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RELATIONSHIP BETWEEN ULTRASONOGRAPHIC CRITERIA, CLINICAL MANIFESTATIONS AND LIFE QUALITY PARAMETERS IN PATIENTS WITH LOWER EXTREMITY VARICOSE VEIN DISEASE

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Comparing the efficacy of modern methods of treatment of the varicose veins disease of the lower extremities requires accurate documentation of the clinical, anatomical and functional situation in each patient using standardized and proven methods. In our study we analyzed the relationship between the diameter of the great saphenous vein determined at the level of the saphenous-femoral joint, for 3 cm distal and in the middle of the thigh, with the duration of reflux. We also studied the severity of clinical manifestations according to CEAP classification, VCSS varicose disease severity scale and quality of life with the help of the AVVQ questionnaire. According to the results of the study, it is the importance of determining the diameter and reflux of the great saphenous vein at the level of saphenous-femoral joint, as there is a statistically significant difference in the mean level of correlation between these indicators and survey areas provided by consensus documents. It has been found that with increasing vein diameter, a more severe clinical class and manifestations of the disease are diagnosed. The relationship between the severity of varicose veins of the lower extremities on the VCSS scale and the assessment of the quality of life using the AVVQ questionnaire was established.

Key words: varicose vein disease, vein diameter, severity, quality of life.

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ВЗАЄМОЗВ'ЯЗОК УЛЬТРАСОНОГРАФІЧНИХ КРИТЕРІЇВ, КЛІНІЧНИХ ПРОЯВІВ ТА ПАРАМЕТРІВ ЯКОСТІ ЖИТТЯ У ПАЦІЄНТІВ ІЗ ВАРИКОЗНОЮ ХВОРОБОЮ НИЖНІХ КІНЦІВОК

Порівняння ефективності сучасних методів лікування варикозної хвороби нижніх кінцівок, вимагає точного документування клінічної, анатомічної та функціональної ситуації у кожного пацієнта з використанням стандартизованих та перевірених методів. У процесі дослідження проаналізовано взаємозв'язок діаметру великої підшкірної вени визначеного на рівні сафено-фemorального зчленування, 3 см дистальніше та на середині стегна, з тривалістю рефлюксу, вираженістю клінічних проявів за класифікацією CEAP, шкалою важкості перебігу варикозної хвороби VCSS та оцінкою якості життя за допомогою опитувальника AVVQ. За результатами проведеного дослідження, встановлено важливість визначення показників діаметру та рефлюксу великої підшкірної вени на рівні сафено-фemorального зчленування, оскільки спостерігається статистично значуща відмінність з середнім рівнем кореляції між даними показниками та зонами обстеження передбачених консенсусними документами. З'ясовано що, зі зростанням діаметра вени, діагностується тяжчий клінічний клас та прояви захворювання. Встановлено зв'язок між показниками важкості перебігу варикозної хвороби нижніх кінцівок за шкалою VCSS та оцінкою якості життя за допомогою опитувальника AVVQ.

Ключові слова: варикозна хвороба, діаметр вен, важкість перебігу, якість життя

The study is a fragment of the research project "Strategy of rapid postoperative recovery in minimally invasive operations on the abdominal cavity, anterior abdominal wall and veins of the lower extremities", state registration No. 0121U109258.

Lower extremity varicose vein disease (LEVVD) involves a number of clinical manifestations, ranging in severity from telangiectasis and varicosity to edema and skin changes that finally lead to the development of venous ulcers. The findings of a large-scale, international study called Bonn Vein Study I suggest that the progression of the disease to more severe clinical manifestations in patients with uncomplicated varicosity makes up from 3.5 % to 7 % per year [15]. The manifestations of lower extremity varicose vein disease (LEVVD) often have a significant negative impact on the patient's quality of life, due to aesthetic changes, chronic pain, decreased mobility, social isolation and other psycho-social problems. Medical costs for this disease make up 2 % of the total public health budget of the developed countries [14].

