



Research Article

A RETROSPECTIVE STUDY AND SCREENING MODELS FOR VARICOSE VEINS

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ABSTRACT

A varix is an abnormally dilated blood vessel with a tortuous course. Varices usually occur in the venous system, but may also occur in arterial or lymphatic vessels. Varicose veins have no specific cause. Varicose veins are more common in women than in men and are linked with heredity. Other related factors are pregnancy, obesity, menopause, aging, prolonged standing, leg injury and abdominal straining. Venous reflux is a significant cause; research has also shown the importance of pelvic vein reflux (PVR) in the development of varicose veins. Varicose veins in the legs could be due to ovarian vein reflux. There is increasing evidence for the role of incompetent perforator veins in the formation of varicose veins and recurrent varicose veins. Furthermore, in this we discussed about possible in vitro and in vivo screening models available for varicose veins.

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INTRODUCTION

Veins that are lengthy, dilated, and twisted are known as varicose veins. The Latin word “varix,” which meaning twisted, is where the word “varicose” originates. Depending on their size and anatomical location, varices can occasionally be categorized as trunk, reticular, or hyphenweb kinds.[Lim CS 2009]

Varicose veins are subcutaneous veins that, when measured while the patient is standing, have dilated to a minimum diameter of 3 mm. They are a portion of a spectrum of chronic venous illnesses that extends from less than 1 mm tiny telangiectasias, popularly known as spider veins, and 1 to 3 mm reticular veins to chronic venous insufficiency, which can cause venous ulcers, hyperpigmentation, and edema. The most widely used terminology to characterize chronic venous disease is CEAP (clinical, etiologic, anatomic, pathophysiologic) [Raetz J, 2019]. Veins move blood from body to heart. When the valves in the veins weaken, they allow blood to flow backward and pool in the veins. It may even pose a threat to life and result in the amputation of the limb that is impacted.

Table with 2 columns: Clinical Classification (C1-C6) and Description (Mild, Moderate, Oedema, Pigmentation, Eczema, Lipodermatosclerosis, Atrophie blanche, Healed ulcer, Active ulcer)

About 25% to 33% of people in Western nations, where leg chronic venous disease is common, suffer from varicose veins. Chronic venous insufficiency (CVI) is associated with fewer skin abnormalities, but ulceration is a serious side effect that requires careful healing and returns in at least two thirds of patients. The condition affects 61% of women and 38% of men in the adult population, according to Polish epidemiological research involving over 40,000 cases. Certain epidemiological studies suggest that there may be an inverse proportion, although overall there seems to be less variation in the disease’s occurrence across the sexes. Varicose veins are defined as long, dilated, and twisted veins [Lee AJ 2015].

Table with 2 columns: Clinical Classification, Description



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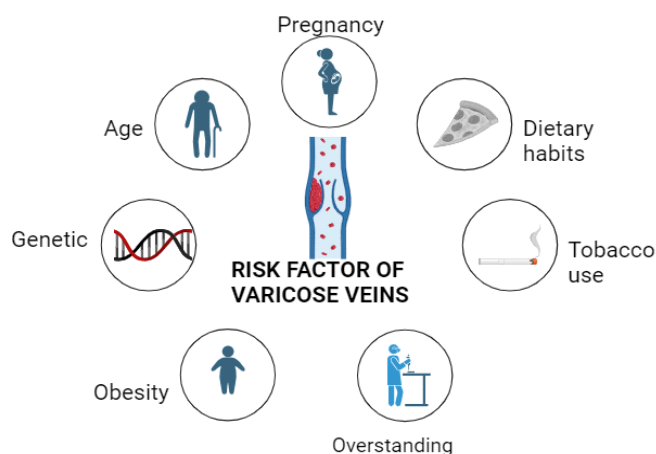
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PATHOPHYSIOLOGY

Varicose vein pathophysiology venous hypertension, a condition in which the veins' defective valves permit blood to flow backward (reflux), is frequently cited as the major cause of varicose veins. Vascular dilatation and tortuosity are brought on by elevated venous pressure in this situation. The hypothesis of primary valvular incompetence postulates that some people may be born with an insufficient number of valves or with genetically weak valves that weaken with age, causing progressive venous dilatation and varicosity formation. Research on the histology of varicose veins has demonstrated a notable increase in collagen production and a disruption of the layers of muscle fibers in comparison to normal veins. The lack of efficient contraction caused by this structural alteration contributes to varicosities development and dilatation. Vein-wall weakness and valve incompetence are closely related. Venous dilation brought on by hypertension may cause the valves to stretch and malfunction, worsening reflux and raising venous pressure even more. The disease is sustained by this dilation and incompetent valve cycle. The formation of varicose veins can also be attributed to incompetent perforating veins, which link the superficial and deep vein systems. Their incapacity can exacerbate venous hypertension and accelerate its evolution, even if they are not usually the main cause. [Fan CM 2003]

RISK FACTOR:

People who work occupations that need them to stand a lot and those who are older are more likely to have varicose veins. The theories that varicose veins are more common in some populations due to social class, smoking, or heredity are not well-supported by the available data. In women, but not in males, obesity is linked to the development of varicose veins. [Sumathi L,2022]



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Pregnancy

Twenty to forty percent of pregnant women have lower extremity varicose veins, accounting for 5.6% of all extragenital

pathology during pregnancy. Pregnancy is the primary cause of the disease's symptoms in 67.2% of individuals with lower extremity varicose veins, and also aggravates the condition in 10.9% of cases. When lower extremity varicose veins occur during pregnancy, the relationship between the condition and altered hormone levels is confirmed when 12% of expectant mothers receive a diagnosis during the first trimester. The illness is discovered in the second trimester of pregnancy in 87.9% of instances. This is particularly valid for women who are expecting, giving birth, or going through the postpartum phase.

The risk of thrombotic problems multiplies several times during pregnancy. Furthermore, 5.5 times as many cases of venous thrombosis and pulmonary thromboembolism are reported in pregnant women compared to non-pregnant women, and 3-6 times as many cases are reported after childbirth compared to pregnancy [London NJ,2000].

