



International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	IMPACT OF PHYSICAL ACTIVITY ON SYMPTOM SEVERITY AND QUALITY OF LIFE IN CHRONIC VENOUS DISEASE: A SYSTEMATIC REVIEW
----------------------	--

DOI	https://doi.org/10.31435/ijitss.1(49).2026.4924
------------	---

RECEIVED	18 November 2025
-----------------	------------------

ACCEPTED	25 January 2026
-----------------	-----------------

PUBLISHED	11 February 2026
------------------	------------------

LICENSE



The article is licensed under a **Creative Commons Attribution 4.0 International License**.

© The author(s) 2026.

This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

IMPACT OF PHYSICAL ACTIVITY ON SYMPTOM SEVERITY AND QUALITY OF LIFE IN CHRONIC VENOUS DISEASE: A SYSTEMATIC REVIEW

Paweł Grzesikowski [PG] (Corresponding Author, Email: pawelgrzesikowski@op.pl)
Non-Public Healthcare Institution Łużyckie Medical Center, Lubąń, Poland
ORCID ID: 0009-0006-4312-1664

Jakub Kubiak [JK]
Józef Struś Multispecialist Municipal Hospital, Poznań, Poland
ORCID ID: 0009-0006-3776-7901

Paulina Klich [PK]
Józef Struś Multispecialist Municipal Hospital, Poznań, Poland
ORCID ID: 0009-0005-4871-2351

Kinga Bekier [KB]
Józef Struś Multispecialist Municipal Hospital, Poznań, Poland
ORCID ID: 0009-0007-0320-3291

Hanna Nowicka [HN]
Hipolit Cegielski Medical Center, Poznań, Poland
ORCID ID: 0009-0001-3676-1894

ABSTRACT

Objectives: Chronic venous disease is a common and progressive condition that affects the veins of the lower limbs and significantly reduces quality of life. It often leads to symptoms such as leg pain, edema, fatigue, and in advanced stages, skin changes and venous ulcers. This narrative review explores current research on the impact of physical activity on symptom severity and quality of life in patients with chronic venous disease.

Methods: A literature search was conducted using PubMed and Google Scholar, focusing on studies published up to the year 2025, with particular emphasis on studies from 2015 to 2025. The following keywords were used: Chronic venous disease, chronic venous insufficiency, physical activity, symptom severity, quality of life.

Conclusions: Results consistently show that physical activity is associated with reduced pain, edema, and fatigue, as well as improved physical functionality. Furthermore, physical activity was also shown to improve quality of life. Despite the positive impact of physical activity, many patients do not meet physical activity guidelines. Physical activity is an effective and low-cost approach to improving both symptom severity and quality of life in patients with chronic venous disease; however, clinical guidelines should aim to improve long-term adherence.

KEYWORDS

Chronic Venous Disease, Chronic Venous Insufficiency, Physical Activity, Symptom Severity, Quality of Life

CITATION

Paweł Grzesikowski, Jakub Kubiak, Paulina Klich, Kinga Bekier, Hanna Nowicka. (2026) Impact of Physical Activity on Symptom Severity and Quality of Life in Chronic Venous Disease: a Systematic Review. *International Journal of Innovative Technologies in Social Science*. 1(49). doi: 10.31435/ijitss.1(49).2026.4924

COPYRIGHT

© The author(s) 2026. This article is published as open access under the **Creative Commons Attribution 4.0 International License (CC BY 4.0)**, allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

Introduction:

Chronic venous disease (CVD) is a common and progressive condition of the circulatory system, which is often left undiagnosed in the early stages. If left neglected and untreated, it can lead to the development of chronic venous insufficiency (CVI) and venous ulcers. This disease significantly reduces the quality of life (QoL) of patients and is a serious therapeutic, aesthetic, and socio-economic problem. The initial symptoms of CVD are pain, edema, and fatigue in the lower extremities, which usually worsen at the end of the day. As the disease progresses, chronic edema and tropic skin changes develop, resulting in skin stiffening, hyperpigmentation, and atrophy (Nicolaides & Labropoulos, 2019).

