Clinical Study protocol: «Study of venous outflow from the lower limbs in patients with pelvic varicosities as a new strategy for compression treatment of pelvic varicose veins and varicose veins of the lower limb»

NCT: no

Date: May 4, 2023

Compression therapy is basic treatment for chronic venous disease (CVD) of the lower limbs. Numerous studies have demonstrated the efficacy and safety of compression therapy in relieving symptoms such as pain, venous edema, leg heaviness and fatigue, as well as accelerating the healing of venous ulcers. It has been established that compression therapy is indicated for patients with both minimally expressed manifestations of CVD and severe forms of the disease. At the same only one study has been conducted to assess the correction of venous outflow from the lower limbs and pelvis in patients with pelvic varicose vein (PVV) and pelvic congestion syndrome (PCS). However, the incidence of this pathology ranges from 15 to 30% in the female population. The cost to the healthcare system of treating these patients in the United States exceeds $2 billion. To date, the options and indications for compression therapy in patients with concomitant PVV and CVD have not been defined. The rational use of compression in this cohort of patients may contribute to the improvement of effective conservative treatment. In addition, inappropriate prescription of compression to patients with pelvic venous disease (which can be observed in real clinical practice) may discredit this simple, effective and safe therapeutic method. In addition, the research devoted to the problem of compression treatment of PVV will contribute to the development of new special compression products aimed at accelerating venous outflow from the pelvic organs. It can be assumed that this will serve as a stimulus for obtaining new data on the therapeutic effects of compression and create conditions for the creation of new technological directions in the production of compression knitwear.

Aim: To study the venous outflow disturbance of the lower limbs in patients with PVV and to develop a new compression treatment strategy for patients with PVV and CVD.

Study goal:

- To study the status of venous outflow from the lower limbs and pelvis in patients with concomitant PVV and CVD.;
- To identify correlations between the degree of impairment of venous outflow from the pelvis and the severity of impairment of the lower extremity musculo-venous pump (MVP) as the main peripheral determinant of venous return from the lower limbs.;
- To study the influence of the duration and extent (involvement in the pathological process) of pelvic venous reflux on the degree of venous outflow disturbance of the lower limbs;
- To develop ultrasound and radionuclide criteria for the severity of pelvic congestion syndrome;

- To study the possibility of using the coefficient of pelvic congestion syndrome (Cpcs) as a predictor of venous outflow disturbance of the lower limbs;
- To establish the criteria for correcting venous outflow disturbances in the lower limbs with compression based on the severity of pelvic congestion syndrome;
- To evaluate the effectiveness of compression therapy for CVD in patients with PVV (PCS) and impaired venous outflow from the lower extremities and the musculo-venous pump function.

Material and methods.

This study enrolled 90 female patients, including 40 patients with PVV and PCS, 40 patients with combined PVV and CVD, and 10 patients with CVD without pelvic vein pathology.

Clinical study:

All patients undergo examination by a physician-researcher who documents patient complaints, medical history, and physical examination findings in individual medical records. Chronic pelvic pain (CPP) and pain in the lower limbs will be assessed with a visual analog scale (VAS), which is a horizontal line 10 cm long, with each centimeter representing 1 point. The severity of pain on the VAS is estimated as follows: 0 points - no pain; 1-3 points - mild pain; 4-6 points - medium pain; 7-8 points - severe pain; 9-10 points - worst pain.

Diagnostics:

Duplex ultrasound (DUS) of the lower limb veins will be performed on all patients. Transabdominal and transvaginal DUS will be performed on all 90 patients, too. Radionuclide venography of the left or right lower limbs (depending on the side of the lesion) will be also performed in all patients. Additionally, the single-photon emission computed tomography (SPECT) of the pelvic veins with *in vivo*-labelled red blood cells (RBCs) will be performed in all patients (n=90).

