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Quality of Life in Venous Diseases of the Lower Limbs

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Additional information is available at the end of the chapter

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Abstract

Chronic venous diseases of the lower limbs are one of the common and disabling conditions with clinical signs and symptoms ranging from spider veins, to varicose veins or even to venous ulceration, effecting patient's quality of life negatively, particularly in relation to the domains of pain, physical function and mobility. It is not only a serious medical condition but also an undeniable physical and psychosocial problem and has a severe impact on a patient's quality of life. Quality of life is defined as individuals' perception of their position in life and refers to the patient's ability to enjoy normal life activities. It is a common and subjective term that has a number of dimensions described as patient-reported outcomes. There are numerous factors that affect person's quality of life negatively. Some of those are social relationships, economic status, physical health, psychological status, environmental conditions (living place or work), pain and especially chronic diseases. We conducted a review about quality of life in chronic venous diseases of the lower limbs to identify how person's quality of life is affected. Therefore, this chapter will focus on the effect of the chronic venous diseases on the person's quality of life.

Keywords: quality of life, chronic venous disorders, evaluation, body image, varicose veins

1. Introduction

Chronic venous disorders (or in other name chronic venous diseases) (CVDs) are widespread problem and can vary from asymptomatic insufficiency of venous valves to chronic leg ulcers [1]. The importance of venous disorders is determined by the socioeconomic influence of disease according to its severity and the number of affected person [2]. Although it does vary, it is revealed that the venous disorders have high prevalence in the community. Approximately 23% of the adult population have varicose veins and 17% have chronic venous insufficiency (CVI) (which is one of the CVD), in all age groups. In addition, it clinically varies from minimal lower leg edema to severe leg ulcers [3].

CVI is a condition that the blood flow within the veins is insufficient, resulting in pooling of blood in the veins, especially in the lower limbs. It can be resulted from by several venous disorders, particularly in chronic situations. It is characterized by permanent lower limb venous hypertension as a result of venous reflux and/or occlusion and insufficient calf muscle pump function [4]. It represents severe phase of CVD and denotes some symptoms such as edema, skin changes, and venous ulcer [5].

CVI is commonly characterized by a condition including diseases in the venous system of the lower extremities [6]. There are a lot of reports about prevalence in CVI, and its variation is very large. This difference may result from the differences in the definition of venous insufficiency and in the methods used for clinical evaluation of the signs and symptoms [7]. There is a study reported that CVI varies between 1 and 17% in men and 1 and 40% in women [8]. However, it is predicted to be as high as 50% in the general population especially in industrial countries [2, 9].

To understand effects of CVI on the quality of life and health outcomes, it is necessary to know the venous anatomy and pathophysiological mechanism. Therefore, we first decided to begin giving information about the anatomy and pathophysiology of the disease.

2. Anatomy of the venous system

Functionally, the peripheral venous system is assumed as a reservoir to store blood and as a canal to return blood to the heart [10]. Depending on activating peripheral muscle pumps and a series of valved conduits to return blood against gravity, the venous system in the lower limbs is more complex than the arterial system [11]. The deep, superficial and most of perforating veins include bicuspid valves opening just one direction [12]. Veins are consisted of three layers, which are intima, media, and adventitia as the similar arteries, although having much thinner vessel wall than arteries [13]. In addition, they have a weaker muscular layer and less elastic tissue when compared with arteries [14].

To classify the veins in the lower limbs, it is considered the relationship between veins and the muscular fascia and location in either the superficial or deep compartment. In this context, they are separated into three groups. These include the deep veins, the superficial veins and the perforating veins. The deep veins are located between the large muscle groups of the lower limb inside the myofascial compartments beneath the muscular fascia [15, 16]. The superficial veins are located above the deep fascia and drain the microcirculation of cutaneous tissue. The perforating veins are responsible for connection between the superficial and deep veins. There is also another group of veins named as communicating veins connecting veins within the same system (deep to deep, superficial to superficial) [15]. In normal situations, muscles contraction generates pressure during contractions in the fascial compartment and this is directly transferred to the veins. Whereby, venous blood flow is directed to the heart via competent valves in the venous system [16]. When muscle pump relaxes, blood begins refill to the deep venous system. Veins become swollen as the vein is filled by antegrade flow in prolonged standing positions. Therefore, the valves within the veins begin to open and

pressure to rise. By dint of muscle pump contraction, the veins begin to discharge and venous pressure decrease [10].

In the lower limbs, as we mentioned above, contraction of the calf muscle provides a significant mechanism to push and direct blood flow within the veins toward the heart. Blood in the deep veins starts to empty throughout the muscle contraction, and blood flows from the superficial to the deep veins via the perforating veins. Therefore, the pressure in the venous system decreases during ambulation [17]. Venous reflux or obstruction at any time in superficial or deep veins is related to venous disease and the clinical manifestations of CVI. An increased pressure in the venous pressure causes a retrograde elevation of pressure into the venules (thinner veins) of the skin. This leads to continuous elevated ambulatory venous pressures (as known commonly venous hypertension) that have been related to development of leg ulcers in advanced stages [18].

3. Pathophysiology of venous disorders

Rising venous pressure and occurring impairment in blood flow by several mechanisms lead to develop venous pathology [19]. It may result from valvular incompetence in superficial, deep or perforator veins, venous tributaries, or obstruction in veins, or a combination of these mechanisms [10]. Congenital causes, repetitive infections, trauma or inflammation resulted from deep vein thrombosis (DVT) may damage the valves. Obesity, pregnancy, a pelvic mass and previous history of DVT may cause obstruction in veins [20]. Abnormal formation of veins and arteries as a congenital disease (arteriovenous malformations) [21] or insufficient of the calf muscle pump caused by fatigue, immobility, or decreased ankle mobility resulting from neuromuscular or orthopedic diseases also contribute to this process [22]. Damage the valves results in reverse flow or leakage in the closed valves [23]. In addition, high pressure begins to enter into superficial veins, when the failure of valves in the saphenofemoral and saphenopopliteal junctions (between the deep and superficial systems) emerges. It can also enter the superficial system due to malfunction of the perforator valves. As the consequence of this situation, veins start to dilate and varicose veins begin to form and spread to the extremity [10].

