEASES

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ABSTRACT

Background: Chronic venous disease (CVD) is a prevalent vascular disorder, primarily characterized by venous hypertension, valvular insufficiency, and ulceration. Emerging evidence suggests a potential association between CVD and cardiovascular diseases (CVDs), including hypertension, ischemic heart disease, and heart failure. This study investigates whether CVD serves as an independent risk factor for CVDs by assessing their prevalence and clinical overlap. Methods: two complementary analyses were conducted. The first examined the prevalence of CVDs in 536 patients with CVD, while the second assessed CVD in 125 inpatients with CVDs. Patients were classified using CEAP criteria, and data analysis included multivariate regression models adjusted for cardiovascular risk factors. Results: among CVD patients, 49.66% also had CVDs, with hypertension (31.2%) being the most common. CVD prevalence increased with disease severity, from 29.5% in CEAP C0-C2 to 70.5% in C3-C6. In cardiovascular patients, 70.4% exhibited CVD, with hypertension (78.2%) and ischemic heart disease (70.5%) as leading comorbidities. Conclusions: the study highlights a strong epidemiological link between CVD and CVDs, emphasizing the role of endothelial dysfunction, chronic inflammation, and hemodynamic alterations in their coexistence. Early screening and integrated vascular management are essential, and future longitudinal studies are needed to establish causality and develop targeted therapeutic approaches.

Keywords: chronic venous disease, cardiovascular diseases, hypertension, ischemic heart disease, heart failure, CEAP classification, venous insufficiency, endothelial dysfunction.

INTRODUCTION

Chronic venous disease (CVD) encompasses a spectrum of venous disorders characterized by venous insufficiency, varicosities, and, in advanced cases, venous ulcers. Globally, CVD affects a significant proportion of the population, with prevalence rates increasing with age. Cardiovascular diseases (CVDs), including hypertension, coronary artery disease, and heart failure, remain the leading cause of mortality worldwide, with a projected 23 million deaths annually by 2030. The clinical intersection

between CVD and CVDs raises important questions about the pathophysiological mechanisms linking these conditions. Both share common risk factors, including aging, sedentary lifestyles, obesity, and genetic predisposition. This study investigates whether CVD serves as an independent risk factor for CVDs. [1-4]

Defined by Nicolaides as “the decompensation stage of lower limb circulation, with the signs and symptoms caused by venous hypertension as a result of structural and functional venous anomalies”,

CVD is an inflammatory, progressive affliction that influences the entire human organism. Due to its high prevalence, its severe complications, its socioeconomic implications and the significant impact on the patients' quality of life, CVD remains a public health concern comparable to diabetes, cancer and cardiac failure (CF). Along with the determining or causing factors, an important role in the onset and progress of the disease belongs to the favoring factors, also known as CVD risk factors, among which we mention cardiovascular pathologies. This article aims to analyze the correlations between the two medical conditions. If the role of CVDs in the progression of CVD is well-established, could CVD itself increase the risk for CVDs? [5,6]

MATERIALS AND METHODS

To support our hypotheses, the investigation consisted of two complementary studies.

The first study focused on the prevalence/frequency of CVDs among patients diagnosed with CVD was performed on a number of 536 patients diagnosed with CVD, selected from an examination lot of 987 subjects, both women and men, aged between

RESULTS

Nearly half (49.66%) of the people suffering from CVD included in our first study also suffered from CVDs, the most frequent being arterial hypertension (AHT), ischemic heart disease (IHD) and heart failure (HF),

18 and 85, of both rural and urban provenance, who have, in 2024, sought care at the Dermatology Department of the "Anton Cincu" Hospital in Tecuci for various dermatological pathologies.

The second study examined the prevalence/frequency of CVD among patients diagnosed with CVDs and the evolution of CVD in relation to the moment of the cardiovascular diagnosis. It was performed upon a number of 125 inpatients from the Cardiology Department of the same hospital, who were admitted in the hospital between January and April 2024.

For each study subject we have respected the CEAP clinical criteria for the diagnosis of CVD, we have analyzed the personal history based on the personal medical records provided by the patients, only taking into account the diagnoses confirmed by specialists.

Clinical data, including medical history, CEAP classification, and diagnostic findings, were documented. Diagnoses were confirmed using imaging and clinical evaluations.