Treatments:

Compression therapy with either class 1 or class 2 compression stockings will be administered to 90 patients with PVD and/or CVD. The selection of the compression class was based on the CEAP class and the severity of tibial MVP abnormalities according to radiophlebography data. The researcher will select the size of the compression product according to the standard scheme after verifying the diagnosis by pelvic and lower extremity vein DUS and radionuclide assessment of venous outflow from the pelvic and lower extremity veins (radionuclide venography and SPECT).

General information

Title: «Study of venous outflow from the lower limbs in patients with pelvic varicosities as a new strategy for compression treatment of pelvic varicose veins and lower limb varicose vein disease»

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Rationale and basic information/ Abstract

Currently, the term "varicose veins" implies not only the pathology of the superficial veins of the lower limbs, but also the pelvic veins. As yet, no epidemiological studies have investigated the frequency of the combination of pelvic and lower limb varicose veins, but in some studies the authors point to a combination of lower limb varicose veins and pelvic varicose veins (PVV) in 30-60% of patients. In this scenario, we are discussing the disease's clinically manifested forms, where lower limb varicose veins are visually identified and pelvic veins are identified by ultrasound and manifest as symptoms of pelvic congestion syndrome. There is no evidence of a concomitant occurrence of asymptomatic or latent forms of varicose veins in the lower limbs and PVV. (In this cases during duplex ultrasound angioscanning (DUS), pathological blood reflux is detected in the dilated superficial veins of the lower limbs and pelvis. However, there are no symptoms or signs of the disease.) As a result, it is not possible to assess the true prevalence of the combination of CVD and PVV.

At the same time, it is evident that dilatation and reflux in pelvic veins cannot but affect the clinical course of CVD in general and lower limb varicose vein disease in particular. Multiple studies from our clinic and foreign colleagues have substantiated this claim. It is caused not only by anatomical links between pelvic veins and lower limbs (perineal, clitoral perforating veins, tributaries of internal iliac veins), but also by common triggering mechanisms and similar pathogenesis of lower limb varicose vein disease and PVV.

Considering the above, valid questions arise about the effect of pelvic varicose veins with reflux on lower extremity venous outflow:

1. How does asymptomatic pelvic vein dilation with reflux impact venous outflow from the lower extremities and the clinical manifestations of CVD?

2. Does symptomatic pelvic vein dilation with reflux affect venous outflow from the lower limbs and clinical manifestations of CVD?

3. Does vulvar vein dilation affect venous outflow from the lower limbs and CVD clinical manifestations?

4. Is the severity or exposure of pelvic congestion syndrome a predictor for the development of lower limb venous outflow disorders?

5. How does the severity of clinical manifestations of PCS correspond to the severity of hemodynamic disturbance, as determined through instrumental research methods?

These questions have significance not only in academic and scientific domains. They are directly related to the strategy and tactics of treating patients with a combination of varicose veins of

lower limbs and PVV, PCS and CVD, since the following fundamental issues have not yet been resolved:

1. Do asymptomatic patients with instrumental detection of PVV and lower limb varicose vein require correction?

2. Is it appropriate to utilize compression knitwear in patients with an asymptomatic course of instrumentally confirmed venous outflow disorders with a combination of pelvic and lower extremity varicose veins?

3. Can the coefficient of pelvic venous congestion be utilized as a quantitative indicator to prescribe compression treatment for venous outflow disorders in the lower limbs of asymptomatic patients without signs of CVD? In other words, can the coefficient of pelvic venous congestion be used as a reference index for correcting the evacuative function of the tibial MVP in patients without clinical manifestations of CVD?