In normal conditions, most of perforator veins are inactive. When the venous hypertension develops, they begin to open, and leakage of the blood occurs from deep to superficial veins [24]. Changing in the microcirculation contributes to the macrocirculatory hemodynamic disturbances [25]. If venous hypertension is not treated, it causes changes in the skin with hyperpigmentation, fibrosis in subcutaneous tissue and eventually ulceration [10].

4. Risk factors

There are some risk factors defined leading to development of CVI such as heredity, age, female sex, obesity, pregnancy, prolonged standing conditions (**Figure 1**).

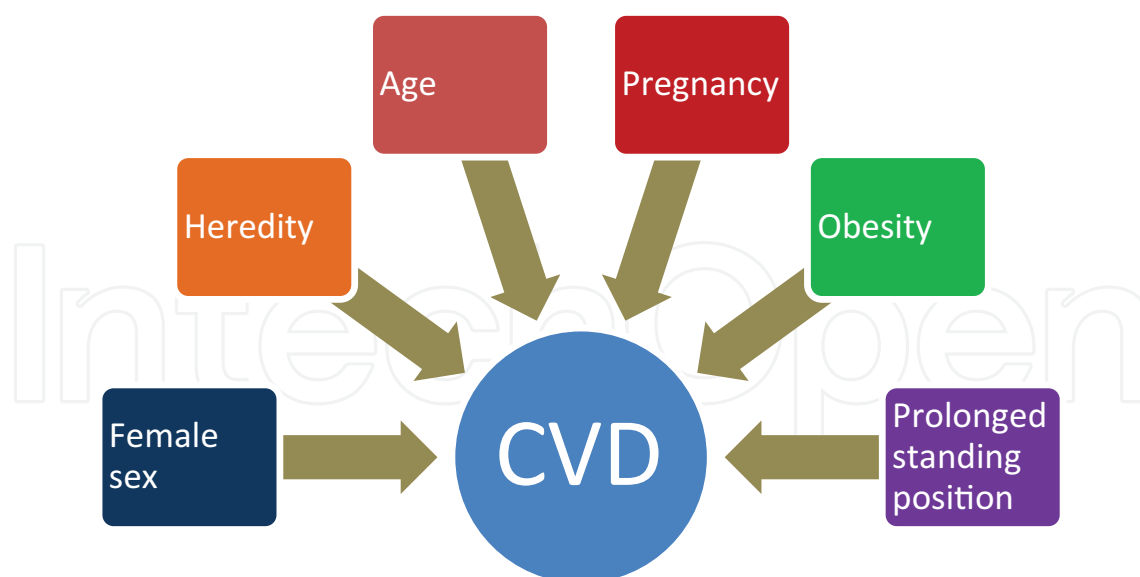


Figure 1. Risk factors of chronic venous disorders.

Several studies have revealed older age as the most important risk factor for CVI. It is more common especially in female adults than male [3, 26]. However, in the Edinburgh Vein research, it has to be reported that varicose veins were more common among males in the general population [27]. Obesity is another risk factor leading to CVI. It is stated that having more than 30 a body mass index (BMI) increases the risk for CVI significantly in both sexes, especially in males [28]. In addition, it is found that a relationship between severe obesity (BMI ≥ 40) and increased limb symptoms without anatomic evidence of CVD. Therefore, it is suggested that the obesity itself is a factor, which contributes to the venous insufficiency [29, 30]. A positive family history, also, is shown to be a predisposing factor for varicose veins or venous disease [28, 31].

5. Symptoms

Symptomatic varicose veins are not assumed as a life-threatening situation, but it is generally progressive, and if progress, it may result in ulceration on the skin [32]. As we emphasized, CVI is a chronic disease seen with the many symptoms ranging from aching of the legs, varicose veins, telangiectasia, muscle cramps, swelling, pruritus, fatigue, throbbing, itching of the skin, to sense of heaviness in lower limbs [33] (**Figures 2 and 3**).

The symptoms of CVI cause considerable morbidity in patients, decreasing on quality of life (QoL) [34]. It is reported that the symptoms are worse especially in women [35]. Some symptoms are exacerbated by the prolonged standing position such as fatigue, heaviness and pain [36]. Therefore, when the patient is being evaluated, these symptoms should questioned with daily activities and work, especially in patients who must be stand for a long periods of time. In general, symptoms are worse at the end of the day. Exercise for lower limbs, mobilization and leg elevation may help relief in symptomatic signs [37].

Symptoms of Chronic Venous Disorders	
Varicose veins Aching of the legs Telangiectasia Muscle cramps Swelling	Pruritus Fatigue Throbbing Itching of the skin Sense of heaviness in lower limbs

Figure 2. Symptoms of chronic venous disorders.