Genetics

They showed that the chance of developing varicose veins was 20% in cases where neither parent had the disorder, 25% in cases where men and women had the problem, and 90% in cases where children had parents with the condition. This suggested autosomal-dominant inheritance with variable penetrance. Both inherited and environmental influences can cause changes in the local RNA expression of a gene. Regulation elements located elsewhere in the same gene and signals from other genes can change the expression of the promotor region of a gene. This is complicated by the processes of epigenetics and the effects of microRNAs on genes. Consequently, the relationship between the genome sequence, gene expression, and cellular dynamics cannot be fully explained by gene expression data alone. Furthermore, a limited approach that is frequently employed in numerous investigations is looking simply for genetic polymorphism variation inside the promoter regions of genes demonstrating variable RNA production. [Dustova NK,2019]

Obesity

Obesity and other diseases are associated with increased femoral vein pressure and diameter and decreased femoral vein flow. As a result, there may be less shear stress and possibly more inflammation. These central effects are likely to favour the onset and progression of lower limb venous disease in the old and immobile, even though improved calf muscle pump function may be able to counteract this increase in venous outflow resistance in young, otherwise fit persons (LLVD). An disparity between the amount of energy required by the body for obesity is caused by a multitude of biological processes, such as physical development, activity, and health maintenance. Being overweight or obese is one of the risk factors for varicose veins. This is because the foot cannot support the weight of the body, which restricts blood flow and results in the development of varicose veins in the foot. Larger, unusually shaped veins that usually appear on the feet are called varicose veins. Varicose veins on the legs affect one in five people; women are more prone than men to develop them. Varicose veins occur when one or more valves cannot seal. This weakens the blood vessel walls even more by stretching the veins and slowing the flow of blood. Vein weakening causes an increasing number of valves to lose their

ability to seal correctly. Gradually, the veins grow larger and more pronounced, resembling thick, twisted chains beneath the skin. [Krysa J ,2012]

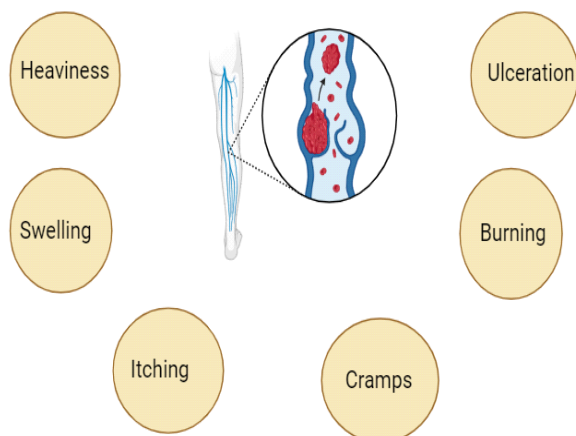
Diet

In patients with diverticular disease, the development or progression of varicose veins may have been facilitated by constipation and a low-fiber diet. The lipid profiles of patients with varicose veins are usually normal. Consequently, despite contradictory data, nutrition may have some bearing. [vies HO]

SYMPTOMS

Leg discomfort is typically the most frequently reported symptom among individuals with venous illness in population-based research. In the National Venous Screening Program, 77% of patients reported having leg pain; 29% reported having moderate pain, and 19% reported having severe or excruciating pain. Legs that are tense, heavy, painful, aching, swollen, itchy, and restless are common symptoms.

COMMON CAUSES OF VARICOSE VEINS



The majority of patients report that standing for an extended amount of time or sitting with their legs in a dependent position makes their pain worse. Discomfort related to ankle edema is often less noticeable in the morning and more noticeable in the evening. Walking or other workouts utilizing the calf muscle pump may help some people with their symptoms, although this is not always the case. [Widyarningsih TS,2018]

The distal limb primarily the ankle and lower calf is usually where the worst symptoms are observed; however, certain reflux patterns may create symptoms in their patients that are related to the sites of normal venous hypertension. Despite the fact that there is much overlap with other Diseases of the lower limbs that can cause discomfort, edema, and pain are frequently signs of venous insufficiency. In addition to diseases that might be associated with venous insufficiency, the patient’s medical history and physical examination could reveal signs of musculoskeletal issues. These ailments include renal insufficiency, congestive heart failure, arthritis, and other illnesses as well as reasons for discomfort in the central nervous system. [Cesarone MR,2002]

EPIDEMIOLOGY

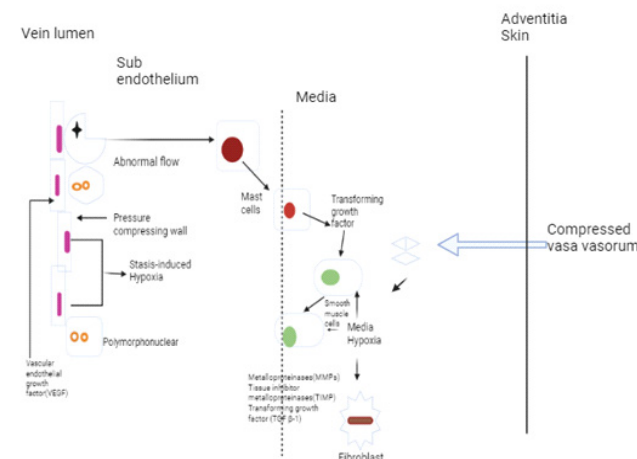
Venous disease is extremely common; cases similar to this

have been reported worldwide. Spider veins are small, dilated intradermal venules with a diameter of about 1 mm that can be found in up to 80% of persons. The prevalence of varicose veins varies; reports range from 20% to 64%. [Renitha K,2015]

Primary varicose veins

Primary varicose veins (PVs) typically affect the lower limbs and are dilated, incompetent superficial veins. They are the most common symptom of chronic venous insufficiency and have the following traits. Anatomical abnormalities in the venous wall, familial predisposition, and elevated venous pressure are often associated with the development of primary varicose veins. Unlike subsequent varicose veins, primary varicosities are not caused by earlier deep vein thrombosis or other underlying venous diseases. One of the primary causes of the development of varicose veins is valve incompetence. Intravenous valve problems result in increased vein pressure and retrograde blood flow. Studies reveal that the composition of the connective tissue in varicose veins varies, including the amounts of collagen and elastin. This variation may weaken the venous wall and result in dilatation. Prolonged sitting or standing may make the condition worse by increasing vein pressure. [Marston WA,2010]

Secondary varicose veins



Secondary varicose veins may be caused by underlying illnesses that lead to elevated venous pressure and damage to the venous valves. Unlike primary varicose veins, which are typically caused by genetic valve incompetence, secondary varicose veins are often associated with other medical disorders, such as Deep Vein Thrombosis (DVT): Vascular thrombus in a deep vein can damage the valves, causing reflux and varicose vein development. Long-term Venous Insufficiency (LDVI): This condition is brought on by the veins’ inefficiency in returning blood to the heart, usually due to obstruction or dysfunction.