4. How effective is compression in correcting impaired venous outflow from the lower limbs in PVV patients?

The severity of the clinical course of lower limb CPV is determined by objective symptoms such as pain, edema, trophic disorders, and venous ulceration. In patients with CVD, the severity of the disease course determines the development of pelvic congestion syndrome (PCS), which is manifested by chronic pelvic pain (CPP), hypogastric heaviness, and dyspareunia. CPP and dyspareunia are the main indicators of the severity of the clinical course of PCS. It has been demonstrated that PCS exacerbates the symptoms of CVD. Thus, correlating the severity of pelvic pain to the degree of pelvic venous fullness (coefficient calculated by pelvic venous scintigraphy) allows us to assume the presence of venous outflow disorders of the lower extremities. According to this hypothesis, the presence and severity of venous outflow disorders of the lower limbs can be determined not only by the results of instrumental examination of the pelvic and limb veins, but also by clinical assessment of the severity of CPP.

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Objectives of the study

To examine the correlation between impaired venous outflow from the pelvis and venous outflow from the lower limbs, to identify predictors of impaired venous outflow from the lower limbs in patients with PVV without clinical manifestations of CVD, to determine indications for the use of compression therapy of the lower limbs in patients with PVV but without symptomatic CVD based on the severity of disturbances in venous outflow from the pelvis.

Primary endpoint of the study

To investigate the impact of varicose veins of the pelvis and pelvic congestion syndrome on the venous outflow of the lower limbs and the function of the muscular-venous pump of the lower limbs.

Secondary endpoint of the study

To assess the efficacy and comfort of utilizing compression stockings of class 1 and 2 in the treatment of lower limbs venous outflow disorders and correction of lower limb muscular-venous pump dysfunction in patients with PCS in combination with subclinical and clinically manifested lower limb CVD.

Study design

This is a single-center, prospective, comparative cohort study. The duration of the study is from 1/4/2023 to 1/12/2023. The study includes 90 patients (40 patients with symptomatic PVV without CVD, 40 patients with asymptomatic PVV and symptoms of CVD, 10 patients with lower limb varicose vein disease (CVD) without PVV.

Inclusion criteria:

• Patient age group: 18-40 years;

• Presence of pelvic varicose veins according to DUS data;

• Reflux in the pelvic veins for more than 1 second before this DUS;

• Reflux in the superficial veins of the lower limbs.

Exclusion criteria:

• Menopause;

• Pregnancy;

• Postthrombotic syndrome;

• Suspicion of May-Turner syndrome;

• Ultrasound signs of nutcracker syndrome.

Before being included in the study, every patient signs a voluntary informed consent form to participate in the research.

The study enrolled 90 female patients, including 80 patients with PVV and 10 patients with CVD without PVV. All patients undergo a physician examination and receive DUS of pelvic veins and lower limbs, regardless of the presence or absence of clinical manifestations of diseases of pelvic veins and lower limbs. Then the patients are classified into three groups based on clinical and ultrasound evaluation. The first group (n=40) comprises patients with symptomatic PVV, including pelvic pain, dyspareunia, and heaviness in the hypogastrium, but without symptoms or signs of CVD. The second group (n=40) consists of women with asymptomatic PVV but with indications of CVD. The third group consists of 10 patients with varicose veins in the lower limb, without PVV or PCS symptoms. All patients undergo radionuclide venography of the lower limbs and emission computed tomography (SPECT) of the pelvic veins with in vivo labelled red blood cells (RBC). Quantitative indicators of the function of the lower extremity muscle-venous pump (MVP) and the pelvic venous congestion syndrome coefficient (Cpvc) are objectively assessed, using the results of radionuclide venography and single-photon emission computed tomography (SPECT). These indicators include average radiopharmaceutical transport time from regions of interest, and objectively represent blood venous flow from the veins of the lower extremities and the pelvis. Compression treatment using class 1 or 2 stockings is prescribed for patients with impaired venous outflow from the lower limbs and impaired venous evacuation function of the lower leg vein duct, depending on the class of CVD according to CEAP. Follow-up examinations, including clinical evaluations and radionuclide studies with SPECT of the pelvic veins, are performed 10 days after the initial clinical examination and radionuclide phlebography to evaluate the efficacy of the compression treatment.

Radionuclide venography with single-photon emission computed tomography (SPECT) of the pelvic veins and repeated clinical examinations are performed to evaluate the efficacy of the compression treatment 10 days after the initial clinical examination. Figure 1 displays the study's design.