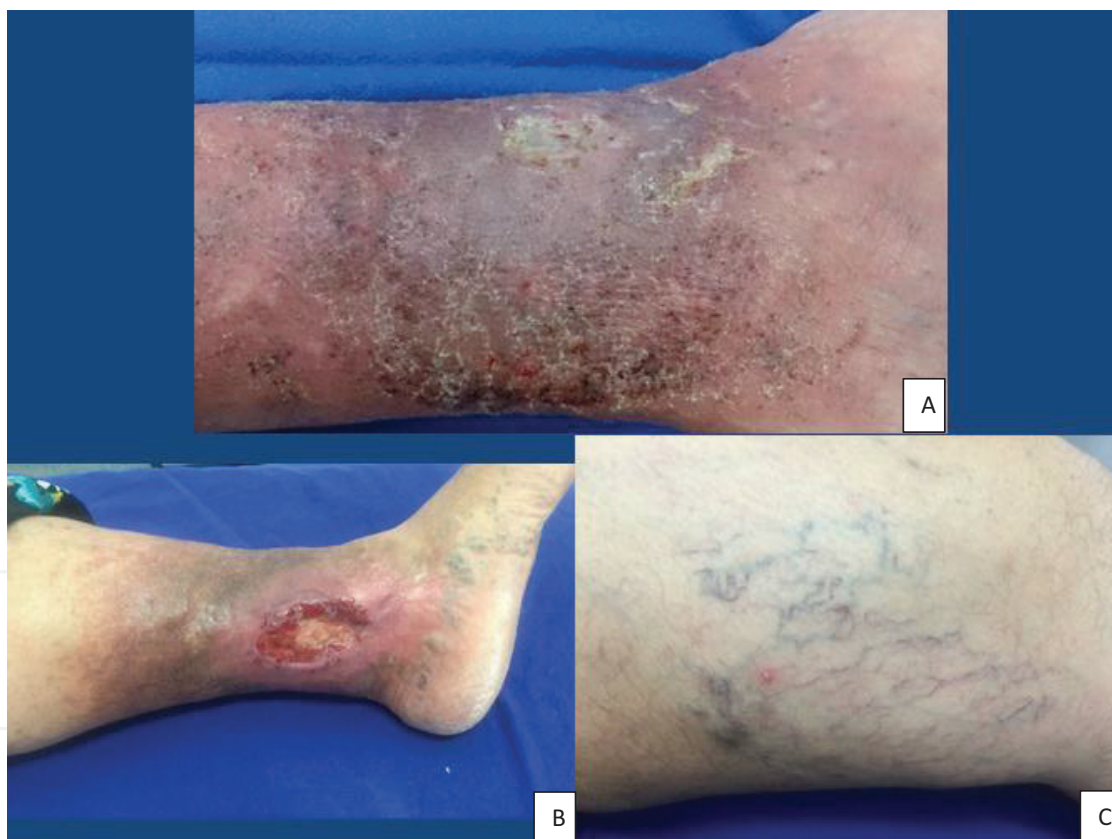


Figure 3. Clinical signs of chronic venous disorders: A: skin changes, B: venous ulcer, C: telangiectasia and reticular veins.

In patients developing chronic outflow obstruction, venous claudication may occur during activities such as walking or climbing stairs. It is also stated that there is an association between QoL scores to severity of disease. Patients indicating the more severe signs and symptoms reported the worse QoL scores [37].

6. Classification

CVI, due to the nature of the disease, presents various signs and symptoms, and this creates a significant challenge to determine severity of disease, to interpret and compare published reports in the literature, objectively. It may be classified using clinical, anatomical, hemodynamic, or patient reported criteria. The challenges resulted from inconsistent reports emerged an applicable and standardized classification system for venous disease [38].

Although there are some classification methods to determine and classify severity of disease, Clinical Etiological Anatomical Pathophysiological (CEAP) classification and Venous Clinical Severity Score (VCSS) are the most using system among them.

6.1. Clinical etiological anatomical pathophysiological (CEAP) classification

The CEAP classification was developed in 1994 the American Venous Forum to describe the severity and etiology of lower limb venous disease, and it was revised in 2004. Thanks to the adoption of this system, correlation among different studies and clinics, and meaningful communication about CVD could be done easily, in a standard way [39]. It serves as a systematic guide in the routine clinical examination of patients with an accurate diagnosis. In the classification of CEAP, there are four parameters. These are clinical indications (C), etiologic factors (E), anatomic dispersion (A), and underlying pathophysiologic manifestations (P) [40]. Detailed information is given in **Table 1**.

There are two version of CEAP: basic version and extended version. The basic version is developed for practical intent. It does not require training for using it and is commonly used in day-to-day care. In addition, its primary aim is using for clinical application; however, it can be used as well as for the purpose of research. The CEAP classification system is an objective and well-constructed

CEAP classification system			
Clinical	Etiologic	Anatomic	Pathophysiologic
C ₀ : There is no any signs of venous disease	Ec : Congenital	As : Superficial veins	Pr : Reflux
C ₁ : Telangiectases or reticular veins			
C ₂ : Varicose veins	Ep : Primary	Ap : Perforator veins	Po : Obstruction
C ₃ : Edema			
C _{4a} : Pigmentation or eczema on the skin	Es : Secondary (post-thrombotic, post-traumatic)	Ad : Deep veins	Pr,o : Reflux and obstruction
C _{4b} : Lipodermatosclerosis or atrophie blanche			
C ₅ : Healed venous ulcer	En : There is no cause determined	An : There is no venous location identified	Pn : There is no venous pathophysiology determined
C ₆ : Active venous ulcer			

Table 1. CEAP classification system.

instrument, although it has shortage in detecting key symptoms of venous disease. It is reported that the deviations of CEAP scores between different physicians are not significant [41].

In the study, conducted by Kahn et al. [37], it is found that clinical values of CEAP in patients with venous diseases were significantly associated with generic and disease-specific QoL. Their results emphasized that CVD has an adverse effect on QoL, proportionally severity of disease. In addition, it is showed that the variables of sex, age, country, duration of CVD, BMI, education level, and presence comorbidities were associated with QoL scores.