Recent large-scale meta-analyses and statistics conducted by the National Institute for Health and Care Excellence (NICE) revealed that conservative treatment of lower extremity varicose vein disease with compression stockings is inferior to active surgical approaches (endovenous thermal ablation, surgery or foam sclerotherapy) in terms of cost effectiveness. [8]. Treatment comparison requires accurate documentation of the clinical, anatomical and functional states before treatment is prescribed. Measurements of the diameter and duration of the primary superficial vein reflux (great and small saphenous veins) can serve as surrogate parameters of the disease severity and provide criteria for planning interventions and monitoring the results [11].

Recently, there has been a tendency to take into account the diameter of great and small saphenous veins for the stratification of patients requiring surgical treatment. In particular, the reimbursement in some countries depends on the criteria of vein diameter, thus in the US the insurance companies reimburse the cost of treatment if the diameter of small saphenous veins is between 3.5 and 5 mm and 4.5–5.5 mm for great saphenous veins [4]. Obviously, the purpose of such criteria is to provide an objective measure to differentiate patients who want intervention for aesthetic reasons from those who require intervention due to the development of chronic venous insufficiency, which has a significant impact on the quality of life associated with health [12]. Although there is some evidence that the CEAP clinical class is associated with larger vein diameters and quality of life scores [5], however, the literature is less likely to link quality of life indicators to the diameter of saphenous vein [9].

Comparison of the efficacy of modern methods of lower extremity varicose vein disease treatment requires accurate documentation of the clinical, anatomical and functional states of each patient using standardized and proven techniques.

However, even the recommendations of the International Union of Phlebology (UIP) [2] on the measurement of great saphenous vein (GSV) diameter in different areas are not properly validated. Therefore, there is a need to establish the importance of sonographic criteria for great saphenous veins and analyze their relationship with the clinical manifestations of lower extremity varicose vein disease and patient's quality of life, to standardize examination protocols and choose optimal treatment approaches.

The purpose of the study was to analyze the relationship between sonographic criteria (diameter and reflux) of the great saphenous vein with clinical manifestations of lower extremity varicose vein disease, its severity and the patient's quality of life.

Materials and methods. In order to achieve the target goal, an open, prospective trial was being conducted on the clinical basis of the Department of Surgery of Postgraduate Education of Ivano-Frankivsk National Medical University from 2018 to 2021, involving consecutive patients seeking assistance with clinical manifestations of lower extremity varicose vein disease. All the patients were informed of the details of the study. The inclusion criteria included: diagnosed clinical manifestations of lower extremity varicose vein disease C2-C6 according to the CEAP classification [7]; the occurrence of reflux in the system of great saphenous vein from sapheno-femoral junction (SFJ) to at least the mid thigh; patients over 18 years of age; submitted informed consent. The exclusion criteria involved: the occurrence of reflux in the sapheno-popliteal junction and deep veins of the lower extremities; the history of deep vein thrombosis, obliterating diseases of the lower extremity arteries; severe systemic diseases (cancer, decompensation of cardiovascular diseases, severe kidney and liver failure), as well as pregnancy. Duplex ultrasound was performed by an experienced specialist by means of ultrasound scanning with Affiniti 70 (Philips, Koninklijke N.V) system, equipped with linear sensor of 7.5 MHz. GSV was examined in the upright position using toe movements, manual compression and decompression, as well as the Valsalva maneuver to assess the retrograde flow and duration of reflux. The GSV diameter was measured by applying the ultrasonic transducer transversally without pressure over three regions: the sapheno-femoral junction, and according to international recommendations [2] 3 cm away from the SFJ and in the middle of the thigh. Reflux lasting for more than 0.5 seconds in the GSV and more than one second in the deep venous system was considered pathological.

The VCSS scale was used to assess the severity of lower extremity varicose vein disease [13]. Patients were asked to complete the Ukrainian-language copy of the specialized phlebological questionnaire for life quality assessment – Aberdeen Varicose Vein Questionnaire (AVVQ) [1]. All the questionnaires were filled out in the clinic to ensure 100 % completion. Patients who refused or were unable to complete the life quality questionnaires were not included in the study. In case of varicose veins of both lower extremities, the leg with more pronounced clinical manifestations was analyzed. This approach was not used to assess the quality of life due to the mixed nature of the common and separate questions of the AVVQ questionnaire for both limbs.

Patients' main clinical data were documented and presented in the table 1.