1. *A clinical examination* comprises of complaints and medical history review, physical examination, checking of local vascular status and evaluating pain severity using the visual

analogue scale (VAS). VAS aids in identifying the severity of CPP. Additionally, to clinically assess the severity of CVD, the Revised Venous Clinical Severity Score (rVCSS) will be utilized. The clinical examination is conducted prior to DUS, radionuclide venography, and ECT. Then, after ten days of receiving compression treatment, the patients undergo a control clinical examination.

2. *Duplex ultrasound scanning (DUS)* of the lower limb veins is performed following a clinical exam to evaluate patency and status of the valve apparatus in the deep, superficial, and perforating veins. In addition to examining the veins in the limbs, DUS is used to assess the condition of the vulvar/perineal veins;

3. This is followed by *transabdominal and transvaginal ultrasound* of the pelvic veins, which includes assessing the patency of the pelvic, iliac, inferior vena cava and renal veins, measuring their diameters, determining the presence of blood reflux through the pelvic veins (gonadal, parametrial, uterine). The left renal vein (LRV) condition is analyzed by determining the vessel diameter at the point of intersection with the superior mesenteric artery and at the kidney gate. Blood flow velocity is measured at these locations, and the ratios of diameters and velocities are calculated to evaluate the degree of LRV stenosis.

4. *Radionuclide venography.* The procedure is performed using a gamma camera and integrated computer. While the patient is upright, 370 MBq of 99mTc pertechnetate is injected into one of the dorsal veins of the foot after a tourniquet has been applied in the area of the ankle joint. With the assistance of a gamma camera detector, we track the transit of the radiopharmaceutical in the tibial (muscular-venous pump of the lower leg), popliteal, femoral, and iliocaval segments. During the investigation of the tibial pump, the patient performs flexion-extension movements in the ankle joint with a fixed heel to activate the calf pump. The gathered data is recorded on the magnetic-optical disk of the computer and then mathematically processed. To investigate the evacuation function of the muscular venous pump (MVP) of the leg an analytical computer program is used to identify areas of interest in the tendon, muscular portions of the leg veins, and the popliteal vein. Then, activity-time curves are constructed to estimate the evacuation time of the radiopharmaceutical from the MVP of the leg. This provides the average transportation time of the isotope. The average isotope transport time is inversely proportional to the volumetric velocity of blood flow. The longer the isotope's average transport time, the slower the blood flow velocity through the deep veins of the leg, and vice versa.Additionally, the rate of blood flow in the tibial veins is measured, providing information on the lower leg's MVP function. Analyzing a panoramic image of the veins from the foot to the inferior vena cava allows for an objective evaluation of deep vein patency and identification of any venovenous discharges that indicate pathology. Normally, only the deep veins in the examined limb are contrasted, while the saphenous and perforating veins are not visualized. The activity-time plot identifies the quick escalation and decline of isotope activity in the area of concern. The average time required to transport in the tendon area of the leg is normally 6-8 s, in the muscle part - 10-12 s, in the popliteal vein - 12-16 s.

5. *The single-photon emission computed tomography (SPECT) of the pelvic veins with in vivo-labelled red blood cells (RBCs).* In order to assess the status of the pelvic veins with the radionuclide, 2 ml of Perfotech solution is injected into the cubital vein for the in vivo

labeling of red blood cells. After 20 minutes, 370 MBq of 99mTc-pertechnetate is injected into one of the veins on the dorsum of the foot. Radionuclide venography is performed as described above. Twenty minutes after administering the radiopharmaceutical and RFG (the necessary time for 99mTc-pertechnetate and autoerythrocytes to bind), single-photon emission computed tomography (SPECT) of the pelvic veins is conducted. The patient lies horizontally on her back, with the gamma camera detector centered above the womb. In order to obtain a tomographic image of the distribution of the labeled erythrocytes in the pelvic veins, 32 projections are made in a circular path with the gamma camera detector rotated 360°, using a 30-second exposure for each frame. The acquired information is analyzed using the SPECT Protocol software package, which generates sections in three projections (sagittal, transverse, and coronal) with a slice interval of 8 millimeters. The radiopharmaceutical utilized is non-reactive to the venous wall and does not stick to the vessels. The labeled red blood cells only amass in regions with heightened blood accumulation, such as varicose veins, liver, and spleen.