Prevalence rates were analyzed using multivariate regression models adjusted for age, sex, and other risk factors.

which aligns with the objectives of our study. Of the 536 patients, 266 of them presented CVDs. Hypertension affected 31.2% of CVD patients, IHD affected 11% and HF affected 7.46% of our selected patients (Figure 1).

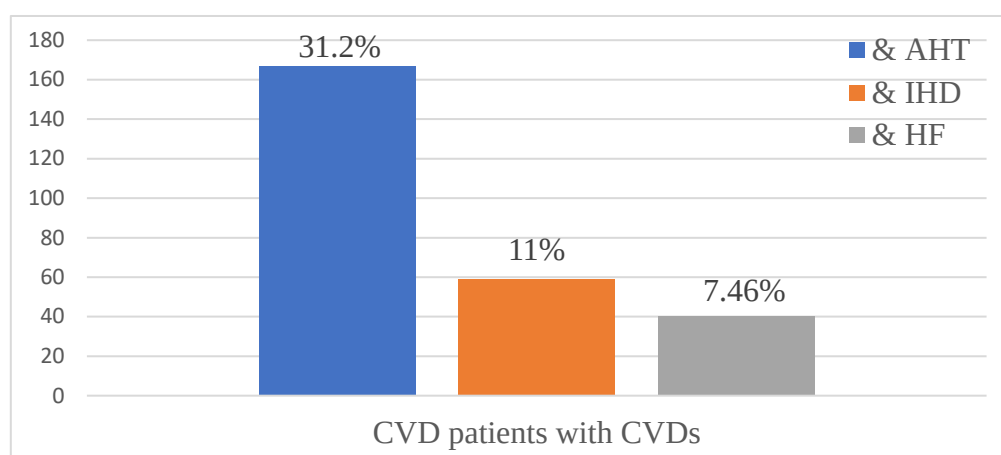


Figure 1. Frequency of comorbidities: AHT, IHD and HF among patients with CVD.

By stratifying the CVD patients with CVDs by the CEAP clinical stages, we remarked on the fact that the prevalence of CVDs increases with the severity of CVD, according to the CEAP stages. Out of the 266 patients with both

CVD and cardiovascular disease, 29.5% were classified as stages C0-C2, while 70.5% patients were affected by C3-C6 CVD (Figure 2).

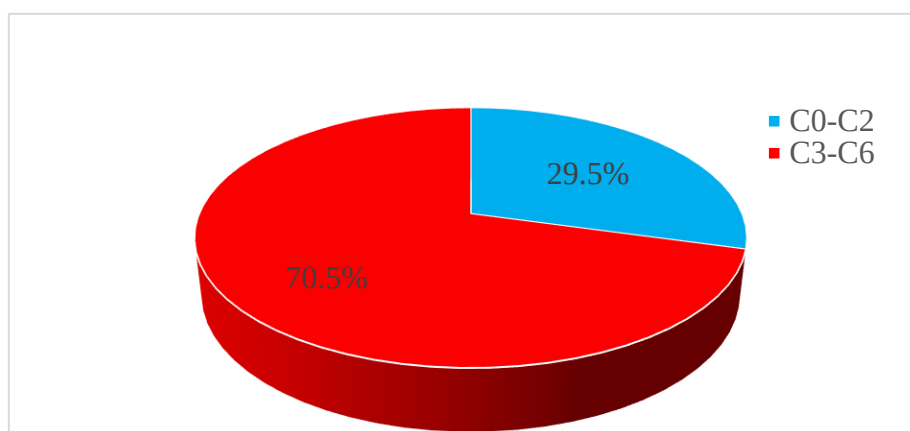


Figure 2. Grouping of cases with CVD according to severity of the disease.

In the second study, using clinical examinations, we diagnosed 88 (70.4%) patients among the 125 patients who were hospitalized for cardiovascular afflictions. 37 (29.6%) of the examined patients did not present, at the time of the evaluation, objective signs or subjective symptoms suggestive of venous impairment.

Analyzing the frequency of CVD among these patients, we ascertained that 78.2% of

the patients with hypertension also presented with CVD manifestations. 73.5% of the patients suffering from heart failure in the III and IV NYHA stages also had CVD, and the frequency of CVD among IHD was 70.5%. Frequently, hospitalized patients associated two or all three of the studied cardiovascular pathologies. A total of 88 patients were diagnosed with both CVDs and CVD. Most cardiovascular patients who also had CVD

were classified based on the CEAP clinical criteria into CEAP classes C3 and C4 (64.77%). A history of venous ulcers was

present in 4.54% of cases, but no patient had active venous ulcers at the time of examination (Figure 3).