Trauma or Injury Secondary varicosities may be brought on by modifications to the venous architecture brought on by previous leg injuries. Blockage Conditions that obstruct blood flow, such as tumors or other masses, can result in increased venous pressure and the subsequent development of varicosities. Secondary varicose veins can also result in skin changes, discomfort, and swelling like primary varicose veins. They may also be connected to more significant issues like venous ulcers or skin infections due to the underlying venous insufficiency.

Usually, the underlying cause of secondary varicose veins needs to be addressed for optimal management. This could involve anticoagulation for DVT, compression therapy, or surgery to return normal venous function. [Bootun R,2016]

MECHANISM OF ACTION

Complex interactions between biochemical, physiological, and structural components mediate their production.

Mechanism of venturination and dysfunctional valve formation in varicose veins. Venous valve problems are the primary cause of varicose veins since they normally prevent blood from flowing backward. Venous pressure increases and blood can reflux (flow backward) in varicose veins when these valves malfunction. This reflux may be the result of structural changes. Primary structural changes in the valves could make them “leaky,” which would worsen reflux and result in additional changes to the venous wall. Furthermore, in the vicinity of the valve junctions, there may be localized dilatation of the venous wall, which may have the secondary effect of valve incompetence.

By increasing the hydrostatic pressure inside the veins, this makes the condition worse. Differences within the Venous Wall. The increase in venous pressure causes significant structural and functional changes in the vein wall. The metalloproteinases, or matrix MMPs, Elevated venous pressure causes an increase in the expression and activity of MMPs, which are enzymes that break down extracellular matrix proteins. This degradation leads to vein dilatation and weakening, endangering the structural integrity of the vein wall. inflammatory reaction Leukocyte infiltration and activation are hallmarks of the inflammatory response that is triggered by increased pressure-induced endothelial cell injury. Fibrosis is aided by this inflammation and can result in varicose veins and chronic venous insufficiency (CVI). It also plays a part in further harm to the vein wall. The Function of Hydrostatic Pressure The hydrostatic pressure in the venous system can lead to matrix degradation in individuals with a genetic predisposition, obesity, or a prolonged standing period, among other potential contributing variables. The mechanical stretch caused by high pressure activates MMPs. It causes the vein wall to become even more fragile and the extracellular matrix to disintegrate. Chronic venous blood shortage - cycle of rising pressure and more dilatation brought on by ongoing wall dilatation and valve dysfunction causes varicose veins, a clinical indicator of chronic venous insufficiency [Gandhi RH,1993].

Treatment Methods

The majority of the time, a medical history and physical examination are utilized to identify CVD. A comprehensive clinical history of the patient should consider any pertinent family medical history, individual history of thromboembolism, CVD, or other illnesses, as well as the presence of specific symptoms associated with the disease. To examine the legs for signs of edema, swelling, skin abnormalities, reticular veins, varicose veins in the main and

A physical examination should be performed while standing, taking into account minor saphenous vein basins, scars from healed venous ulcers or procedures. The most often used diagnostic technique is colour duplex ultrasonography, or CDU.

The morpho-haemodynamic changes in the affected limbs can be determined using the CDU, a non-invasive, repeatable, and user-friendly approach. Moreover, anatomical anomalies including varicophlebitis, thrombophlebitis and venous reflux are tested for using CDU. For individuals with severe stages of CVD (CEAP stage 3 and higher), a CDU examination is recommended before to any vascular surgery. Checking peripheral pulses in the lower extremities and recording the ankle brachial index (ABI) are important steps in ruling out peripheral artery disease (PAD). [Sudhakar Pachiappan,2020]

Sclerotherapy

Foam Sclerotherapy

In a minimally invasive method known as foam sclerotherapy, a sclerosant solution—typically sodium tetradecyl sulfate (STS)—is combined with air to form a foam. When varicose veins are injected with this foam, they collapse and are eventually absorbed by the body. A clot forms inside the vein as a result of the foam’s irritation and inflammation of the vein wall. Varicose vein symptoms are lessened and the vein’s appearance is diminished over time as the body absorbs the treated vein. Preparation: Under local anaesthetic, foam sclerotherapy is often carried out in an outpatient setting.

The injection can be guided by an ultrasound, particularly in deeper veins. Infusion the vein that is intended is injected with the foamed sclerosant. Because the foam is visible on ultrasonography, the practitioner can make sure the vein is sufficiently filled. Following procedure care to help maintain the vein tight and encourage healing, a compression bandage or stocking is placed to the treated area after the injection. In order to improve circulation, patients are usually encouraged to walk promptly after the surgery.

Effectiveness research indicates that foam sclerotherapy can be more effective than traditional liquid sclerotherapy, particularly for larger veins. Studies have shown that foam sclerotherapy can achieve vein closure rates of 67-97% within a few weeks to two years post-treatment. Most patients require only one session, but some may need additional treatments depending on the extent of their varicose veins. Advantages minimally invasive Foam sclerotherapy does not require incisions, which reduces recovery time and minimizes scarring. Quick recovery patients can often return to normal activities within a few days, making it a convenient option for those with busy schedules. The procedure is generally less expensive than traditional surgical options, such as vein stripping.