Normally, the gonadal veins are not contrasted, with either an absence or slight accumulation of radiopharmaceuticals in the pelvis venous plexus. To eliminate potential errors in the assessment of pelvic venous stasis, mathematical calculations of areas of interest are utilized due to the possibility of weak contrast of intrapelvic veins, caused by low activity of labeled red blood cells and errors in radiopharmaceutical administration. The gamma camera's computer equipment enables calculation of pulse numbers from the region of interest. The gamma camera captures radiopharmaceutical radiation activity in pulses per second, which quantitatively represents the content of labeled red blood cells within the region of interest. To ensure the objectivity of collected data, a ratio of pulse counts from two standard regions of interest is utilized - the veins of the uterus and parametrium, and the common iliac vein on each side. This is necessary as the speed of blood flow in pelvic veins can vary between patients. This ratio is known as the pelvic venous congestion coefficient (Cpvc). The labeled erythrocyte activity in this vessel remains the most stable value, while the activity of erythrocyte-phosphate-pertechnetate complexes in the venous plexuses relies on their varicose transformation and blood deposition. Normally, Cpvc does not exceed 0.5. An increase in this ratio indicates the presence of pelvic venous congestion due to stagnation of blood in the venous plexus of the pelvis. The higher the Cpvc, the more pronounced the pelvic venous congestion and stagnation of blood in the pelvic veins.

6. *Compression treatment.* Compression stockings of class 1 and 2 will be utilized as a method of compression therapy. The selection of compression class relies on the CVD classification as outlined by CEAP and the existence of impairments in the evacuation function of the lower extremity MVP in regards to the radiophlebography data of the lower limbs. The patient is instructed to wear these stockings for 10 consecutive days, 8 hours daily, following which repeated clinical and radionuclide examinations will be conducted to evaluate the efficacy of the treatment. The comfort level of the compression socks will be evaluated using a visual analog scale. This 10 cm long horizontal line assigns 1 point to each centimeter. Based on patient assessments, the following gradations of comfort will be identified: 9-10 points - complete absence of discomfort, comfortable wearing of the knitwear for 8 hours or more; 7-8 points - minor short-term mild discomfort (mild discomfort: a feeling of squeezing, sliding), which does not interfere with wearing the knitwear for 8 hours; 4-6 points - average severity of discomfort, the patient has difficulties using the stockings for 8 hours; 1-3 points - severe degree of discomfort, inability to use compression stockings.

Data from clinical examinations, ultrasound, and radionuclide studies are documented in the patient's personal medical record.

Safety of research and treatment

If any side effects or adverse events occur due to the administration of radiopharmaceuticals or use of compression products, they are reported and all necessary measures are taken to control these side effects and adverse reactions.

Follow-up

For a period of two months following the study's conclusion, each patient will undergo monitoring in order to identify the presence of any side effects or adverse events. Furthermore, continuous assessment of the treatment's efficacy will be conducted during this period**.**

Data processing and statistical analysis

The data of interest are analyzed using the MS Excel program to create summary tables. Statistical analysis is performed using MS Excel, Statistica 6.0, and the VassarStats online calculator (open source project). The arithmetic mean (M) and standard deviation (SD) were calculated. Qualitative variables are compared using Fisher's exact test, and quantitative variables are compared using Student's criterion or Mann-Whitney U test, as appropriate. Statistical significance was assumed at P value under 0.05.