Data Processing. In order to perform statistical calculations, all the indices were collected in a special database (Access®; Microsoft, Richmond, Virginia, USA) and passed statistical analysis using StatPlus software (AnalystSoft, USA, 2021) license No. 2-2405609903. The mean values and their standard errors were determined. Pearson correlation coefficient was calculated to compare the diameters of the veins with other parameters, thus the parameters with $p < 0.05$ were considered statistically significant. Regression analysis was used to study the relationship between quality of life and symptoms measures (VCSS, AVVQ, and CEAP) and vein diameter. Positive coefficients point out that an increase in the independent variable will increase the dependent variable, and negative coefficients indicate a decrease.

Clinical characteristics of patients

	Number of patients (n=285)
Age	50.4±8.6
Sex M/F	92/193
Extremities right/left	172/113
C class (CEAP)	
C2	86 (30.2 %)
C3	145 (50.9 %)
C4a	21 (7.4 %)
C4b	13 (4.6 %)
C5	15 (5.3 %)
C6	5 (1.7 %)

Results of the study and their discussion. Based on the ultrasound examination of the venous system of the lower extremities, the following results were diagnosed: the average GSV diameter measured at the SFJ level is 12.08 ± 5.07 mm, and the duration of reflux is 2.47 ± 0.51 s. Measurement of GSV parameters carried out in accordance with the international recommendations of the UIP determined the following data: the average diameter of GSV at the level of 3 cm distal from the SFJ was 8.82 ± 4.31 mm, the duration of reflux was 2.13 ± 0.81 s, measured in the middle of the thigh 7.69 ± 1.62 mm and 2.81 ± 1.83 s, respectively. Men and women had the equivalent maximum diameter of the great saphenous vein and the duration of reflux at all detection points.

Analysis of the relationship between the studied GSV parameters showed the following features: in none of the studied GSV zones, there is no statistically significant relationship between the vein diameter and the duration of reflux. fig.1.

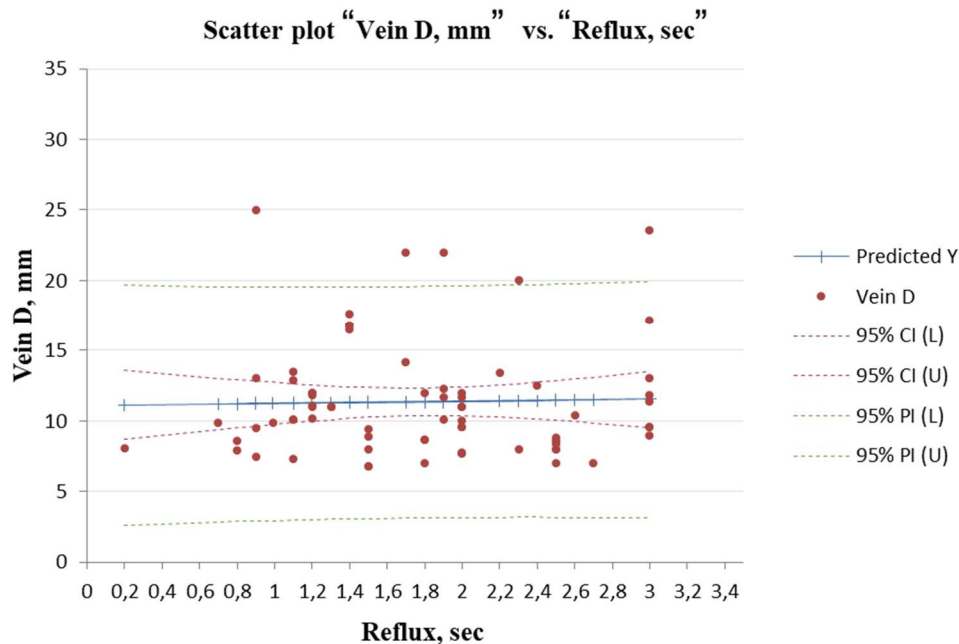


Fig. 1. Linear regression diagram of GSV diameter and reflux duration.