Long-Term Efficacy: Although foam sclerotherapy has demonstrated encouraging short to medium-term results, long-term data is still being evaluated to understand its durability compared to traditional surgical methods. Common side effects include skin discoloration, lumps under the skin, and temporary inflammation. More serious but rare complications can include visual disturbances, chest tightness, and even stroke, especially in patients with pre-existing conditions.

Patients with varicose veins can benefit from foam sclerotherapy, especially those looking for a less intrusive option. Although patients should weigh the advantages and disadvantages of the treatment with their healthcare professional to choose the best course of action for their particular problem, it provides effective outcomes with a relatively short recovery period.[

Atkins E,2008]

Liquid sclerotherapy

Sodium tetradecyl sulfate (STS) is a common sclerosant solution that is injected into the vein during liquid sclerotherapy. This solution irritates the blood vessel's lining, forcing it to collapse and adhere to one another. This results in a blood clot inside the vein. The treated vein gradually disappears from view as the body consumes it. A dermatologist or vascular specialist typically performs the operation in the patient's doctor's office. To reduce the risk of bleeding during therapy, patients may need to refrain from taking certain medications, such as ibuprofen or aspirin. Direct injection of the sclerosant into the vein is done with a tiny needle. During the injection, patients - especially those with bigger veins - may feel some slight discomfort or cramping. Depending on how many veins need to be treated, the total process normally takes between 15 and 30 minutes.

Efficiency Results are often seen by patients three to six weeks after starting treatment. For tiny, superficial veins, liquid sclerotherapy works well; however, foam sclerotherapy or other alternate therapies may be necessary for larger veins. Although studies indicate that foam sclerotherapy may be more effective for larger veins due to its capacity to cover a larger surface area and displace blood within the vein more effectively, liquid sclerotherapy has been shown to be beneficial.

Most common side effects usually goes away in a few days to weeks. Patients may also feel discomfort, redness, elevated areas at the injection site, and bruising. Slight ulceration at the injection site, allergic responses, and inflammation are among the more significant but uncommon adverse effects that may occur. These consequences are uncommon, but have been documented in cases of high-volume foam injections, including visual problems and stroke. For the purpose of determining risks, patients and doctors should review medical histories. Following Surgery: Care following the treatment, the treated area is typically covered with compression bandages or stockings to aid in healing and stop blood from returning to the treated vein. Shortly after, walking is advised for patients to improve circulation. Although patients can usually return to their regular activities right after, they are usually advised to refrain from heavy lifting and vigorous activity for a few days after treatment. For varicose and spider veins, liquid sclerotherapy is a tried-and-true minimally invasive treatment option. It has a short recovery period and removes tiny veins efficiently. To find out if they are good candidates for the surgery and to go over the possible risks and advantages, individuals should speak with their healthcare professional. [Jarošíková R,2023]

Radiofrequency ablation

RFA uses radiofrequency energy to heat and target particular tissues, causing them to be destroyed. Many medical disorders, such as malignancies, irregular heart rhythms, and chronic pain syndromes, are frequently treated with this method. Production of heat, a radiofrequency probe is used in the treatment, and it emits energy, heating the tissue around it. The heat kills the intended tissue, which may include tumor cells or the nerves that transmit pain. Concentrated care RFA is a precise therapy choice since it is made to cause

the least amount of damage to the nearby healthy tissues. RFA is usually carried done in an outpatient environment.

To make the area where the probe will be implanted numb, patients may be given local anaesthetic. To help patients relax throughout the treatment, light sedation may be given in certain situations. To precisely direct the probe to the targeted region, the doctor use imaging methods like fluoroscopy (X-ray) or ultrasound.

After inserting the probe into the region of interest, radiofrequency waves are transmitted. The targeted tissue is destroyed by the heat produced. For instance, in pain treatment, certain nerves may be targeted throughout the process in order to block pain signals. The length of the process varies based on the complexity and number of regions treated, typically lasting 15 minutes to 2 hours. RFA is frequently used to treat disorders with chronic pain, especially those involving the neck, lower back, and arthritic joints. Those who have not responded to prior therapies may have great pain reduction.

RFA reduces the size and symptoms of varicose veins by sealing up the afflicted veins. It is an excellent treatment for this condition. RFA is useful for shrinking tumours, especially those located in the lungs, kidneys, and liver. Patients who are not candidates for conventional surgery frequently use it. RFA is used in cardiology to improve cardiac rhythm control by destroying aberrant electrical pathways in the heart that lead to arrhythmias. Most of the time, patients can go back home that same day. The injection site may bruise or cause mild discomfort, but most people are able to return to their regular activities in a day or two. Follow-up sessions could be required to assess the procedure's efficacy and track progress, depending on the ailment being treated. Typical side effects temporary soreness, bruising, swelling, and discomfort at the injection site are a few of these. Complications can include bleeding, infection, and tissue injury, however these are uncommon. There is a chance of heart block or other arrhythmias in cardiac applications. Before having RFA, patients who take blood thinners or have specific medical conditions may need to address the risks with their healthcare physician.

Especially for chronic pain and varicose veins, radiofrequency ablation is a flexible and efficient therapy option for a number of medical issues. For several people, it is an advantageous option due to its little invasiveness and capacity to accurately target afflicted tissues. Consultation with a healthcare expert is necessary to ascertain whether RFA is suitable for a certain set of circumstances and to comprehend the possible dangers and advantages, just like with any other medical therapy.[Smith PC,2009]

Ambulatory Phlebectomy

Ambulatory phlebectomy is an outpatient procedure that removes superficial varicose veins through a series of small incisions in the skin. Dermatologic surgeons and vascular specialists. Local anaesthesia is used, and patients typically do not feel pain during the procedure. The Procedure marking the veins by using visual examination and doppler ultrasound to mark the veins to be removed. Incisions Small incisions, as tiny as 1 mm, are made in the skin adjacent to the vein. The incisions are typically 2-3 cm apart. Vein removal by a small hook-like instrument and fine clamps are used to extract the vein in small segments through the incisions. After the

procedure, a compression bandage or stockings are applied to the treated area. Varies based on the number of veins treated. Patients can typically walk immediately after the procedure and resume normal daily activities, with some bruising and swelling. Ambulatory phlebectomy is commonly used to treat visible, bulging. Incisions as tiny as 1 mm are made in the skin adjacent to the vein. After the procedure, a compression bandage or stockings are applied to the treated area. Patients can typically walk immediately after the procedure and resume normal daily activities, with some bruising and swelling. Often the day after the procedure. [Bi M, Li D,2020]