It is worth distinguishing two basic terms: CVD is a general term that includes various morphological and functional abnormalities of the venous system, while CVI refers to more advanced stages of CVD and is associated with symptoms such as chronic edema, skin changes, and venous ulcers. According to the Clinical, Etiological, Anatomical, and Pathophysiological (CEAP) classification, CVI corresponds to categories C3-C6 (Eklof et al., 2009). The CEAP classification is an international standard for clinical assessment of CVD, based on symptoms, etiology, anatomy, and pathophysiology (Lurie et al., 2020).

A German observational study conducted by Kirsten et al. (2021) on a cohort of 19,104 employees estimated the prevalence of CVD at 21.1% and CVI at 4.3%. Nevertheless, prevalence data could have been underestimated due to the exclusion of individuals above the age of 70. Additionally, this study confirmed that the prevalence of CVD and CVI is higher in women than in men (Kirsten et al., 2021). Estimated data on the prevalence of CVI in the general population is difficult to specify. Discrepancies often arise from study methodology and/or population composition. Current data suggests that CVI prevalence ranges from 1% to 17% in men and 1% to 40% in women and is higher in more developed and highly industrialized countries (Beebe-Dimmer et al., 2005).

CVD is one of the most common diseases of the circulatory system and represents a significant problem in the daily life of patients. Considering the risk factors of CVD, such as excessive body mass, low physical activity (PA), and a sedentary lifestyle, it can be assumed that introducing PA regimens may improve therapeutic outcomes. This review aims to analyze current literature on the influence of PA on symptom severity and QoL in patients with CVD.

Methodology:**Study Design:**

This narrative review focuses on providing an overview of the current knowledge on the effects of PA on symptom severity and QoL in CVD. A comprehensive literature search was conducted using PubMed and Google Scholar, considering publications up to 2025, with particular focus on studies published between 2015 and 2025. Earlier studies were included when recent data were limited or unavailable. The search strategy utilized Boolean combinations of the following terms: ('chronic venous disease' OR 'CVD' OR "chronic venous insufficiency" OR 'CVI') AND/OR ('physical activity' OR 'physical exercise') AND/OR ('symptom severity' OR 'diseases activity') AND/OR ('quality of life' OR 'QoL'). The inclusion criteria included peer-reviewed original research articles, narrative reviews, systematic reviews, and meta-analyses that investigated the impact of PA on symptom severity and QoL in CVD. Exclusion criteria included studies focusing solely on surgical, pharmacological, or compression therapies without assessing PA, as well as case reports, conference abstracts, and non-peer reviewed material. Furthermore, the reference lists of eligible studies were manually reviewed to identify other relevant studies.

Risk of bias:

This narrative review lacks formal standardized review protocols and quality assessment frameworks present in systematic reviews. Inclusion criteria were based on the judgment of the authors, rather than standardized methodological criteria, introducing a potential risk of selection bias. Efforts were made to achieve comprehensive literature coverage through Boolean search strategies in PubMed and Google Scholar; however, a lack of diversity among databases could have resulted in the omission of other relevant studies. Furthermore, studies showing a positive impact of PA on symptom severity and QoL in CVD may have a higher likelihood of publication, introducing a risk of publication bias. Many of the included studies relied on self-reported data of PA levels and associated health outcomes, which may be subject to recall and social desirability bias. Additionally, although this review prioritized literature published between 2015 and 2025 to reflect the current state of knowledge, this could have resulted in relevant older studies being underrepresented. Lastly, interpretive bias may have been introduced by subjective data analysis and a focus on certain findings. The authors strived to present a balanced and comprehensive overview of the current state of knowledge; however, the conclusion should be interpreted with caution and viewed primarily as a foundation for further investigation, rather than conclusive clinical guidance.

Anatomy of the lower limb venous system:

Anatomically, the venous system of the lower limbs is divided into deep and superficial veins, which are interconnected by perforators. The superficial veins drain approximately 10% of the venous blood from the lower limbs. Their primary components are the great saphenous vein and the small saphenous vein. In contrast, the deep veins account for approximately 90% of the venous return from the lower limbs and are characterized by high capacity and low pressure. They include the anterior and posterior tibial veins, the peroneal vein, the soleal vein, and the gastrocnemius vein (Youn & Lee, 2019). Histologically, the vein wall is composed of three layers: the tunica intima, tunica media, and tunica adventitia. A distinguishing feature of veins is the presence of valves, which ensure unidirectional blood flow (Kienzl et al., 2024).