The study of the GSV diameter value in the studied areas shows the following results: there is no statistically significant difference between the GSV diameter measured at the SFJ level and 3 cm distal, $r=0.567$, $p=2.57$. The same results are obtained when comparing the diameter GSV in the middle third of the thigh and 3 cm distal to the SFJ ($r=0.622$, $p=1.143$). As for the GSV diameter determined at the SFJ level and the middle third of the thigh, there is a statistically significant difference between these study zones with the average correlation level ($r=0.398$, $p=0.0016$). This trend emphasizes the importance of taking into account the diameter indicators at the level of the sapheno-femoral junction in addition to the areas of measuring the diameter of the great saphenous vein proposed by international regulatory documents.

Of course, measuring the diameter of a vein in the SFJ area is difficult for several reasons: the anatomical location of the GSV in the groin area complicates the location of the ultrasound sensor clearly perpendicular to the vein axis. In addition, the shape of the vein is affected by the junction of the epigastric,

pubdental, anterior and posterior accessory subcutaneous veins, and possible aneurysmal dilatations due to venous reflux in the deep venous system. Therefore, for the correct implementation of the results obtained in the study of the GSV diameter, require appropriate skills and experience in ultrasound diagnosis of the venous system of the lower extremities. However, the duration of reflux in GSV in the groin area is easily identifiable.

Analysis of the relationship between the duration of venous reflux in the GSV studied areas, showed slightly different results: between the duration of reflux on SFJ and in the middle third of the thigh there is no statistically significant difference ($r=-0.114$, $p=0.393$), at the same time, a statistically significant difference with the average level of correlation ($r=0.421$, $p=0.0003$) is observed between the duration of reflux on the SFJ and 3 cm more distally. This can obviously be explained by the drainage of blood flow to the estuarine areas of the GSV and, accordingly, a decrease in blood pressure on the distal venous valves of GSV. This again emphasizes the importance of taking into account both the diameter and duration of reflux in the great saphenous vein at the level of the sapheno-femoral junction.

The results of the patient's clinical examination show that the largest proportion of patients falls on clinical class C3, although 19 % of patients have trophic changes in the lower extremities inherent in clinical class C4-C6. The average CEAP in the study group is 3.28 ± 0.98 . Analysis of the relationship between the GSV diameters in the three study areas and the severity of clinical manifestations of the disease, determined by the CEAP scale, shows that with increasing venous diameter, a more severe clinical class of the disease is diagnosed, fig. 2.

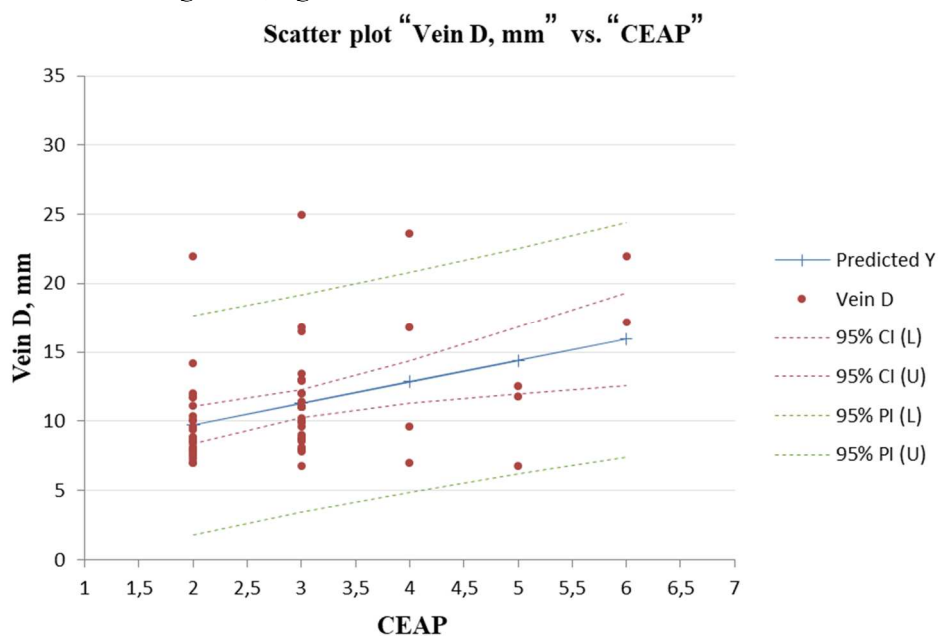


Fig. 2. Diagram of linear regression of GSV diameter indicators at the level of SFJ and severity of clinical manifestations according to CEAP.