VenaSeal

As a non-thermal treatment for varicose veins, Venaseal seals the problematic vein using cyanoacrylate adhesive, directing blood flow to healthier veins. It is recommended for patients with symptomatic venous reflux illness for the permanent closure of superficial truncal veins in the lower extremities, such as the great saphenous vein. Under local anaesthesia, the process usually takes 45 to 60 minutes. To guarantee precise implantation, a catheter is put into the vein with the use of ultrasound guidance. Using a catheter, the medical adhesive is injected into the vein. Vein walls are adhered to one another by light external pressure, resulting in vein closure. The catheter is taken out after the glue has been applied, and the access site is covered with a tiny adhesive bandage. VenaSeal to previous procedures, it is a less invasive choice because it doesn't require thermal energy or tumescent anaesthesia. Following the treatment, patients usually have little discomfort and can resume their regular activities right away. Comparing this treatment to other options, studies have demonstrated lower rates of discomfort and bruising along with high closure rates (over 90%) and long-lasting symptom relief. It is common for the treatment site to experience some pain, itching, or inflammation, which normally goes away in a few weeks. Deep vein thrombosis and allergic responses are uncommon but possible side effects.

When treating varicose veins, the VenaSeal closure system offers a safe and efficient substitute that improves quality of life, significantly reduces symptoms, and requires little recovery time. If this treatment is appropriate for their particular illness, patients should speak with their healthcare professional. A type of hosiery called compression stockings, sometimes referred to as compression socks, is made to put pressure on the legs and ankles. Deep vein thrombosis (DVT), lymphedema, and varicose veins are just a few of the ailments they are frequently used to treat. By gently pressing the legs, compression stockings enhance circulation by encouraging the blood to return to the heart. [Poder TG,2018]

Compression Stocking

By preventing or lessening swelling, the pressure aids in the reduction of fluid accumulation in the ankles and legs. Compression stockings can ease pain and discomfort in the legs by increasing circulation and lowering edema. Compression stocking types. The greatest pressure is applied to the ankle using these stockings, and the pressure decreases progressively up the leg. They are the kind that are most frequently prescribed for anti-embolism tights for those who are less mobile, such those who are confined to a chair or bed, these stockings are made for them. They aid in the prevention of

thrombi, compression socks available over-the-counter. These stockings don't require a prescription and offer a reduced level of compression.

They are often used for long flights or standing for long periods. Compression stockings come in various compression levels, measured in millimetres of mercury (mmHg) 15-20 mmHg Mild compression, often used for long flights or standing for long periods. 20-30 mmHg Moderate compression, commonly prescribed for varicose veins and edema. 30-40 mmHg Firm compression, applied following surgery or for more serious problems like lymphedema.

To make sure your legs fit properly, it's vital to measure them. Overly tight compression stockings can be painful and limit blood flow, while undersized stockings are ineffective. Wear them first thing in the morning since your legs swell the least in the morning when you first wake up, this is the best time to wear compression stockings. Put them on and go about your day Compression stockings should be worn all day and taken off before bed for optimal effects. Before utilizing compression stockings, it's crucial to speak with a healthcare professional, particularly if you have any underlying medical concerns like neuropathy or peripheral artery disease. When it comes to using and caring for your compression stockings, always heed the advice given by the manufacturer or your healthcare professional.

A proper fit and regular use are necessary for compression stockings to be an effective treatment for a variety of medical ailments. It is imperative that you speak with a healthcare professional to determine the right kind and degree of compression for your unique requirements. [Sadick NS,2005]

Laser Ablation

A popular minimally invasive procedure for varicose veins, endovenous laser ablation (EVLA) focuses on treating the incompetence of the great and small saphenous veins (SSV). With the use of concentrated laser radiation, the venous wall is thermally damaged, causing vein occlusion and successfully relieving venous insufficiency symptoms.

A laser fiber is inserted into the afflicted vein under ultrasound guidance as part of the treatment. The laser fiber delivers precise energy that produces heat, causing steam bubbles that cause the blood to boil and harm the endothelium lining. This technique not only provides better cosmetic outcomes and patient satisfaction, but it also lessens the need for standard surgical treatments, which frequently carry higher risks of problems and longer recovery times.

Studies on patients have shown that EVLA has a high success rate; within a year, more than 90% of patients report effective venous occlusion. Because it combines safety, low invasiveness, and efficacy, EVLA has emerged as the go-to alternative for treating varicose veins, marking a significant development in vascular therapy options. [Gibson K,2017]

Exercise:

Enhances the movement frequent exercise improves blood flow, which is especially advantageous for those who have circulatory problems, such as varicose veins. Building muscle exercise serves to promote and enhance the function of the veins by strengthening the leg muscles. Managing your weight

keeping a healthy weight lowers the strain on the veins and lowers the chance of varicose vein development. Exercise improves happiness, energy levels, and cardiovascular health.

Being physically active can lessen the chance of developing new varicose veins and stop existing ones from getting worse. Exercise can help patients recover from varicose vein therapy and get better results overall. Minimal - Efficiency aerobic exercises moving while walking an easy and efficient technique to encourage movement. Without straining the legs, swimming offers a full-body workout.

Exercises particular to the legs raising calf elevate your heels while standing on the edge of a step, then bring them down. Strengthening the calf muscles through exercise aids in the heart's blood pumping function. Leg rises to strengthen the thigh and calf muscles, elevate one leg at a time while lying on your back. Exercises for flexibility and stretching exercises can increase muscular tensile strength and flexibility, which may help ease the pain brought on by varicose veins. Suggestions for efficient physical activity. On most days of the week, try to get in at least 30 minutes of moderate activity. Stop exercising and see a medical expert if you feel any pain or discomfort. Start with shorter workouts if you're new to exercising, and then progressively increase the length and intensity. Maintain hydration to stay hydrated, drink lots of water prior to, during, and after exercise.