Risk factors and pathophysiology:

Many risk factors contribute to the development and progression of CVD. Modifiable risk factors include obesity, smoking, physical inactivity, and occupations involving prolonged standing or sitting. These can be addressed through lifestyle changes and modifications to the external environment. In contrast, non-modifiable risk factors include a family history of CVD or varicose veins (VV), genetic predisposition, older age, and female sex (Labropoulos, 2019; Krizanova et al., 2023).

Circulation in the venous system of the lower limbs presents unique challenges because, unlike arterial circulation, it must overcome the force of gravity. Unidirectional blood flow is maintained by the calf muscle pump in conjunction with competent venous valves. The pathophysiology of CVD involves complex mechanisms, with venous obstruction and reflux being two primary contributors (Ortega et al., 2021). Elevated venous pressure and vein dilation lead to a reduction in fluid shear stress (FSS) on endothelial cells (EC). These cells sense changes in FSS and respond by regulating venous tone (Baeyens et al., 2016).

The endothelial glycocalyx also plays a critical role in regulating vascular tone. It is a protective layer covering the luminal surface of ECs and is composed of glycoproteins, proteoglycans (PG), and glycosaminoglycans (GAG). The glycocalyx functions as a mechanotransducer, converting mechanical signals from turbulent blood flow into intracellular biochemical signals. In addition, it plays a key role in anticoagulation and anti-inflammatory processes. It serves as a selective permeability barrier for macromolecules and prevents the adhesion of platelets and leukocytes. In the context of CVD, damage to the glycocalyx disrupts vascular tone regulation and facilitates the adhesion and transmigration of leukocytes, thereby promoting inflammation (Kienzl et al., 2024; Tarbell & Pahakis, 2006; Tarbell & Cancel, 2016).

During the early phases, the inflammatory activation of ECs increases vascular permeability. This increased permeability, combined with venous stasis, promotes the extravasation of red blood cells, which are subsequently degraded by interstitial macrophages. The excess iron released is stored as hemosiderin, a pigment responsible for the characteristic hyperpigmentation of the lower limbs in patients with CVD. Furthermore, elevated levels of fibrin and hemosiderin further activate macrophages and mast cells, which amplify the inflammatory response and stimulate EC activation (Labropoulos, 2019; Ferris & Harding, 2019). Once activated, ECs exhibit increased expression of adhesion molecules such as selectins, intercellular adhesion molecule 1 (ICAM-1), and vascular cell adhesion molecule 1 (VCAM-1). These molecules facilitate the adhesion of inflammatory cells, including neutrophils, lymphocytes, macrophages, and monocytes, and promote the recruitment of cytokines and matrix metalloproteinases (MMPs). Adhesion molecules and inflammatory cytokines, particularly Transforming Growth Factor Beta (TGF- β), Interleukin 6 (IL-6), Interleukin 8 (IL-8), and VCAM-1 are thought to contribute to the development of venous valve insufficiency (Sprague & Khalil, 2009).

MMPs also play a key role in venous wall remodelling. They are proteolytic enzymes that are involved in the continuous turnover of collagen and elastin in the extracellular matrix (ECM) (Kucukguven & Khalil, 2013). In the early stages of CVD, increased activity and variable expression of several MMP subtypes have been observed (Serralheiro et al., 2017). The consequence of this is the accumulation of collagen fibers and the degradation of elastin in the ECM, leading to increased thickness and stiffness of the venous walls (Dorland & Huveneers, 2017).

A self-sustaining cycle appears to develop, characterized by venous hypertension, vein wall dilation, valve insufficiency, and the subsequent onset of venous stasis. This promotes inflammation, venous wall remodeling, and increased vascular permeability, which leads to further morphological changes. If left untreated, CVD may progress to CVI, leading to chronic pain, edema, and trophic skin changes, and in severe cases, the formation of venous ulcers, which can serve as entry points for infection.