6.2. Venous severity scoring

Although there are many reports that proving the CEAP classification is a useful instrument in classifying venous diseases, there is need more detailed information concerning severity and longitudinal changes of disease in patient during treatment [42]. In the basis of this thought, the American Venous Forum developed Venous Severity Scoring (VSS) from ingredients of the CEAP for measurement of disease severity, in 2000 [43]. The VSS includes three components about scoring of disease. These are the Venous Disability Score (VDS), the Venous Segmental Disease Score (VSDS) and the Venous Clinical Severity Score (VCSS).

VDS is a modification of the original CEAP classification, which is providing disability level, and it evaluates the functional impact of CVD in daily activities. VSDS considers both

The venous clinical severity scoring				
Qualification	Absent: 0	Mild: 1	Moderate: 2	Severe: 3
Sense of discomfort, Pain, aching, fatigue heaviness	No	Sometimes, it does not reflect in Daily activities	Daily, it does not affect daily activities	Daily, it restricts most of activitiy
Varicose veins	No	Few and scattered	Confined to calf or thigh	Involve calf and thigh
Venous edema	No	Restricted foot and ankle	Spreads above ankle but don not pass the knee	Extends to knee or above the knee
Pigmentation of the skin	No or focal	Restricted in perimalleolar area	Diffuse over lower third of calf	Diffuse more than lower third of calf
Inflammation	No	Restricted in perimalleolar area	Diffuse over lower third of calf	Diffuse more than lower third of calf
Skin induration	No	Restricted in perimalleolar area	Diffuse over lower third of calf	Diffuse more than lower third of calf
Number of active ulcers	0	1	2	>2
Duration of ulcer	Absent	Less than 3 months	Between 3 months to 1 year	Unhealing ulcer more than 1year
Size of ulcer	Absent	Diameter <2 cm	Diameter 2–6 cm	Diameter >6 cm
Compression therapy	Not used	Intermittant	Most days	Every day, mostly

Table 2. Venous clinical severity scoring.

anatomical and pathological aspects of CVD to provide score about obstruction and reflux. VCSS was designed the aim of obtaining the severity of venous disease. It evaluates totally 10 clinical parameters, and each item scores graded from absent (score 0) to severe (score 3) [43], which is shown in **Table 2**. The VCSS provides more reliable information about severity of disease in patient's routine activities [44]. It is mentioned that the VCSS scores are associated with QoL measurements [41].

7. Quality of life

The term 'Quality of life' (QoL) is a broad multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life and affected by the culture, individuals' goals, expectations, spirituality, standards and concerns [45, 46]. In another way, it is defined as individuals' perception of their position in life and refers to the patient's ability to enjoy normal life activities [46]. It observes life satisfaction, including everything from physical health, family, education, employment, wealth, religious beliefs, finance and the environment [47]. Therefore, the mean of QoL varies among different people.

There is a consensus in the idea that patients' sights are not stable, and it shifts according to their expectations and perceptions. However, these parameters effecting psychological aspects of disease and degree of symptoms are sometimes underestimated in clinical practice. In order to obtain accurate meaning of QoL in clinical medicine and trials, it is necessary to distinguish between QoL in its more general sense [48]. Consequently, the term 'health-related quality of life' (HRQoL) is derived to obtain more reliable clinical outcomes. Thanks to this idea, clinicians can justify the suitability and cost-effectiveness of the treatment they recommend [49].

The quality of life has subjective and objective indicators, which reflect patient's physical and psychological aspects [50] (**Figure 4**). Objective parameters such as income and physical function can be used in assessing quality of life, but they do not give better opinion about perceiving and experiencing individual's lives. They are better for demonstrating of individual's subjectively perceived QoL, which is critical factor in deciding for treatment and health care policy [51–53]. Subjective evaluations are including psychological domain of pleasure, general happiness and well-being mostly useful to define the experience of life [53] and effectiveness of treatment [54].

There are two basic categories of QoL surveys as generic and disease-specific (**Figure 5**). Both of generic-and disease-specific questionnaires should be used in evaluating QoL, as long as surveys that is reliable, valid, and responsive [55]. For evaluating global sense of well-being and obtaining a subjective measure in efficacy of treatment, generic tools are widely used, and they are appropriate to provide information about QoL in a wide spectrum of disease [56]. Furthermore, in the population with varied circumstances, they enable comparison of measures across populations. However, disease-specific measures are more sensitive in defining effect of treatment and changes in the disease over time [55].