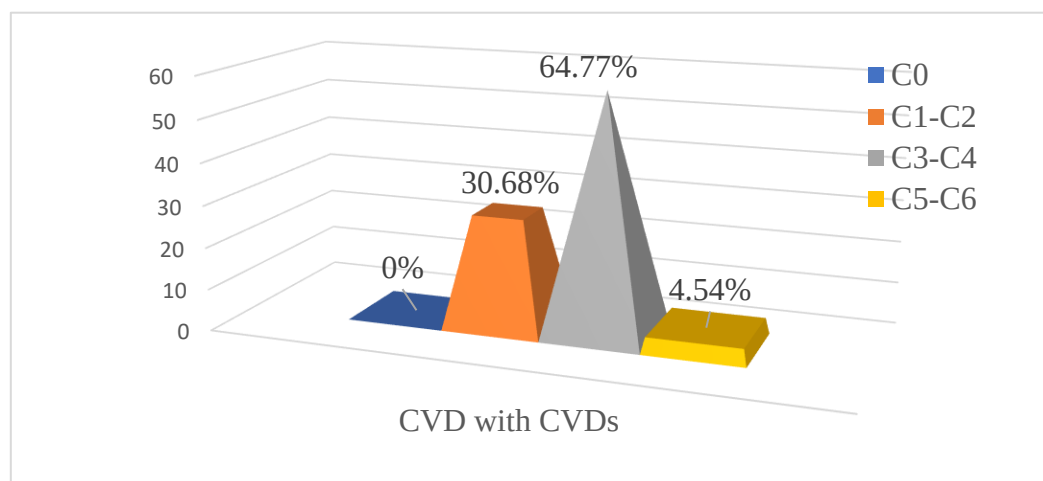


Figure 3. Frequency of CVD in patients with cardiovascular disease.

Comparing the results of the two studies, the prevalence of CVDs in patients with CVD of the lower limbs and the prevalence of CVD in patients with the same CVDs—we observed that the prevalence of CVD among patients with CVDs was significantly higher compared to the frequency of CVDs among patients with CVD:

- 31.2% of patients with CVD had hypertension, and 78.2% of hypertensive patients had CVD.
- 7.46% had heart failure, while 73.5% of heart failure patients also developed CVD.
- 11% had ischemic heart disease, and 70.5% of ischemic heart disease patients had CVD.

CVDs contributed to the onset of venous disease of the lower limbs after 6–15 years of progression.

Example 1: A 59-year-old woman with a healthy lifestyle and a maternal history of venous disease was diagnosed with heart failure and ischemic heart disease at the age of 52. She developed varicose veins at 54 and, by 59, belonged to CEAP class C3.

The progression of skin lesions associated

with the varicose complex was also slow in patients suffering from cardiovascular disease. In most cases, they appeared 10–15 years after the onset of cardiac diseases, progressing over long periods without the development of venous ulcers.

Example 2: A male patient from an urban environment, a smoker, who worked in conditions of prolonged static standing and physical exertion, with no family history of venous disease, developed varicose veins at the age of 45. At 50, he was diagnosed with NYHA class III heart failure and dilated cardiomyopathy. He is currently classified at the age of 78 in CEAP class C4. Trophic skin lesions appeared 17 years after the onset of cardiac disease.

DISCUSSIONS

The relationships observed in the two studies may also be due to the high average age of the population with CVDs, as well as the presence of other risk factors in the studied individuals: heredity, professional activity conditions, lifestyle, pregnancy in women, and obesity.

In the study, we encountered patients

without associated medical pathology who belonged to class C6 (active venous ulcer). They were aged between 35 and 50 years. In all cases, CVD developed secondary to deep vein thrombosis.

Many of the patients admitted to the Cardiology Department, with advanced-stage CVDs (NYHA class IV heart failure), showed minor signs of peripheral venous impairment (C1, C2, C3 CEAP). However, in all of these patients, CVD developed shortly after the worsening of their cardiovascular conditions.