Impact of physical activity on symptom severity in chronic venous disease:

CVD is characterized by venous reflux, increased pressure, and impaired venous return, which manifests in pain, fatigue, leg heaviness, reduced mobility, skin changes, and venous ulcers. PA has been shown to improve venous return, calf muscle pump function, endurance, functional sympatholysis, and microvascular endothelial function, thereby reducing CVD-associated symptoms (Labropoulos et al., 1996; van Uden et al., 2005; Mortensen et al., 2012; Klonizakis et al., 2009).

The results of a study by Keser et al. (2020) suggest that moderate-intensity PA can help to reduce the severity of CVD-associated symptoms, such as pain and fatigue. Furthermore, they highlighted that moderate-intensity PA should be considered optimal. Low-intensity PA showed smaller improvements in symptom severity, while vigorous-intensity PA did not show significantly better improvements compared to moderate-intensity PA, proving it an unnecessary strain on the musculoskeletal system (Keser et al., 2020). Similarly, Aydin et al. (2024) conducted a study involving 105 patients diagnosed with CVI and reported that patients with higher self-reported PA levels reported lower disease severity and pain intensity (Aydin et al., 2024). Espeit et al. (2022) also reported an inverse relationship between PA and fatigue in self-reported CVD symptoms (Espeit et al., 2022). These studies collectively highlight a consistent trend in which patients with greater PA involvement tend to report lower levels of pain and fatigue, indicating a positive effect of PA on symptom severity in CVD patients.

Complementing these findings is a 24-month-long randomized controlled study by Sharifi et al. (2021), which analyzed the impact of aquatic PA on CVI clinical status. Out of 91 patients in the aquatic PA group and 90 patients in the control group, 28% and 3% reached the primary endpoint of a 4-point reduction in the modified Venous Clinical Severity Score (VCSS) after 3 months, respectively. This study shows that supervised aquatic PA led to a notable decrease in CVI symptom severity. Furthermore, patients reported better limb functionality and emotional well-being (Sharifi et al., 2021). A different study by Aydin et al. (2024) supports the findings of higher PA levels leading to increased physical functionality, suggesting that the benefits of PA extend beyond symptom control and include broader improvements in physical performance (Aydin et al., 2024). This relationship may be bilateral, in which higher PA levels lead to symptom reduction, which in turn facilitates the ability to sustain higher loads of PA.

Despite these positive associations, a study by Domingues et al. (2025) points to challenges in the adherence of specific patient groups to PA requirements. They showed that only 36.2% of patients with CVI achieved recommended PA levels, with older age being a significant barrier to achieving PA recommendations. The low adherence rates highlight a practical limitation in leveraging PA as a consistent symptom management tool in clinical practice (Domingues et al., 2025).

In conclusion, current evidence indicates that higher levels of PA are consistently associated with lower pain and fatigue levels, as well as improved functional capacity. This data underscores the crucial role of PA in reducing symptom severity in CVD patients.

Impact of physical activity on quality of life in chronic venous disease:

CVD negatively impacts QoL across multiple dimensions, even in the early stages. A study by Branisteanu et al. (2019) showed that symptoms associated with CVD have a “mild” or “moderate” impact on QoL, and were shown to negatively impact physical, psychological, and social functioning, as well as pain components of the Chronic Venous Disease Quality of Life Questionnaire (CIVIQ-20). The degree to which patients were affected was positively correlated with CVD CEAP severity classification. Physical symptoms such as leg pain, edema, fatigue, skin changes, and occasional bleeding impair mobility and limit daily activity (Branisteanu et al., 2019). These restrictions contribute to an elevated emotional burden and social withdrawal. Additionally, anxiety and depressive symptoms may develop in response to aesthetic and functional decline. A different study by Santiago et al. (2022) compared patient and physician perceptions about the impact of CVD on QoL. This multi-country qualitative study involving 100 patients and 60 physicians revealed a disparity of perceptions. Physicians acknowledged the physical impact of CVD but frequently underestimated the psychosocial and aesthetic toll on patients. Patients reported that CVD disrupted relationships, social interactions, and self-esteem. The study emphasized that comprehensive care must extend beyond symptom control and should incorporate emotional, social, and aesthetic concerns (Santiago et al., 2022).