Exercise is an essential part of living a healthy lifestyle and helps to control varicose veins. Regular exercise helps strengthen leg muscles, improve circulation, and stop varicose veins from getting worse. It can also help slow down the evolution of varicose veins. Before beginning any new fitness program, it is best to speak with a healthcare professional, especially for those who already have medical issues.[Gong JM]

Laser Therapy for Varicose Veins

In endovenous laser treatment (EVLT), varicose veins are heated and sealed up using laser light. Under local anaesthetic, the surgery is carried out under the guidance of ultrasound imaging. The problematic vein is cleansed, and the patient is positioned comfortably. The area is made numb by local anaesthetic. A narrow catheter is inserted into the injured vein under the guidance of an ultrasound, which is utilized to see the vein. The catheter is used to inject a laser fibre into the vein.

The energy released by the laser causes the vein walls to heat up, collapse, and seal shut. Catheter removal following the completion of the laser therapy, the treated region is covered with a compression bandage and the catheter is withdrawn. The advantages of laser therapy minimal interference compared to conventional surgical techniques like vein stripping; EVLT requires fewer incisions and is less invasive. With little recovery time, patients can frequently return to their regular activities soon after the treatment. According to studies, there is a significant degree of success, with treated vein closure rates above 90% after a year.

Patients usually report reduced pain and fewer problems when compared to traditional procedures. At the site of treatment, patients may suffer moderate pain, bruising, or swelling. Usually, these effects go away in a few days. Skin burns, nerve

damage, and deep vein thrombosis are possible side effects, albeit they are uncommon. Patients may not be suitable candidates for EVLT if they have specific diseases, such as severe vascular disease or skin infections. When treating varicose veins, laser therapy is a highly beneficial and less intrusive alternative to traditional surgical techniques. Patients should speak with a healthcare professional about their particular situation to find out if EVLT is the best option for them and to learn about the possible dangers and advantages of the treatment.[Oguzkurt L,2012]

Lose Weight

Dietary Changes

Healthy Diet A diet high in entire foods such as fruits, vegetables, whole grains, lean meats, and healthy fats should be the main focus. This aids in controlling calorie intake and ensuring you receive the essential nutrients. Consider the amounts of food you eat. Measuring serving sizes and using smaller dishes can assist stop overindulging. Eat fewer processed foods that are heavy in fat, added sugars, and empty calories. These foods don't provide you long-lasting satisfaction and can make you gain weight. Water consumption before to meals can aid in decreasing caloric intake and appetite. Try to consume at least 8 glasses (2 litres) of water per day. Observe signs of hunger and fullness. Enjoying your food and knowing when to stop eating can be achieved by eating mindfully and slowly.

Physical Activity

Try to get in at least 150 minutes a week of moderate to intense cardiovascular exercise, such swimming, cycling, or brisk walking. Aim for 300 minutes a week if you want to lose more weight. Include strength training activities twice a week or more. Gaining muscle helps you burn more calories even when you're at rest by raising your resting metabolic rate. Look for ways to maintain your daily activity level. This can be walking during breaks, using the stairs, or participating in physically demanding hobbies.

Behavioural Modifications

Set attainable weight loss objectives, like shedding 1-2 pounds (0.5-1 kg) every week. This strategy is healthier and more sustainable. To keep track of your food intake and exercise, use apps or keep a food diary. Keeping an eye on your development can help you stay responsible and make the required corrections. Think about collaborating with a licensed dietitian or nutritionist, asking friends and family for assistance, or joining a weight reduction support group. Emotional eating can be brought on by high stress. Engage in stress-relieving activities like yoga, meditation, or deep breathing.

Consistency and Patience

Losing weight is a slow process that calls for perseverance and persistence. Instead of looking for short cures, concentrate on adopting durable lifestyle improvements. No matter how tiny, acknowledge and applaud your progress. This can support and strengthen constructive behaviour and motivation. The comprehensive approach to weight loss includes positive behavioural modifications, consistent physical activity, and a balanced diet. You can gradually reach and stay at a healthy weight by implementing small, sustainable lifestyle adjustments. Before beginning any weight loss program,

always get medical advice, especially if you have any underlying medical concerns. [Mahajan DR,2021]

Food for prevention and treatment of varicose vein

Blackberries

Both blackberries and blueberries are well-known for their high antioxidant content, which helps to strengthen veins, reduce inflammation, and promote arterial health. The berries reddish-blue hue also contributes to the improvement of the vascular system and vein integrity. Blackberries contain flavonoids called rutin, which have anti-inflammatory, blood clot-preventing, antioxidant, and vaso-protective properties. Furthermore, blackberries have been shown to lessen capillary sponginess and the chance of developing new varicose veins.

Chia seed or flaxseed

The high-fiber component of flaxseed is well-known for supporting heart health, increasing pressure on the legs and abdomen, and supporting digestive function. If we consume insufficient amounts of fiber, constipation may develop. Varicose veins can occasionally develop as a result of pressure placed on the lower rectum's veins during the process of passing faeces. Flaxseed has the highest concentration of Omega 3 fatty acids (51%–60% Omega 3 oils), among other fatty acids. [Murad MH,2011]

Grapes seeds extract:

The Vitaceae family includes the grape seed that is harvested from *Vitis vinifera* seeds. Strong antioxidants known as oligomeric proanthocyanidins (OPCs) are found in it; in lab and animal tests, OPCs have been shown to increase blood vessel elasticity and reduce the likelihood of fluid leakage, which is the primary cause of leg swelling frequently linked to varicose veins. The antioxidant activity of grape seed extract not only solves the issue of varicose veins, but it also has the ability to shield skin cells, prevent the breakdown of collagen beneath the surface of the skin by enzymes, fortify capillaries, encourage healthy circulation, and effectively deliver nutrients to the skin. The medication assists in lowering blood pressure to the normal range, widening narrowed blood vessels, and increasing capillary permeability. It was also discovered to be beneficial in lessening the varicose vein-related edema, irritation, and pain.