Publication ethics

The study results will be published in scientific journals, presented at scientific forums and conferences, and used for creating methodological recommendations by the Ministry of Health. Additionally, information about the study outcomes will be posted on social networks. The leading role in the publications will be played by S.G. Gavrilov together with A.V. Karalkin, N.Yu. Mishakina, and A.S. Grishenkova included as contributors.

Duration of the study

The project duration hinges on reaching the required number of participants, which is 90. Technical abbreviations are clearly explained upon first use. Patients participate in the study for 10 days, during which they receive ultrasound and radionuclide exams, as well as compression treatment. The writing style is formal, objective, and free from grammatical, spelling, and punctuation errors. Citation and footnote styles follow a consistent format. Physicians examine patients before and on day 10 of compression. Patients receive a repeat radionuclide study after 10 days.

Anticipated difficulties

Difficulties with patient recruitment are anticipated due to the fact that gynecologists see and treat a majority of female patients with pelvic pain. To mitigate this difficulty, correspondence will be sent to women's clinics and outpatient clinics, and communication with gynecological hospitals will be established. There is no anticipated funding hurdle, since the study is being conducted as a part of the University's scientific work and does not require any extra funding.

Responsibilities of Researchers

Sergey Gennadievich Gavrilov, principal investigator

Recruiting patients, conducting interviews, performing ultrasound scans, devising treatment plans, selecting a treatment method, monitoring compliance with study inclusion requirements, documenting procedures, adhering to ethical standards.

Anatoly Vasilievich Karalkin, researcher.

Performing radionuclide studies of veins, documentation, statistical analysis.

Nadezhda Yuryevna Mishakina, researcher.

Performing ultrasound examinations, preparing documentation, statistical analysis.

Anastasia Sergeevna Grishenkova, researcher

Recruitment of patients, repeated examinations of patients, documentation, statistical analysis.

Patient Information

Title of the study: «Study of venous outflow from the lower limbs in patients with pelvic varicosities as a new strategy for compression treatment of pelvic varicose veins and varicose veins of the lower limb»

Organization: Pirogov Russian National Research Medical University

Introduction

Before agreeing to participate in this study, it is vital to thoroughly read, comprehend, and familiarize yourself with the explanation of all proposed procedures. This document outlines the objectives, methodologies, benefits, and potential drawbacks of this study. Furthermore, this document details other procedures that may be presented to you and your right to discontinue your participation in the study at any point. The study results cannot be guaranteed or assured.

Scope and purpose of the study

You are invited to participate in a prospective cohort study to examine the impact of pelvic vein dilation on venous outflow from the lower extremities and the impact of compression therapy on said venous outflow. This study comprises female patients who have pelvic varicose veins, whether or not they exhibit symptoms of chronic vein disease. All consenting patients will receive thorough clinical examinations administered by qualified physicians, ultrasound, and radionuclide studies for the assessment of venous outflow from their pelvic and lower limb veins.

Methods of investigation

Physical examination, duplex ultrasound of pelvic veins and lower limbs, radionuclide phlebography of lower limbs, emission computed tomography. Radiation exposure during radionuclide studies does not exceed 1.96 mSv.

Treatment

Participants in the study found to have lower limb venous outflow disturbance will receive either Class 1 or Class 2 compression treatment. Adherence to specific requirements is mandatory, including following all procedures as directed and reporting any physical or mental condition changes throughout the study.

Possible risks and inconveniences

During radionuclide studies, allergic reactions in the form of erythema may occur in extremely rare cases. Rare cases of contact dermatitis from a skin reaction to the fabric components of compression knitwear have also been reported.

New data

Any significant information obtained during the study that may impact your health will be provided to you.

Voluntary participation/ Dropout

Your participation in this study is voluntary. Refusal to participate will not impact your treatment or access to medical care. You may withdraw from the study at any time, and it is essential that you inform your doctor immediately. Your doctor may remove you from the study for reasons such as non-compliance with instructions, ineligibility, study termination, or administrative reasons.