PA encompassing interventions such as structured exercise, muscle training, and daily functional movement play a vital role in improving QoL in patients suffering from CVD. Evidence from a randomized controlled trial by Karakelle et al. (2021) demonstrated that a structured exercise program, alongside compression therapy, significantly improved key clinical outcomes in CVI patients, compared to the control group. Out of all clinical aspects, including CIVID-20, duplex Doppler ultrasonography, VCSS, visual analog

scale (VAS), circumference measurements, 6-minute walking test, and 10-meter walking test, only hemodynamic status and edema did not show significant improvements compared to the control group. Participants showed meaningful improvements in calf muscle pump function, venous refill times, and clinical severity scores. More importantly, these objective gains translated into enhanced physical functioning and improved reported QoL, underscoring PA benefits in CVD management (Gürdal Karakelle et al., 2021).

Calf muscle and inspiratory muscle training have also been independently tested. A randomized trial conducted by Aydin et al. (2022) compared inspiratory versus calf muscle training and found that both training programs, when paired with compression therapy, improved QoL in all CIVIQ-20 parameters. Calf muscle training paired with compression therapy demonstrated greater improvements in QoL, venous refill times, pain, edema, range of motion, muscle strength, and functionality. On the other hand, inspiratory muscle training paired with compression therapy demonstrated greater improvements in disease severity, as well as inspiratory and expiratory muscle strength. This shows that both calf muscle and inspiratory muscle training can positively impact QoL in CVD patients (Aydin et al., 2022).

The relationship between habitual PA and QoL in people self-reporting CVD symptoms was explored in an observational study by Espeit et al. (2022). Participants who have self-reported CVD symptoms had impaired QoL; however, in this population, higher levels of self-reported PA were associated with a tendency towards improved QoL. This suggests that regular daily movement, even at non-structured levels, can improve QoL in CVD patients (Espeit et al., 2022). These findings align with an earlier study by Keser et al. (2020), which reported that patients who engaged in PA experienced improved QoL. Notably, the study found no significant difference in QoL outcomes between patients reporting moderate-intensity and vigorous-intensity PA. This suggests that moderate-intensity PA may be optimal for improving QoL in individuals with CVD, as vigorous exercise could pose an unnecessary strain on the skeletomuscular system (Keser et al. 2020).

A cross-sectional study by Kiloatar et al. (2021) confirms that even in the early stages of CVD, patients typically maintain low levels of PA, regardless of symptom severity (Kiloatar et al., 2021). Similarly, a study conducted by Erdal et al. (2021) also stated that patients with CVI presented with lower exercise capacity and PA levels. This suggests that early encouragement of PA may be crucial to maintaining physical function and preventing QoL decline (Erdal et al., 2021). This need for early encouragement is confirmed by a study conducted by Özberk et al (2018), in which the QoL of patients suffering from CVD decreased when PA and functional capacity were low (Ozberk et al., 2018). These findings support interventions that target increased PA in patients with CVD.

This data underpins the importance of structured or unstructured PA on the improvement of QoL in CVD. Moderate levels of daily PA, especially in the early stages of the disease, may be particularly impactful. The benefits are multifaceted, including better physical functioning, psychological well-being, and social participation, which contribute to an increased QoL.

Conclusion:

Current evidence consistently suggests that PA can reduce symptom severity and improve QoL in patients with CVD. Notably, non-structured habitual PA also appears to be beneficial. Despite these findings, many patients do not meet PA recommendations, with barriers such as age, reduced mobility, and a lack of awareness contributing to low adherence rates. Clinical guidelines should consider early and sustainable PA interventions. Currently, there is a lack of studies that do not rely on self-reported PA levels and that are not cross-sectional in nature. Future research should prioritize long-term intervention studies and strategies aimed at improving PA adherence, especially in older patients.

Author's contribution:

Conceptualization: JK, PK

Methodology: PG, KB

Software: PK, JK

Check: JK, PK, KB, PG, HN

Formal analysis: PG, HN

Investigation: JK, KB

Resources: PK, PG

Data curation: KB, HN

Writing - rough preparation: JK, PG

Writing - review and editing: PK, HN

Visualization: KB, PG

Supervision: JK, HN

Project administration: PK, KB

All authors have read and agreed with the published version of the manuscript.