Citrus fruit

Lemon, sweet lime, orange, and grapefruit are just a few of the citrus fruit family's well-known members that are nutrient- and vitamin-rich and help maintain strong, healthy bodies. The antioxidants in these zesty citrus fruits help prevent free radicals from damaging blood vessels. Delicious citrus fruits that are widely available have the potential to prevent varicose veins and save lives. Incorporate it into your diet on a regular basis. [Periyasamy S,2020]

***Aesculus hippocastanum* (Horse Chestnut)**

The most commonly prescribed oral treatment for venous edema in Germany is plant extract. Approximately twenty clinical trials have been conducted on the condition and have shown promising results; as a result, the German Commission E has approved the use of plant extract for the treatment of CVI. Additional reports have also supported the use of plants to

treat CVI. Horse chestnut seed extracts (HCSE) are believed to contain a complex mixture of saponins, also known as aescins, together with tannins and flavonoids. Aescins are responsible for the pharmacodynamic effects of horse chestnut, including its anti-oedematous, anti-inflammatory, venotonic, and free-radical scavenging qualities, according to recent studies. [Devi MA,2014]

Fluoric acidum (Hydrofluoric acid)

For ulcers and persistent varicose veins, especially in women with many children, fluoric acidum is used. It is also typical to have eating pain and weakening enlarged blood vessels. The person also wishes to move quickly when walking. When they diminish from touch, sitting, sleeping, warmth, and evening hours, a cold shower will improve symptoms.

Hamamelis (Witch Hazel)

Homeopathic witch hazel, or hamamelis, is used to treat varicose veins in the thighs and legs that are clogged, swollen, painful, or great. The remedy might improve leg overloading, bleeding, and flow. Regular sensations of discomfort, stinging, and freezing run down the legs. Side effects are enhanced by rest and activity in any event, they are made worse by jolting, warmth, touch, sitting, and weight. [31]

MODELS USED FOR SCREENING OF VARICOSE VEINS

***In Vitro* Method**

Smooth muscle cells (SMCs)

In order to evaluate the biological behaviours of the smooth muscle cells (SMCs), the individuals with varicose veins and those with normal veins had their saphenous veins cleaned and the cells were cultured. SMCs were specifically isolated from explants of the veins' medial layer and cultivated in Dulbecco's modified Eagle medium, which was enhanced with additional nutrients and fetal bovine serum. After allowing the cells to multiply, their properties were assessed using a variety of assays. Several crucial strategies were used in the assessment processes. Multiplication of cells: Cell counting and [3H]-thymidine incorporation techniques were used to measure this. To quantify DNA synthesis and total cell growth, cells were first synchronized in serum-free medium and then stimulated with fetal bovine serum. Assay for Migration: The migratory potential of SMCs was assessed using a scratch wound migration assay. 48 hours after making a wound in a confluent cell layer, the amount of cell migration into the wound area was measured. Protein expression analysis: Matrix metalloproteinase-2 (MMP-2) and phenotype-dependent indicators were assessed for expression by Western blotting. The cells' protein extracts were examined for particular indicators of SMC differentiation. collagen synthesis: By incorporating L-[3,4-3H] proline into freshly generated proteins, collagen synthesis was evaluated and insights into the extracellular matrix creation by SMCs were obtained. In this investigation, varicose vein and normal vein patients' saphenous veins were used to separate smooth muscle cells (SMCs). After that, these cells were cultivated to ascertain their biological characteristics. SMCs were extracted from explants of the medial layer of the veins and cultured in Dulbecco's modified Eagle medium supplemented with fetal bovine serum and extra nutrients. The cells were subjected

to additional tests to evaluate their characteristics after being given time to proliferate.

The assessment procedures made use of a number of critical tactics. Multiplication of Cells: Cell counting and [3H]-thymidine incorporation techniques were employed to measure this. Cells were first synchronized in serum-free media and then stimulated with fetal bovine serum in order to assess DNA synthesis and total cell growth. Test of Migration A scratch wound migration experiment was used to evaluate the migratory potential of SMCs. 48 hours following the creation of a wound in a confluent cell layer, the migration of cells into the wound area was measured. Analysis of Protein Expression: The expression of phenotype-dependent markers and matrix metalloproteinase-2 (MMP-2) was evaluated by Western blotting. .. We looked for distinct indications of SMC differentiation in the cell extracts that contained proteins. In order to assess the synthesis of collagen and provide information about the extracellular matrix production by stem cell-like particles, L-[3,4-3H] proline was added to newly produced proteins. [Gawas M,2022]

Endothelial Cell Monolayers

Human saphenous vein segments were extracted from patients undergoing various surgical procedures. To maintain their viability, the segments were promptly submerged and placed in oxygenated Krebs solution. mounting these in order to keep them viable. Following their installation, these vein segments were placed in a specially constructed bypass circuit and subjected to two distinct flow patterns: either non-pulsatile flow representing venous conditions or pulsatile flow mimicking arterial conditions. After 90 minutes of monitoring the impact of flow on endothelial function, the veins were perfused with oxygenated Krebs solution at regulated temperatures. A number of evaluation methods were used to gauge the endothelial cells' survival and functional responses. The effect of flow on endothelial function was observed for ninety minutes, and then the veins were perfused with oxygenated Krebs solution at controlled temperatures. Techniques for Evaluation The survival and functional responses of the endothelial cells were assessed using a variety of evaluation techniques. Assessment: To determine the cells' vitality: Viability Assessment: Tissue ATP concentration was measured, and the values obtained were compared between exposure to varied flow conditions before and after to ascertain cell viability. Vasomotor Response Testing: The veins responses to a variety of pharmacological medications, including bradykinin, substances, such as phenylephrine, sodium nitroprusside, and bradykinin, were assessed by the use of organ chamber testing. Because of this, relaxation responses that were permitted for the assessment of endothelium-dependent and independent responses could be evaluated. The tissue ATP concentration was measured and the findings were compared before and after exposure to different flow conditions in order to determine the vitality of the cells. Vasomotor response testing: The veins' responses to a variety of pharmacological medications, such as bradykinin, sodium nitroprusside, and phenylephrine, were assessed using organ chamber testing. This allowed for the evaluation of relaxation responses.