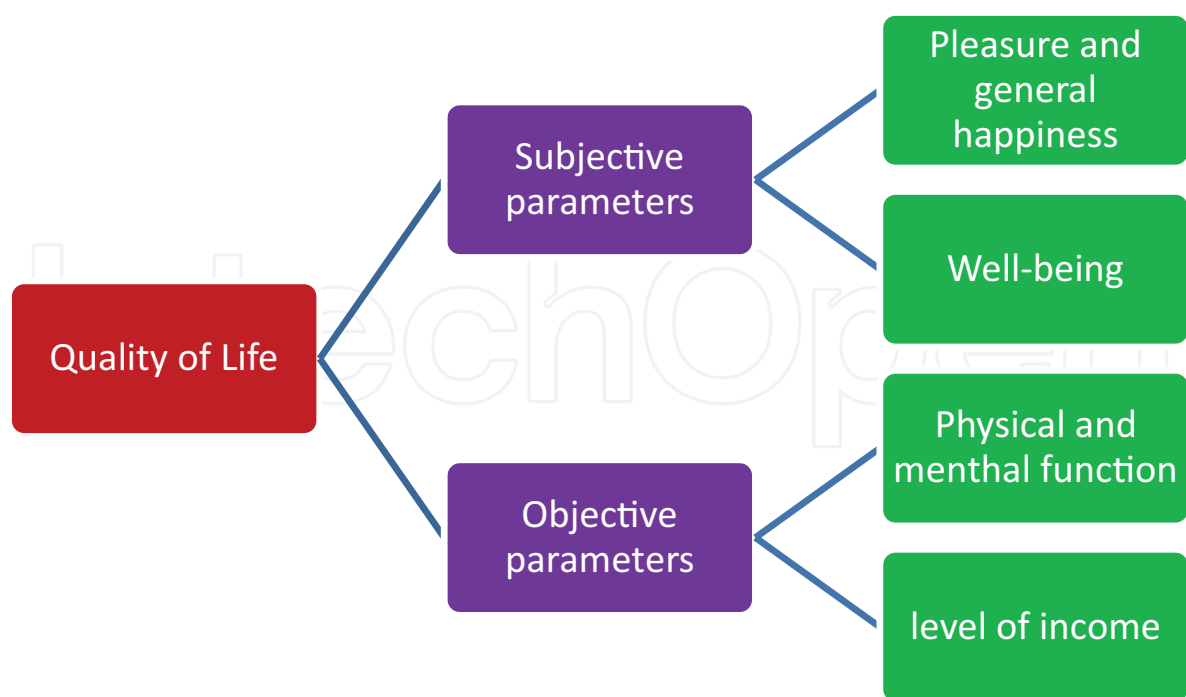


Figure 4. Parameters of quality of life.

Generic Instruments	Disease-Specific Instruments
<ul style="list-style-type: none">• The 36-Item Short Form Health Survey• Nottingham Health Profile• EuroQoL, 5D• Sickness Impact Profile	<ul style="list-style-type: none">• Chronic Venous Insufficiency Questionnaire• Venous Insufficiency Epidemiological and Economic Study• Aberdeen Varicose Vein Questionnaire• Specific Quality of life and Outcome Response – Venous• Assessment of Burden in Chronic Venous Disease• Charing Cross Venous Ulceration Questionnaire

Figure 5. Generic and disease-specific questionnaires.

In particular, in recent years, there is an increasing view that patient-reported QoL is a significant way for evaluating outcomes, especially changes in disease. For chronic conditions such as CVI, evaluation of QoL can provide useful information about burden of disease if it does not captured well by the physician based on other measures [55, 57]. Although mortality rates

are low in some diseases such as CVI, patient satisfaction including resolution of symptoms and improvement in HRQoL is recognized as significant treatment outcome measures [58].

As we mentioned above, CVI is a common circulatory disorder that impairs the return of blood to the heart. It mainly affects the legs, causing varicose veins, thrombosis, edema, and ulceration, which affects QoL. There are many generic and disease-specific QoL assessment tools using in CVI. We aimed to explain these instruments, particularly the most widely used in clinical trials.

7.1. Generic instruments

Generic instruments intend for evaluating general QoL, regardless of the diseases or situation of the patient. They usually can be used in healthy population, too [48].

7.1.1. *The 36-item short form health survey*

A widely used and the most popular well-validated generic quality-of-life instrument is the 36-Item Short Form Health Survey (SF-36) [59]. It is designed to assess generic health status, which is not specific to any age, illness or treatment option [48]. The SF-36 is developed in 1993 using the questions in two categories as physical health and mental health (**Figure 6**). The category of physical health indicates the patient's level of functioning, and mental health indicates of well-being [56]. It contains eight items, which is multidimensional, measuring overall health, functional status and well-being [60]. Besides these items, there are two transition question related to general health and perception of individual's health. These are 'Compared to one year ago, how would you rate your general health now?' and 'In general, would you say your health is: (excellent, very good, good, fair, poor)?', respectively [48]. It is stated that items in the SF-36 detect negative states of health besides the positive aspect; however, some of these dimensions are similar to those in the Nottingham Health Profile [61]. The survey generates a score between 0 and 100, and 0 point indicates worst, 100 indicates best general health perception [60].

Being applicable for a broad range of diseases and thoroughly valid and reliable for measuring QoL are advantages of the SF-36. It is found to be clinically and psychometrically consistent [62] and completed approximately in 5 min, which is admissible in clinical practice [41].

The SF-36 has demonstrated to be a good fit for assessing QoL in the population with CVD. In the studies, it is shown that there is a correlation between the physical component of questionnaire in the patients with CVD and severity of illness. In addition, the strong correlation between all subdomains of the physical components and disease severity measured by the CEAP classification is demonstrated in the literature. However, for the mental component, it is not presented. Correlations between vitality [63] and mental health [64] are poor and inconsistent [38].

Kaplan et al. [63], in their study, used SF-36 to evaluate QoL in patients with CVD, and they found that there was significant correlation between physical component of QoL and severity of venous disease. They also reported that CVD in the lower extremities has a significant effect on physical health.