Funding Statement: The study did not receive special funding.

Conflict of Interest: The authors declare no conflicts of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process.

In preparing this work, the authors used ChatGPT and Grammarly as applications to improve language and readability. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

REFERENCES

1. Nicolaides, A. N., & Labropoulos, N. (2019). Burden and Suffering in Chronic Venous Disease. *Advances in therapy*, 36(Suppl 1), 1–4. <https://doi.org/10.1007/s12325-019-0882-6>.
2. Eklof, B., Perrin, M., Delis, K. T., Rutherford, R. B., Gloviczki, P., American Venous Forum, European Venous Forum, International Union of Phlebology, American College of Phlebology, & International Union of Angiology (2009). Updated terminology of chronic venous disorders: the VEIN-TERM transatlantic interdisciplinary consensus document. *Journal of vascular surgery*, 49(2), 498–501. <https://doi.org/10.1016/j.jvs.2008.09.014>.
3. Lurie, F., Passman, M., Meisner, M., Dalsing, M., Masuda, E., Welch, H., Bush, R. L., Blebea, J., Carpentier, P. H., De Maeseneer, M., Gasparis, A., Labropoulos, N., Marston, W. A., Raffetto, J., Santiago, F., Shortell, C., Uhl, J. F., Urbanek, T., van Rij, A., Eklof, B., ... Wakefield, T. (2020). The 2020 update of the CEAP classification system and reporting standards. *Journal of vascular surgery. Venous and lymphatic disorders*, 8(3), 342–352. <https://doi.org/10.1016/j.jvsv.2019.12.075>.
4. Kirsten, N., Mohr, N., Gensel, F., Alhumam, A., Bruning, G., & Augustin, M. (2021). Population-Based Epidemiologic Study in Venous Diseases in Germany - Prevalence, Comorbidity, and Medical Needs in a Cohort of 19,104 Workers. *Vascular health and risk management*, 17, 679–687. <https://doi.org/10.2147/vhrm.s323084>.
5. Beebe-Dimmer, J. L., Pfeifer, J. R., Engle, J. S., & Schottenfeld, D. (2005). The epidemiology of chronic venous insufficiency and varicose veins. *Annals of epidemiology*, 15(3), 175–184. <https://doi.org/10.1016/j.annepidem.2004.05.015>.
6. Youn, Y. J., & Lee, J. (2019). Chronic venous insufficiency and varicose veins of the lower extremities. *The Korean journal of internal medicine*, 34(2), 269–283. <https://doi.org/10.3904/kjim.2018.230>.
7. Kienzl, P., Deinsberger, J., & Weber, B. (2024). Chronic Venous Disease: Pathophysiological Aspects, Risk Factors, and Diagnosis. *Hamostaseologie*, 44(4), 277–286. <https://doi.org/10.1055/a-2315-6206>.
8. Labropoulos N. (2019). How Does Chronic Venous Disease Progress from the First Symptoms to the Advanced Stages? A Review. *Advances in therapy*, 36(Suppl 1), 13–19. <https://doi.org/10.1007/s12325-019-0885-3>.
9. Krizanov, O., Penesova, A., Hokynkova, A., Pokorna, A., Samadian, A., & Babula, P. (2023). Chronic venous insufficiency and venous leg ulcers: Aetiology, on the pathophysiology-based treatment. *International wound journal*, 21(2), e14405. Advance online publication. <https://doi.org/10.1111/iwj.14405>.
10. Ortega, M. A., Fraile-Martínez, O., García-Montero, C., Álvarez-Mon, M. A., Chaowen, C., Ruiz-Grande, F., Pekarek, L., Monserrat, J., Asúnsolo, A., García-Honduvilla, N., Álvarez-Mon, M., & Bujan, J. (2021). Understanding Chronic Venous Disease: A Critical Overview of Its Pathophysiology and Medical Management. *Journal of clinical medicine*, 10(15), 3239. <https://doi.org/10.3390/jcm10153239>.