A statistically significant, average correlation relationship is observed between the studied values ($r=0.365$, $p=0.004$).

The average assessment of the severity of clinical manifestations determined on the VCSS scale is 7.34 ± 3.41 points and demonstrates that the relationship with the diameter of GSV is the same as in the analysis of clinical manifestations according to CEAP. A statistically significant correlation between VCSS and vein diameter in the studied areas was determined: at the level of SFJ ($r=0.345$, $p=0.004$), in the area 3 cm distal to SFJ ($r=0.517$, $p=0.00005$), at the middle level thighs ($r=0.497$, $p=0.0004$). In the studied patients with an increase in the diameter of the GSV, there is an increase in the scores determined by the VCSS scale. As for the duration of reflux, there is no statistically significant relationship between the duration of reflux and CEAP and VCSS scores. The analysis of CEAP and VCSS indicators did not show a significant difference between men and women. However, there is a simultaneous increase in these two indicators in patients. ($r=0.5108$, $p=0.00029$).

An increase in the severity of clinical manifestations of the disease with age is observed both on the VCSS scale and in accordance with the CEAP classification. Both indicators show a statistically significant correlation, but between the VCSS scale and age this relationship is moderate strength ($r=0.4401$, $p=0.0007$), and between clinical manifestations according to CEAP classification and age, the relationship is weak strength ($r=0.269$, $p=0.038$). Obviously, these results demonstrate the progression of the disease with age in

the absence of adequate treatment. Quality of life indicators significantly complement the characteristics of the pathological process in patients with varicose veins of the lower extremities and are important criteria for assessing the impact of LEVVD on the patient's condition. The average rating of quality of life using the AVVQ questionnaire is 21.29 ± 6.72 points. Analysis of the ratio of vein diameter indicators measured in the three study areas and AVVQ indicators showed a weak statistically insignificant correlation index. Regression analysis of the LEVVD severity of on the VCSS scale and the AVVQ quality of life assessment showed a positive relationship between the studied indicators. fig. 3.

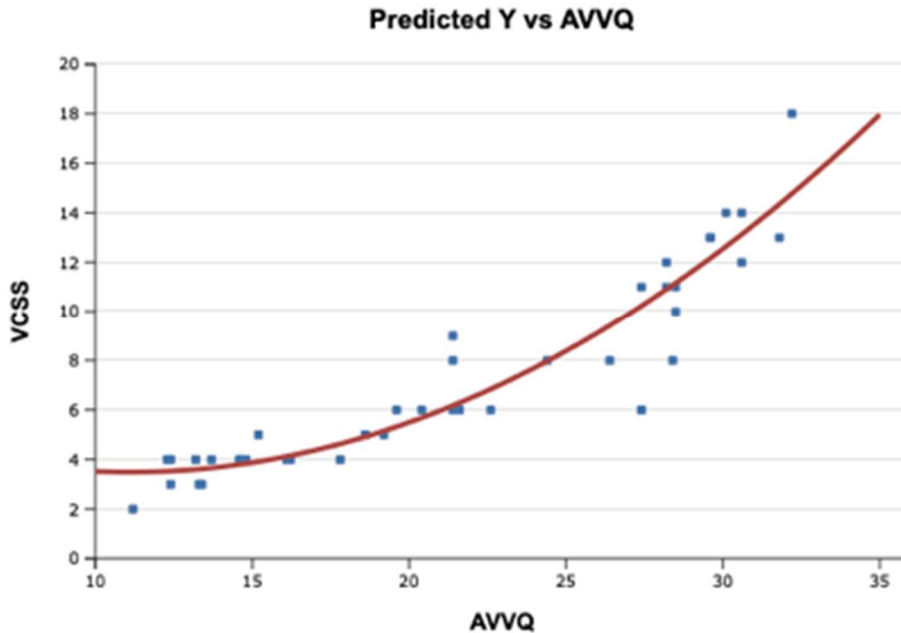


Fig. 3. Polynomial regression diagram of VCSS and AVVQ.