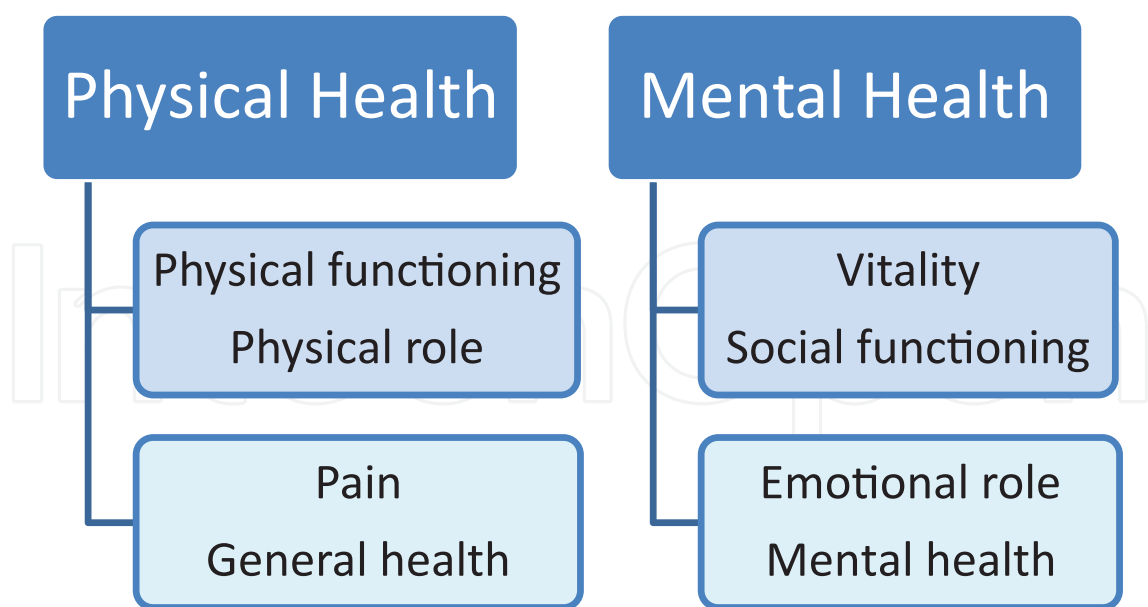


Figure 6. Scales of SF-36.

Darvall et al. [34] conducted a study including 284 patients to determine whether there is any relationship between symptoms in lower limb and generic HRQoL in patients with untreated varicose veins. To obtain data they used SF-12 (shortened version of SF-36) and CEAP. In conclusion, they presented that both physical and mental HRQoL are meaningfully worse in patients with lower limb symptoms regardless of clinical grade of disease. Furthermore, they emphasized that generic HRQoL instruments can be used for comparing effect of treatments.

7.1.2. Nottingham Health Profile

Apart from SF-36, the Nottingham Health Profile (NHP) is another generic instrument designed with a view to measure QoL. Emotional, social and physical health parameters, which are affected by the disease, can be assessed with the NHP for a wide spectrum of illness and situation. It measures subjective health status in sleep, emotional reactions, physical mobility, social isolation, pain, and loss of energy. The questions in each area are answered by 'yes' or 'no' [65]. An example for each section is given in **Table 3**.

In a study, the SF-36 is compared with the NHP in patients with chronic limb ischemia in different degrees. As a result of this study, it is demonstrated that the SF-36 has more internal consistency among patients with mild ischemic symptoms, but the NHP has greater sensitivity to change in patients with more severe ischemia [66].

The NHP is a short questionnaire, and easy to complete. In the NHP, expressions and sentences are not complicated and confounding. It is used frequently both in medical (although it was not designed for that purpose) and non-medical situations to evaluate general health status of individual. However, it is less sensitive in detecting the minor changes in health status and identifying particular problems [48].

Parameters	Examples of questions	Yes	No
Pain	I have pain at night		
Energy	I am tired all the time		
Sleep	I take pills to help me sleep		
Physical mobility	I can walk about only indoors		
Social isolation	I feel lonely		

Table 3. Examples of questions from the NHP.

There are also two other less common instruments evaluating general health status: EuroQoL, 5D (EQ-5D) and Sickness Impact Profile (SIP). We preferred to mention about the most widely used questionnaires to give information related to ingredients and general aspects of them.

7.2. Disease-specific instruments

Disease-specific surveys evaluate factors associated with specific diseases and effect of treatment. In this way, the sensitivity in treatment options and outcomes can increased in comparison with generic instruments, for evaluating QoL in venous diseases [56]. There are four instruments specific to venous disease, which have been used and validated. For evaluating venous diseases with full scope, the Chronic Venous Insufficiency Questionnaire (CIVIQ) and the Venous Insufficiency Epidemiological and Economic Study (VEINES) should be preferred, while the Aberdeen Varicose Vein Questionnaire (AVVQ) and the Charing Cross Venous Ulceration Questionnaire (CXVUQ) are suitable to address particular aspects of venous disease [67].

7.2.1. Chronic Venous Insufficiency Questionnaire

Chronic Venous Insufficiency quality of life Questionnaire (CIVIQ) was developed in France to create a disease-specific QoL instrument should be preferred in place of the generic QoL instruments [68]. Owing to psychometric evaluations and linguistic validity in many countries, it has been the most widely used QoL instrument in venous diseases [66]. According to CEAP classification, the CIVIQ is more sensitive to evaluate QoL for patients in between C0 and C4 clinical grade, because the items in this questionnaire are developed to obtain outcomes about effect of particularly varicose veins and edema on QoL, not venous ulcers [41].

Since CIVIQ was developed, it has undergone some changes. In the first version of the CIVIQ, four areas may evaluate including physical, psychological, social and pain, which is accepted as having effect on QoL. There were different numbers of questions in each category, and this made it difficult to calculate a compound score [68]. Therefore, the idea that there is a need to correction in the CIVIQ is aroused. A new revised version of the questionnaire is named as the CIVIQ-20, which allows weighting the categories equally to obtain a global score.

Nevertheless, it is proved that both versions of the CIVIQ are valid, reliable and consistent for measuring QoL [68, 69]. The items are scored according to the five-point Likert scale [70]. The items of CIVIQ are given in **Table 4**.

There is also the third version of the CIVIQ as CIVIQ-14. The CIVIQ-14 was designed to facilitate its use in clinical areas with the factorial stability of its previous version [71]. It is built by removing 6 items and one dimension causing to the factorial instability in the CIVIQ-20 questionnaire. The 14 remaining items covered three dimensions as physical, pain and psychological [72].

The data obtained with CIVIQ are entirely trustworthy in terms of reflecting the effects of the disease according to self-reporting by the patient with CVD. The CIVIQ was shown to be reliable owing to having good internal consistency, reproducibility and responsiveness [73]. Unlike the AVVQ which are going to be mentioned later, it is more sensitive to making allowance for the more psychological effects on the QoL resulting from CVI [41].