11. Baeyens, N., Bandyopadhyay, C., Coon, B. G., Yun, S., & Schwartz, M. A. (2016). Endothelial fluid shear stress sensing in vascular health and disease. *The Journal of clinical investigation*, 126(3), 821–828. <https://doi.org/10.1172/jci83083>.
12. Tarbell, J. M., & Pahalakis, M. Y. (2006). Mechanotransduction and the glycocalyx. *Journal of internal medicine*, 259(4), 339–350. <https://doi.org/10.1111/j.1365-2796.2006.01620.x>.
13. Tarbell, J. M., & Cancell, L. M. (2016). The glycocalyx and its significance in human medicine. *Journal of internal medicine*, 280(1), 97–113. <https://doi.org/10.1111/joim.12465>.
14. Ferris, A. E., & Harding, K. G. (2019). An overview of the relationship between anaemia, iron, and venous leg ulcers. *International wound journal*, 16(6), 1323–1329. <https://doi.org/10.1111/iwj.13192>.
15. Sprague, A. H., & Khalil, R. A. (2009). Inflammatory cytokines in vascular dysfunction and vascular disease. *Biochemical pharmacology*, 78(6), 539–552. <https://doi.org/10.1016/j.bcp.2009.04.029>.
16. Kucukguven, A., & Khalil, R. A. (2013). Matrix metalloproteinases as potential targets in the venous dilation associated with varicose veins. *Current drug targets*, 14(3), 287–324. <https://doi.org/10.2174/138945013804998972>.
17. Serralheiro, P., Novais, A., Cairão, E., Maia, C., Costa Almeida, C. M., & Verde, I. (2017). Variability of MMP/TIMP and TGF- β 1 Receptors throughout the Clinical Progression of Chronic Venous Disease. *International journal of molecular sciences*, 19(1), 6. <https://doi.org/10.3390/ijms19010006>.
18. Dorland, Y. L., & Huveneers, S. (2017). Cell-cell junctional mechanotransduction in endothelial remodeling. *Cellular and molecular life sciences : CMLS*, 74(2), 279–292. <https://doi.org/10.1007/s00018-016-2325-8>.
19. Labropoulos, N., Giannoukas, A. D., Nicolaidis, A. N., Veller, M., Leon, M., & Volteas, N. (1996). The role of venous reflux and calf muscle pump function in nonthrombotic chronic venous insufficiency. Correlation with severity of signs and symptoms. *Archives of surgery (Chicago, Ill. : 1960)*, 131(4), 403–406. <https://doi.org/10.1001/archsurg.1996.01430160061011>.
20. van Uden, C. J., van der Vleuten, C. J., Kooloos, J. G., Haenen, J. H., & Wollersheim, H. (2005). Gait and calf muscle endurance in patients with chronic venous insufficiency. *Clinical rehabilitation*, 19(3), 339–344. <https://doi.org/10.1191/0269215505cr809oa>.
21. Mortensen, S. P., Mørkeberg, J., Thaning, P., Hellsten, Y., & Saltin, B. (2012). Two weeks of muscle immobilization impairs functional sympatholysis but increases exercise hyperemia and the vasodilatory responsiveness to infused ATP. *American journal of physiology. Heart and circulatory physiology*, 302(10), H2074–H2082. <https://doi.org/10.1152/ajpheart.01204.2011>.
22. Klonizakis, M., Tew, G., Michaels, J., & Saxton, J. (2009). Exercise training improves cutaneous microvascular endothelial function in post-surgical varicose vein patients. *Microvascular research*, 78(1), 67–70. <https://doi.org/10.1016/j.mvr.2009.03.002>.
23. Keser, İ., Özdemir, K., Erer, D., Onurlu, İ., & Bezgin, S. (2020). Differences in pain, fatigue, and quality of life in patients with chronic venous insufficiency based on physical activity level. *Türk gogus kalp damar cerrahisi dergisi*, 28(1), 76–83. <https://doi.org/10.5606/tgkdc.dergisi.2020.18068>.
24. Aydın, G., Aloğlu Çiftçi, E., Atıcı, E., Akgöl, A. C., & Tuncer, M. A. (2024). *Physical activity in patients with chronic venous insufficiency: Its relation with disease severity, pain, fatigue, and functionality*. *Türk Fizyoterapi ve Rehabilitasyon Dergisi*, 35(3), 382–388. <https://doi.org/10.21653/tjpr.1521503>.
25. Espeit, L., Rimaud, D., Le Mat, F., Cudel, C., Micol, I., Bertoletti, L., Chaigneau, C., Millet, G. Y., & Lapole, T. (2022). Fatigue, physical activity, and quality of life in people self-reporting symptoms of chronic venous disease. *Journal of vascular surgery. Venous and lymphatic disorders*, 10(5), 1147–1154.e1. <https://doi.org/10.1016/j.jvsv.2022.04.016>.
26. Sharifi, M., Bay, R. C., Karandish, K., Emrani, F., Snyder, R., D'Silva, S., & ATLANTIS Trial (2021). The randomized, controlled ATLANTIS trial of aquatic therapy for chronic venous insufficiency. *Journal of vascular surgery. Venous and lymphatic disorders*, 9(4), 961–970. <https://doi.org/10.1016/j.jvsv.2020.10.016>.
27. Domingues, W. J. R., Germano-Soares, A. H., Cucato, G. G., de Souza, L. C., Brandão, E. K. S. S., Souza, E. L. D. C., da Silva E Silva, T. R., Arêas, G. P. T., Costa, C., Campelo, P. R. D. S., Dos Santos, N. J. N., Silva, G. O. D., & Simões, C. F. (2025). Physical activity levels in patients with chronic venous insufficiency. *Phlebology*, 40(1), 47–54. <https://doi.org/10.1177/02683555241273153>.
28. Branisteanu, D. E., Feodor, T., Baila, S., Mitea, I. A., & Vittos, O. (2019). Impact of chronic venous disease on quality of life: Results of vein alarm study. *Experimental and therapeutic medicine*, 17(2), 1091–1096. <https://doi.org/10.3892/etm.2018.7054>.
29. Santiago, F. R., Ulloa, J., Régner, C., Peudon, T., Braund, E., Fradet-Aubignat, C., & Giancesini, S. (2022). The impact of lower limb chronic venous disease on quality of life: patient and physician perspectives. *Journal of comparative effectiveness research*, 11(11), 789–803. <https://doi.org/10.2217/ce-2022-0054>.
30. Gürdal Karakelle, S., Ipek, Y., Tulin, O., & Alpagut, İ. U. (2021). The efficiency of exercise training in patients with venous insufficiency: A double blinded, randomized controlled trial. *Phlebology*, 36(6), 440–449. <https://doi.org/10.1177/0268355520985759>.