Expected benefit

Compression therapy is a safe and effective method for treating CVD. It relieves the symptoms of venous insufficiency such as pain, edema, leg heaviness and fatigue. Treatment duration depends on disease severity, identified disorders, and planned surgical intervention as revealed through ultrasound and radionuclide exams. Compression treatment is usually recommended for patients exhibiting clinical symptoms of venous disease such as leg pain, edema, and heaviness. However, patients with a combination of pelvic varicosities may have disruptions in venous outflow from their lower extremities that do not produce clinical symptoms but can cause them. In such instances, patients require compression therapy, which does not cause any significant complications or side effects, but improves venous outflow from the legs. You will undergo ultrasound and radionuclide studies to determine the extent of disturbances in venous outflow from the lower limbs and the impact of pelvic varicosities on the functional state of the veins in the lower limbs. Based on conducted studies, identifying factors that lead to decreased venous outflow will enable doctors to prescribe compression treatment for patients with pelvic varicosities who currently do not experience leg vein problems. However, without proper treatment, they may develop them in the future. This study has practical significance in improving treatment quality for patients with pelvic varicose veins and preventing the development of venous insufficiency in the lower limbs, which can cause edema, pain, and leg heaviness. The results hold not only scientific but also practical significance.

Confidentiality

All medical records and research materials that can identify you will be kept confidential and will not be disclosed in accordance with applicable laws. In the event that the study results are published in medical literature, your identity will remain undisclosed. Monitors, auditors, representatives of the Ethics Committee, and authorities will have access, subject to confidentiality, to the original medical records to verify the accuracy of clinical trial procedures. By signing the Informed Consent Form, you consent to this access. If you have any questions about your examination and treatment of pelvic varicose veins or require additional information, please contact the research staff: Sergei Gennadievich Gavrilov (mobile phone: +7 (916) 9299947); Karalkin Anatoly Vasilievich (mobile: +7 (915) 9909555); Mishakina Nadezhda Yuryevna (mobile: +7 (916) 3480739, Grishenkova Anastasia Sergeevna (mobile: +7 (926) 1132119).

Informed consent form

Informed consent

I (full name), _____
informed by the doctor-researcher (full name)_____
about all aspects of the planned clinical trial.

I received information about the aim and objectives of the clinical trial, information about the methods of examination and treatment, the essence of ultrasound, radionuclide studies and compression treatment, its positive and negative aspects, the benefits and risks of participating in the clinical trial, my rights and responsibilities. I have been warned about possible complications and adverse events of ralionuclide testing and compression treatment, and about my actions in the event of these complications.

I had the opportunity to discuss with the research doctor all the questions that interested me and was satisfied with the answers I received.

I am informed that I will be included in the study only after I have undergone a complete examination (in accordance with the Protocol) and my medical and physical condition meets the conditions for inclusion in this study.

I voluntarily, knowingly agree to take part in a clinical study devoted to the study of venous outflow from the pelvis and lower limbs and the possibilities of compression treatment of various disorders of venous outflow from the lower limbs. I am informed that I have the right to refuse or at any time to discontinue participation in this study.

I agree to follow instructions, cooperate in good faith with the study physician, and immediately report to him any problems with my health.

I am advised that if my health is harmed by compression treatment or a medical procedure covered by a clinical, ultrasound or radionuclide study plan, I will receive medical treatment that will be reimbursed by the insurance company with which I am insured.

I am informed that information about me and the results of my examination will be confidential and can only be disclosed to official representatives while maintaining anonymity.

By signing the Informed Consent form, I give my permission to access the medical data obtained in the study by those responsible for conducting the clinical trial, representatives of the Ethics Committee, and official representatives of the Ministry of Health of the Russian Federation.

I received a signed and dated copy of the Patient Information with a 5-page informed consent form.

Patient's signature

Full name patient

Date

(filled out by the patient)

Signature of the research physician

Full name doctor-researcher

Date

(filled out by the research doctor)