Also, a statistically significant, strong correlation was observed between the studied indicators ($r=0.9204$). At the same time, there was a statistically insignificant, weak correlation between CEAP and AVVQ ($r=0.0156$, $p=0.0928$).

The diameter of the great saphenous vein is a common parameter that is often measured and recorded while examining patients with lower extremity varicose vein disease. However, even the recommendations of the International Union of Phlebology (UIP) [2] do not suggest proper validation for measuring the diameter of GSV in different areas. Yet, there are some reports in the literature [10] as to whether different measurement areas of GSV correlate with each other and whether the examination of these well-defined areas makes it possible to predict the clinical situation better. Thus the investigation made it possible to reveal a statistically significant difference with the average level of correlation ($r=0.398$, $p=0.0016$) between the GSV diameter determined at the SFJ level and the middle third of the thigh; while there were no statistically significant changes while comparing the diameter of the GSV in the middle third of the thigh and 3 cm below the SFJ. The obtained results emphasize the importance of taking into account the indicators of GSV diameter at the level of the sapheno-femoral junction in addition to the areas to be examined due to consensus documents.

Analysis of the relationship between the duration of venous reflux in the examined areas of GSV showed a statistically significant difference with the average level of correlation ($r=0.421$, $p=0.0003$) between the duration of reflux on SFJ and GSV trunk defined 3 cm below, as the duration of the reflux is one of the criteria for determining the patient treatment strategies.

The investigation analysis shows positive correlation between the diameters of the great saphenous veins and the CEAP clinical class [5, 11]. These data were confirmed by our research work, which showed a tendency with increased vein diameter and worsening of clinical manifestations ($r=0.365$, $p=0.004$).

The obtained study results show that the average VCSS is 7.34 ± 3.41 points and is defined as moderate, a statistically significant correlation between VCSS and vein diameter in all examined areas. The works of Gibson et al. [3], and Lane et al [5], showed weak but significant correlation of VCSS, with maximum diameters, while Mendoza et al. reported a strong significant correlation of diameters on the SFJ and the proximal region of the thigh [11].

Analysis of the relationship between vein diameter and life quality assessment measured by AVVQ showed a weak statistically insignificant correlation index. These results are consistent with the study performed by Lattimer et al [6], who revealed that the AVVQ and VCSS did not correlate with the initial

GSV diameter. However, the regression analysis of lower extremity varicose vein disease severity according to the VCSS scale and life quality assessment showed a positive relationship between the studied indicators, which makes the AVVQ life quality questionnaire, a synchronous tool for assessing patients with lower extremity varicose vein disease.

Conclusions

1. The obtained study results prove the importance of determining ultrasonographic criteria (diameter and reflux) of the great saphenous vein at the level of sapheno-femoral junction, as there is a statistically significant difference with the average level of correlation between the diameter of the great saphenous vein ($r=0.398$, $p=0.0016$), the duration of venous reflux ($r=0.421$, $p=0.0003$) defined in the area of sapheno-femoral junction and in the areas of examination suggested by the consensus documents, which may improve the diagnosis and help to choose the appropriate treatment options.

2. The analysis of the relationship between the diameter of the great saphenous vein in the examined areas and the severity of clinical manifestations of the disease, determined by the CEAP scale showed a statistically significant, medium correlation index ($r=0.365$, $p=0.004$), with a positive linear regression coefficient (the larger the vein diameter the more severe clinical class of disease is diagnosed).

3. There is a statistically significant correlation between the severity of varicose vein disease of the lower extremities on the VCSS scale and the diameter of the vein in the examined areas: at the level of sapheno-femoral junction ($r=0.345$, $p=0.004$), 3 cm below the previous level ($r=0.517$, $p=0.00005$) and mid-thigh ($r=0.497$, $p=0.0004$). The increase of the GSV diameter in the examined patients shows clear tendency for higher scores as defined by the VCSS scale.

4. It is possible to observe the statistically significant strong correlation ($r=0.9204$) between the severity of lower extremity varicose vein disease on the VCSS scale and the life quality assessment measures using the AVVQ questionnaire, which shows the synchronism of objective and subjective perception of the disease by both a doctor and a patient.

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