Items of CIVIQ-20	1	2	3	4	5
1. Intensity of pain in legs					
2. Interferes with work or daily activities					
3. Sleeping poorly					
4. To stand for a long time					
5. Climbing stairs					
6. In crunching/kneeling					
7. Walking briskly					
8. Travelling by car/plane/bus					
9. Doing housework					
10. Going to parties					
11. Performing sport activities					
12. Feel on edge					
13. Getting tired easily					
14. Feel like a burden people					
15. Feeling weaker and stiffer					
16. Embarrassment to show legs					
17. Easily irritable					
18. Impression of being disabled					
19. Difficulty getting up in the morning					
20. Do not feel like going out					

Table 4. The items of CIVIQ.

7.2.2. *Venous Insufficiency Epidemiological and Economic Study*

The Venous Insufficiency Epidemiological and Economic study (VEINES QoL/Sym) evaluates the epidemiology and outcomes of CVD [74]. Unlike the generic QoL questionnaires lacking determining detailed information and lower sensitivity for CVD, the purpose of the VEINES QoL/Sym is to present a whole picture of the effect of CVD in the lower limbs [41].

Through the agency of the VEINES, it is evaluated that QoL and symptoms in many conditions in CVD ranging from telangiectasia, varicose veins, skin changes, edema to leg ulcers [38]. Psychometric analyzes revealed that the questionnaire was valid and reliable, as well as manifests correlation with SF-36 and clinical grading according to CEAP. Furthermore, it is stated that the questionnaire is reliable and valid for evaluating of QoL and symptoms in patients with acute deep vein thrombosis (DVT) [75].

The questionnaire includes 35 items in two categories as the VEINES quality-of-life questionnaire (VEINES-QoL) is containing 25 items for evaluating QoL, and the VEINES symptom questionnaire (VEINES-Sym) containing 10 items measuring symptoms of disease. With the VEINES QoL/Sym, physical symptoms can measured more effectively than psychological and social aspects especially in patients with lower limb venous disease ranging from uncomplicated varicose veins to DVT, and the higher scores are associated with the better QoL outcomes [75].

7.2.3. *Aberdeen Varicose Vein Questionnaire*

Aberdeen Varicose Vein Questionnaire (AVVQ) developed by the Garratt et al. [76] in 1993 as a patient-based questionnaire for measuring especially varicose vein outcomes. It is more specific for disease, particularly focuses on symptoms and questions related to varicose veins [41].

There are some issues that can examined by the AVVQ such as social situation and physical symptoms including pain, edema in lower limbs, venous ulcers, using compression therapy and the impact of varicose veins on routine activities. The questionnaire contains 13 questions and is scored from 0 to 100. The higher scores indicate more severe effect of disease (0 point—no effect, 100 point—severe effect) [76]. It is demonstrated in a study matched the AVVQ scores with SF-36 in the literature that there is significant correlation between the AVVQ and SF-36 outcomes [77]. Additionally, there is evidence reporting the AVVQ is reliable, is associated with patient symptoms significantly, and is considered to be greater responsive and sensitive than generic QoL questionnaires [49].

Being short and easy to complete are some of advantages the AVVQ. It is particularly suitable for assessment of uncomplicated varicose vein and outcomes of treatment. In addition, it allows measurement and evaluation of treatment effects on daily life, if it is used in combination with generic questionnaires, such as the SF-36 or NHP [41].

7.2.4. *Specific Quality of life and Outcome Response—Venous*

Specific Quality of life and Outcome Response Venous (SQOR-V) is another disease-specific questionnaire separated to five domains about emotional problems, appearance, and limitation in movements, physical discomfort and risk to health. It contains 46 questions that are based on patient reported symptoms not clinical signs [78].

The SQOR-V gives more sensitive assessment in functional impact of CVD in patients with the class C1–C3 according to CEAP classification system and was designed especially for this purpose. There is evidence that the SQOR-V has a significant correlation with the AVVQ [78], but it should be pointed out that the AVVQ more sensitive than SQOR-V in demonstrating ulceration, varicose veins and other skin changes resulted from CVD [79].

7.2.5. Charing Cross Venous Ulceration Questionnaire

The Charing Cross Venous Ulceration Questionnaire (CXVUQ) was developed to provide a reliable measure for QoL in patients with venous ulcers. Prior to development of the CXVUQ, there was not available any reliable questionnaire evaluating effect of venous ulcer on QoL and treatment outcomes [67].

7.2.6. Assessment of Burden in Chronic Venous Disease

Assessment of Burden in Chronic Venous Disease (ABC-V) was developed by Guex to evaluate directly burden of disease caused by varicose veins. It is a specific tool for evaluating of disease severity and treatments outcomes [80].

8. Discussion

Patients suffering from CVD, causing such as leg ulcers, edema, venous stasis, venous hypertension, etc., are demonstrate worse QoL. This is resulted from sustained discomfort in effected area especially in lower limbs, pain, limited mobility and prolonged healing time. Furthermore, particular treatment options and their financial cost have a significant impact on QoL [81]. It has been preferred to determine the effects of disease and treatment methods on disease from the point of view of the patient, especially in recent years [67]. There are two ways to follow outcomes of effects of venous diseases. One of these is using patient-perceived and reported QoL measurements, another one evaluating clinical signs and symptoms by the physician reports. It is reported that there are many definitions and measuring methods of QoL. Even so, it is defined that there are some key concepts of QoL, which include reliable assessment of the disease's functional effect on daily life activity, focusing on the patient's point of view and feelings, and a taking into account of physical, social and psychological issues [56].