31. Aydin, G., Yeldan, I., Akgul, A., & Ipek, G. (2022). Effects of inspiratory muscle training versus calf muscle training on quality of life, pain, venous function and activity in patients with chronic venous insufficiency. *Journal of vascular surgery. Venous and lymphatic disorders*, 10(5), 1137–1146. <https://doi.org/10.1016/j.jvsv.2022.04.012>.
32. Kiloatar, H., Aras, O., Korkmaz, M., & Vural, A. H. (2021). An evaluation of quality of life, physical activity level and symptoms in patients with early stages of chronic venous disease. *Journal of vascular nursing : official publication of the Society for Peripheral Vascular Nursing*, 39(4), 108–113. <https://doi.org/10.1016/j.jvn.2021.07.007>.
33. Erdal, E. S., Demirgüç, A., Kabalcı, M., & Demirtaş, H. (2021). Evaluation of physical activity level and exercise capacity in patients with varicose veins and chronic venous insufficiency. *Phlebology*, 36(8), 636–643. <https://doi.org/10.1177/02683555211002339>.
34. Ozberk, S., Karadibak, D., Ozalp Karabay, D., & Polat, M. (2018). The Relationship Between Quality of Life, Functional Capacity, Physical Activity and Performance Levels in Chronic Venous Disease. *Journal of Updates in Cardiovascular Medicine*, 6(3), 97-101. <https://doi.org/10.32596/ejcm.18.00397>.