Immunohistochemistry: This method evaluated the expression of leukocyte adhesion-related proteins, including CD31,

E-selectin, P-selectin, and ICAM-1, as well as the preservation of endothelium. The quantification of staining regions for these proteins was achieved by computer-aided image analysis. Endothelial Cell Isolation and Culture: Using collagenase digestion, endothelial cells were extracted from saphenous veins and cultivated in plates coated with fibronectin. A modified ELISA approach was used to evaluate the upregulation of ICAM-1 in response to various flow conditions, which were both endothelium-dependent and independent.[Gami B,2011]

IN VIVO Models

Deep venous thrombosis (DVT)

Mice weighing between 20 and 25 grams (g) were anesthetized with 2% isoflurane, put in a dorsal recumbent position, and an aseptic midline laparotomy was used to reach the inferior vena cava (IVC). 7–0 Prolene sutures were used to ligate the venous side branches. The back branches held their patent. A 25G stainless-steel needle connected to a 30G silver-coated copper wire KY30-1-GRNis placed against the anterior wall (anode) of the exposed caudal IVC in the electrolytic IVC model (EIM). The circuit is completed by implanting a second wire subcutaneously (cathode). A range of current intensities applied for 10 to 45 minutes (min) at 100 to 300 micro-amperes (μ Amp) were evaluated to determine the ideal settings for consistent thrombus development (data not shown). Grass S48 square wave stimulator and constant current unit were used to apply a current of 250 μ Amp for 15 minutes. The electrolysis products produced by the direct current damage the endothelium surface of the IVC, creating an environment that is thrombogenic and encouraging the formation of thrombus. Without using any current, the needle was inserted into the IVC for 15 minutes in sham animals. To confirm the existence of a blood flow channel, ultrasound (US) imaging of the IVC was performed at baseline and two days after EIM. To evaluate plasma sP-Sel during euthanasia, blood was drawn via cardiac puncture, and the IVC/thrombus was removed for thrombus weight (TW), morphometrics, P-selectin and vWF staining, scanning electron microscopy (SEM), and transmission electron microscopy (TEM).[Hooda R,2018]

Ferric chloride induced venous injury

During the preparation, isoflurane was used to induce anaesthesia in male Sprague-Dawley rats weighing 327±370 g. Subcutaneous (sc) administration of the analgesic buprenorphine (0.03 mg/kg) and glucose (50 mg/ml), 1 ml (Pharmacia), was performed prior to the cessation of the initial anaesthesia. All animals in the experiment were housed in separate cages with free access to food and water throughout their stay. The oral and subcutaneous injection of the medication or vehicle preceded the anaesthesia by 15 ± 20 min. The inferior vena cava was visible when the abdomen was opened after anaesthesia by a midline incision. Just caudal to the left renal vein, a blunt needle measuring 0.9 mm and 20G was used to tie a cotton thread tightly around the vein to create a stenosis in the inferior vena cava. After that, the needle was taken out. The exterior surface of the inferior vena cava, caudal to the stenosis, was then treated with a circular piece of filter paper, 5 mm in diameter, containing 3.5 ml of ferric chloride (8% w/w) dissolved in water, iron(III)- chloride hexahydrate, FeCl₃. The application was left on for five minutes before being removed.

The viscera was covered with 1.5 ml of warm saline, the skin and muscle layers were sewn up in two layers using 3±0 silk surgical sutures, and the inhalation anaesthesia was stopped. The animal was re-anesthetized 1, 3, or 5 hours after the ferric chloride was applied. After reopening the abdomen, blood samples were taken in 0.13 mol/l trisodium citrate (9:1) from the aorta to be analysed for melagatran or anti-FXa activity in plasma. The inferior vena cava was opened, the rat's heart was sliced, and the thrombus was removed to determine its moist weight right away. Each rat had two doses, one subcutaneous injection (1 ml/kg) and one peroral administration (5 ml/kg), via gavage, 30 minutes prior to the placement of the inferior vena cava stenosis, in a randomized research that effectively blinded the technician. The study included four groups of thirty rats each: subcutaneous (saline) and oral (water); oral H 376/95 (10 mmol/kg) plus subcutaneous vehicle; subcutaneous H 376/95 (3 mmol/kg) plus oral vehicle; and subcutaneous dalteparin (120 IU/ kg) plus oral vehicle. Ten rats were killed in each of these four groups at the one, three, and five-hour marks following the administration of the ferric chloride. [Xiao Y,2009]

Thrombosis in the deep iliac vein

Six healthy domestic pigs with a mean weight of 46.5 kg had their deep iliac veins induced to thrombosis using 12 different methods. The governmental committee on animal affairs gave its approval to the protocol. A solution of thiopental (3–30 mg/kg body weight and hour) was injected into an ear vein as needed following an intramuscular injection of 30 mg ketamine, 2.5 mg xylazine/kg of body weight, and 1 mg atropine/animal for premedication. Throughout the entire experiment, mechanical ventilation was maintained and the animals were intubated. In order to insert two 10F sheaths, the jugular vein underwent surgical preparation on both sides. A 0.035-inch hydrophilic guidewire and a 4F multipurpose catheter were used to catheterize the iliac veins on both sides through the sheaths. By administering intravenous contrast media, the common femoral vein and the iliac veins may be seen during fluoroscopy.

After that, 6F sheaths were inserted and the femoral veins on both sides were pierced. Two occlusion-balloon catheters were inserted into the common iliac veins via the jugular approach. To minimize blood flow during homeostasis and maximize the likelihood of effective thrombus induction, each balloon catheter was inflated close to a segment with minimal collateralization. Then, for thrombus induction, a 3-ml solution of Thromborel was gradually administered distal to the balloon (via the balloon catheter's guidewire lumen). The balloons were deflated after an hour, and to demonstrate the existence and severity of thrombosis, computed tomography (CT) and fluoroscopy were carried out as detailed further in the text. Digital subtraction angiography (DSA) and CT

scans showing visible thrombus material across a distance of [60 mm] were considered to have successfully induced thrombus. Furthermore, pulmonary artery CT was y o n e both following mechanical thrombectomy and thrombus generation. [Golledge J,1997]

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