These findings support the hypothesis that as CVD progresses (CEAP C3-C6), the likelihood of cardiovascular involvement increases. The stratified CEAP analysis demonstrated that patients in advanced stages of venous disease exhibited nearly double the prevalence of CVDs compared to those in early-stage CVD (C0-C2).[1,7-10]

Given the multitude of risk factors contributing to the onset and progression of CVD, and without access to a statistical model that allows for the exclusion of other risk factors, it is difficult to quantify the role of CVD in the development of CVDs.

The relationship between CVD and CVDs may stem from shared risk factors, including chronic inflammation, endothelial dysfunction, and hemodynamic disturbances. Advanced CVD stages (C3-C6) are characterized by systemic inflammation and venous stasis, which can exacerbate cardiovascular risk.[11-14]

CVD is characterized by venous hypertension, valvular incompetence, and chronic inflammation, which may contribute to systemic vascular dysfunction. The mechanisms by which CVD may predispose to cardiovascular disease are multifactorial and involve:

- Endothelial dysfunction: endothelial integrity plays a crucial role in both venous and arterial homeostasis. CVD is

associated with increased vascular endothelial growth factor (VEGF) expression, endothelial permeability, and leukocyte adhesion, all of which contribute to systemic endothelial dysfunction. Impairment of nitric oxide (NO) synthesis, a key vasodilatory molecule, has been observed in both CVD and arterial atherosclerosis. Defective NO pathways result in increased vascular resistance, impaired microcirculation, and greater susceptibility to hypertensive disorders.[7,11-13,15-18]

- Inflammation and oxidative stress: CVD is associated with low-grade systemic inflammation, as evidenced by elevated levels of C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- α). These inflammatory mediators are similarly implicated in atherogenesis and arterial thrombosis. Persistent inflammation leads to extracellular matrix remodeling, increased deposition of fibrotic material in vessel walls, and vascular rigidity, which are hallmarks of both chronic venous insufficiency (CVI) and CVDs.[7,17-22]
- Hypercoagulability and hemodynamic dysregulation: venous stasis in CVD creates a hypercoagulable state, increasing the risk of deep vein thrombosis (DVT). The presence of chronic thrombotic events has been associated with an elevated risk of myocardial infarction and ischemic stroke. Prolonged venous hypertension in advanced CVD (CEAP C4-C6) may contribute to reduced venous return and cardiac preload alterations, ultimately impacting left ventricular diastolic function.[23-25]

The current findings align with prior research that has examined the link between venous insufficiency and cardiovascular morbidity. By studying the specialized

literature, we found the desired information in the Gutenberg Health Study (Germany), one of the largest population health studies, conducted in Germany over 10 years. It included 15,000 individuals aged 35–74, randomly selected from the population registry in the Mainz region. The study aimed to analyze risk factors, medical pathology within the target population, and existing correlations. The Gutenberg Health Study demonstrated that individuals with CVD had a 46% increased risk of developing cardiovascular disease, independent of traditional risk factors such as age, smoking, and diabetes.[26-28]

The Edinburgh Vein Study (UK) highlighted that individuals with symptomatic varicose veins were significantly more likely to develop arterial hypertension and metabolic syndrome, emphasizing the systemic nature of vascular pathologies.[25,29,30]

A study conducted in France reported that among patients with CEAP C4-C6 disease, 80% had concomitant arterial abnormalities, further supporting the hypothesis that severe venous disease is a marker of systemic cardiovascular pathology.[6,31-33]

Calculating the prevalence of CVDs within the evaluated population, the authors of the study noted that it was higher among individuals with CVD, increasing significantly as the evolutionary stage of venous disease progressed.

Using a multivariate regression statistical model, adjusted for age, sex, and cardiovascular risk factors, they observed that the risk of cardiovascular disease association was 46% higher in individuals with CVD compared to those without, increasing with the CEAP evolutionary stage, from 33% in class C2 to 40% in class C3.

The incidence of CVDs increases proportionally with the CEAP evolutionary stage, thus demonstrating that CVD is an

independent risk factor for CVDs.

In the context of the information presented, given that CVD is the most prevalent condition in the world (83.6%), neglected by $\frac{3}{4}$ of patients, and that by 2030, 23 million deaths worldwide are estimated to be caused by CVDs (which are the leading cause of death in our country), as it is an independent predictor for all-cause mortality, and because it is easy to diagnose – just by "looking" at the legs of our patients – we emphasize the importance of diagnosing and treating the disease in its early stages.[26,34-39]

Given the high prevalence of both conditions and their shared risk factors, early diagnosis and integrated management of CVD could play a critical role in preventing cardiovascular complications.