There are many study investigated QoL in patients with CVI. In the study conducted by the dos Santos Crisóstomo et al. [82], using CIVIQ to evaluate effect of manual lymphatic drainage (MLD) on HRQoL and symptoms in patients with CVI, revealed that a four-week period of MLD treatment, which comprised approximately 40 min duration sessions, provide improvement in CVI, especially in terms of clinical severity of disease mostly associated with edema, symptoms and pain HRQoL. Furthermore, thanks to this research, it was demonstrated that the MLD had good effect on CVI and pain HRQoL, and it could still be observed after only 4 weeks of follow-up. On the other hand, it was found that MLD has not any changing effect on the physical, social, or psychological components of HRQOL. Another study carried out by Molski et al. [83] reported that MLD decreased the clinical severity of disease and lower limb

volume in patients with CVD, and improved QoL. They also reported that if MLD was started in the preoperative period, there would have been better improvement in quality of life.

Patients with venous ulcers are known as having poor HRQoL [84, 85], and there is a global concern about the link between HRQoL and venous ulcers. For defining health policies, obtaining information about clinical outcomes and determining effect of venous ulceration emerged that the importance of studying by HRQoL in patients with venous ulceration [85]. In a study investigating the relationship between venous ulcer and HRQoL, González de la Torre et al. [86] reported that venous ulcers had negative effect on patients' HRQoL, especially in their emotional status. Additionally, the association with the degree of the wound and decreased HRQoL was found in the study. In another study carried out by Birks et al. [87], it is reported that generic questionnaires were reasonably well to measure HRQoL in patients with venous leg ulcers.

As mentioned before in this chapter, there are some disease specific questionnaires to measure QoL, and each has some advantages and limitations. Kuet et al. [79] conducted a study to evaluate the relationship between the AVVQ and the CIVIQ-14. Their purpose was to compare disease-specific QoL tools with generic QoL and clinician-driven tools. They used the AVVQ, CIVIQ-14 and EQ-5D to measure QoL, and CEAP classification and the VCSS to obtain information about severity of disease. In conclusion, it is reported that there was a strong correlation between the two disease-specific QoL (the AVVQ and CIVIQ-14). There was a significant correlation also found between these disease-specific QoL questionnaires and the generic QoL (EQ-5D). Furthermore, there was existed a strong relationship between the clinical scoring system and disease-specific QoL questionnaires.

There is many factors effect QoL, and evidences demonstrate increasingly significant correlation between questionnaires and clinical severity of disease. Shepherd et al. [78] carried out a study in patients undergoing treatment for symptomatic veins to investigate the relationships between clinical severity of disease and QoL. Assessments were applied by using CEAP and VCSS to evaluate severity of disease, and SF-12 (generic), the AVVQ (disease-specific) and the Specific Quality of life and Outcome Response-Venous (SQOR-V) questionnaires to measure QoL. As a result, strong positive correlation was found between the AVVQ and the SQOR-V. In addition, the correlation between the AVVQ to SF-12 and the VCSS also was found statistically significant.

As mentioned, venous disorders demonstrate a lot of clinical condition, which are effect individual in many ways. Post-thrombotic syndrome (PTS) is one of a widespread clinical condition seen in patients especially after deep venous thrombosis (DVT) and is characterized with symptoms such as pain, edema and skin changes [88]. Effect of PTS on the QoL has been investigated for years and decreased QoL in patients developed PTS and is demonstrated in many studies [89, 90]. Furthermore, in patients having prior DVT history, QoL and clinical severity of disease are worse in comparison with patients having other forms of CVD [91]. Broholm et al. [90] found that PTS was associated with worse both in disease-specific (measured with VEINES-QOL/Sym) and generic (measured with SF-36) QoL. In addition, they stated that there was a significant negative correlation between PTS and the VEINES-QOL/Sym scales.

The fact that increased clinical degree of venous disease was commonly associated with deteriorating health outcomes and QoL has been proven by many studies. Carradice et al. [92] in their study which is conducted with the aim of to explore the impact of venous disease, and assess any gradual direct effect of clinically advanced disease on HRQoL, evaluated 561 patients with the having different clinical degree of venous disease according to CEAP clinical grade. From those, 456 patients had C2–6 and 105 patients had C0–1 clinical degree, which is assumed as a control group. They also used VCSS system to determine severity of disease. To evaluate QoL, they use SF-36 and EQ-5D as generic instruments, and the AVVQ as a disease-specific instrument. As a result, they reported that there was a significant correlation between severity of disease and deterioration in both disease-specific and generic QoL for all clinical grades, in particular in patients with more severe grade had worse QoL scores.

In conclusion, chronic venous disorders are globally common problem, and with the clinical properties, it has great impact on the QoL. To know how disease affects patient's quality of life, and whether there will be any change in the condition of disease in the course of the treatment, it is essential to use valid and reliable disease-specific assessment tools when patients are evaluated by the clinician. Therefore, it should not be considered only physical findings, when evaluating changes in the state of the disease, but also patient's satisfaction and sense of well-being should be assessed. Through the evaluation of all physical and mental aspects of the disease, the effectiveness of treatment outcomes and changes in burden of disease can be assessed more objectively.

To determine level of QoL, there are some general and disease-specific questionnaires, which are developed particularly for patients with venous disorders. The SF-36 and the NHP are most widely used to determine QoL both in patients and healthy population. However, it is proved that using disease-specific questionnaires is more sensitive and reliable for measuring QoL in patients with CVD. The negative effect of CVD on the QoL has been proved in many studies by using different disease-specific instruments, but there is not any consensus which questionnaire is the best among them. The CIVIQ, VCSS, AVVQ, SQOR-V and CXVUQ are mostly used for evaluation QoL in patients having venous disease, and all are sensitive in detecting QoL levels specifically for venous diseases.

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