The interplay between CVD and CVDs has been a subject of increasing interest due to their shared pathophysiological mechanisms, overlapping risk factors, and high prevalence within the aging population. Traditionally, CVD has been regarded as a localized venous pathology, yet mounting evidence suggests it may be a component of a broader vascular dysfunction that predisposes individuals to cardiovascular morbidity. This study sought to elucidate the potential role of CVD as an independent risk factor for CVDs, by examining its prevalence among patients diagnosed with cardiovascular conditions, as well as the reciprocal relationship in those initially diagnosed with CVD.

The clinical significance of the association between CVD and CVDs underscores the need for an integrated vascular approach, which involves:

- Early screening and risk assessment: given the significant overlap in patient populations, routine cardiovascular risk assessment should be incorporated into the management of CVD. This may include

blood pressure monitoring, lipid profiling, and echocardiographic evaluations in patients with advanced venous disease. Similarly, patients diagnosed with CVDs should be screened for signs of venous insufficiency, especially those with sedentary lifestyles, prolonged standing, or a history of venous thrombosis.

- Targeted therapeutic strategies: the presence of both CVD and cardiovascular disease warrants optimized medical management, including: antiplatelet therapy for patients with both atherosclerosis and chronic venous insufficiency, venous compression therapy in patients with heart failure to reduce venous pooling and improve lower limb circulation, anti-inflammatory and antioxidant interventions, such as flavonoid-based treatments (e.g., diosmin, hesperidin), which have been shown to have beneficial effects on both venous tone and arterial endothelial function.
- Lifestyle modifications and patient education: addressing modifiable risk factors (obesity, smoking, sedentary behavior) is critical in preventing disease progression in both venous and cardiovascular disorders. Exercise regimens focusing on calf muscle strengthening and mobility improvements can enhance venous return and reduce cardiovascular risk.

While this study provides valuable insights into the relationship between CVD and CVDs, several limitations should be acknowledged:

- Cross-sectional design: the study

establishes associations but does not confirm causality. Longitudinal cohort studies are needed to determine whether CVD independently predicts cardiovascular events over time.

- Potential confounders: while adjustments were made for major cardiovascular risk factors, additional variables such as genetic predisposition, inflammatory biomarkers, and endothelial function tests could further clarify underlying mechanisms.
- Diversity of study population: larger, multi-center studies with diverse ethnic and demographic cohorts are needed to validate findings and assess generalizability.

Future research should focus on exploring mechanistic pathways, particularly the role of chronic systemic inflammation, venous hypertension, and endothelial dysfunction in cardiovascular morbidity. Developing predictive models that integrate the CEAP classification and cardiovascular risk scores is essential for identifying high-risk patients, enabling early intervention and personalized management strategies. Longitudinal studies are essential to establish causal relationships between CVD and CVDs, providing deeper insights into their pathophysiological connections and potential shared risk factors. Assessing the impact of therapeutic interventions, including pharmacological treatments that simultaneously target venous and arterial dysfunction, is crucial for optimizing patient outcomes and developing integrated management strategies for coexisting vascular disorders.

CONCLUSIONS

CVD is not merely a localized venous condition but a systemic disorder with implications for cardiovascular health. Our findings highlight the need for heightened

clinical vigilance and multidisciplinary approaches to manage patients with coexisting CVD and CVDs. This study highlights the strong association between CVD and CVDs, emphasizing shared pathophysiological

mechanisms such as systemic inflammation, endothelial dysfunction, and hemodynamic alterations. CVD should no longer be viewed in isolation but rather as a potentially modifiable contributor to cardiovascular risk.

Given the high comorbidity rates, early screening, multidisciplinary management, and targeted vascular therapies may lead to improved patient outcomes and reducing cardiovascular risk.

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Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of “Anton Cincu” Hospital in Tecuci.

Informed Consent Statement

Written informed consent for participation in the study and for publication of this paper was obtained from the patients.

Data Availability Statement

The data presented in this study are available on reasonable request from the corresponding authors.

Conflicts of Interest

The authors declare no conflict of interest.

Author's contribution

The authors GS, IDF, SST, MAB, and FCFM had an equal scientific contribution to this research as NM, the first author.

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