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Original Research Paper

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VARICOSE VEINS – REFLECTION OF FACTS

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ABSTRACT Varicose Veins are abnormally dilated, tortuous & serpiginous veins of the Superficial Venous System (GSV/SSV) seen in the lower limbs. They can be caused by existing /inherited valve dysfunction, decreased vein elasticity, or valve damage from prior thrombotic events. The result is pooling of blood in the veins, increased venous pressure, and subsequent vein enlargement. As a result of high venous pressure, branch vessels balloon out, leading to varicosities. Varicose veins are likely a result of multiple genetic and environmental factors, rather than a single gene mutation. The mere presence of genetic predisposition does not guarantee that a person will develop varicose veins, but lifestyle factors such as prolonged standing, obesity, prolonged hormonal therapy, and certain conditions that demand prolonged bed rest without activities of the lower limbs, like Orthopedic surgeries, Trauma, etc.

KEYWORDS : VHL (Von Hippel-Lindau syndrome, Hyperhomocysteinemia (HH CY), LDS (Lipo dermato sclerosis, Thrombophlebitis, Chronic venous insufficiency (CVI),Sclerotherapy

INTRODUCTION

Varicose veins are characterized by subcutaneous dilated, tortuous veins greater than or equal to three millimeters, involving the saphenous veins, saphenous tributaries. (1)

Varicose veins are considered a common clinical manifestation of chronic venous disease.(2)

Not withstanding the cosmetic challenges with varicose veins, the associated superficial axial venous reflux should be evaluated.(3)

Varicose vein entity includes a vast majority of clinical and pathological manifestations, from limited leg discomfort to swelling and non-healing ulcers.(4,5)

Varicose veins constitute a progressive disease, and remission of the disease does not occur, except after pregnancy and delivery. (6)

Multiple intrinsic and extrinsic factors include - age, gender, pregnancy, weight, height, race, diet, bowel habits, occupation, posture, previous DVT, and genetics.(7)

Varicose vein is one type of venous insufficiency which falls under the broad heading of superficial venous disease(8)

Varicose veins are ectatic, tortuous vessels of the superficial venous system that are at least 3 mm in size, are a common problem with significant impact on the patient's quality of life. (9)

They are more than a simple cosmetic issue; the presence of varicosities carries an increased risk for the development of superficial vein thrombosis.(10)

Dilatation of varicosities may be due to failure of these valves in the lower extremity, allowing backward transmission of the pressure gradient from the deep system to the superficial through the saphenofemoral junction (SFJ) (11)

Anatomic, ultrasound, and plethysmographic studies have demonstrated that the presence of valvular incompetence is widely distributed throughout the leg in affected individuals. (12,13)

Increased venous pressures have been shown to correlate with increased severity of disease (14)

Varicose veins are part of the spectrum of chronic venous disease and include spider telangiectasias, reticular veins, and true varicosities.(15)

Generalized symptoms consist of aching, heaviness, cramping, throbbing, restlessness, and swelling in the legs (16)

Symptoms are often worse at the end of the day, especially after prolonged standing, and usually resolve when patients sit and elevate their legs. Women are significantly more likely than men to report lower limb symptoms (17)

Signs of a more serious underlying vascular insufficiency may include changes in skin pigmentation, eczema, infection, superficial thrombophlebitis, venous ulceration, loss of subcutaneous tissue, and lipodermatosclerosis (18)

When venous disease is severe or interventional therapy is being considered, venous duplex ultrasonography is the modality of choice (19)

Treatment options for varicose veins include conservative management and interventional therapies such as Endo venous thermal ablation, endovenous sclerotherapy, and surgery (20)

What are Varicose Veins?

Varicose Veins are abnormally dilated, tortuous & serpiginous veins of the Superficial Venous System (GSV/SSV) seen in the lower limbs. Varicose Veins are seen only in human beings (A consequence of erect posture).

Causes of Varicose Veins:

This can be broadly divided into 02 categories –

1) (A) Hereditary – Transmission of defective genes to progeny
   (B) Genetic – Causes like gene mutations and others like Hyperhomocysteinemia.
2) Individual / Other Causes

1(A) Hereditary Causes and Genetic Mutations :

Note: Varicose Veins are considered a multifactorial condition, with no single gene is responsible for it, but several genes have been linked to an increased risk of developing the condition, like

- FOXC2 – Mutations in FOXC2 are associated with lymphedema–distichiasis syndrome & varicose veins are commonly observed as one of its phenotypic abnormalities. FOXC2 can lead to primary venous valve failure, which is a major factor in the development of varicose veins.
- EFEMP1, which encodes Fibulin-3, a glycoprotein that helps maintain the integrity of elastic tissues, has been linked to Varicose Veins in some studies.

Other Genes Responsible are :

- MTHFR (Methylene tetrahydrofolate reductase)
- THBD (Thrombomodulin)
- Complement factor B(CFB) – rs4151657 – Recently identified in the complement factor 'B' gene as a risk factor for varicose veins.

It is important to note that varicose veins are likely a result of multiple genetic & environmental factors, rather than a single gene mutation.

VHL (Von Hippel-Lindau Syndrome)

A homozygous cytosine to thymine mutation (598C>T) in the VHL gene is associated with an increased risk of varicose veins.

- PIE 201: Mutations in PIE 201, which encodes a mechanically active ion channel involved in sensing vascular shear stress have been linked to varicose veins & lymphoedema.
- Other genes that are responsible, according to – The National Institutes of Health (NIH) & OAE, are:
- CAS Z1, PPP3R1, EBF1, STIM2, HFE, GATA2, NFATC2, SOX9 & Proteins (MICB, CD209) as potential candidates for varicose vein development.
- The NIH identified 08 varicose veins-related proteins, including 03 deleterious proteins (COLEC 11, IRF3, SARS2) & 05 protective proteins (LUM, POSTN, RPN1, RSPO3, VAT1)

1(B) Hyperhomocysteinemia:

(HH CY) or elevated homocysteine levels is linked to an increased risk of varicose veins, primarily due to its impact on the vein wall development & also thrombosis.

HHCY can damage the inner lining of blood vessels i.e endothelium, leading to increased blood clotting & potentially hindering blood flow in the veins, which can contribute to the development of varicose veins.

Mutations in genes like MTHFR can lead to HHCY, increasing the risk of varicose veins.

- HHCY – Some studies suggest that HHCY can contribute to venous valve failure, which can lead to the development of varicose veins.
- HHCY – is also associated with venous insufficiency, a condition where the veins are unable to properly return blood to the heart. This can lead to increased venous pressure & fluid stasis in the lower limb, further contributing to the formation of varicose veins.

2. Individual / Other Causes for Varicose Veins:

- Advanced Age
- Gender – More of female gender
- Obesity – excess weight puts additional pressure on veins, particularly in the legs.
- Pregnancy – Hormonal changes and the growing foetus can increase pressure on the veins
- Occupations – which demand prolonged standing like Teachers, Lecturers, Security guards, salesmen, shop keepers, Traffic police men, Bus conductors, etc, and prolonged sitting professionals like IT personal and computer operators.

What Happens When Venous Blood Accumulates in the Legs:

- Blood gets accumulated (stagnated) in the veins and leads to over-dilatation and tortuosity of the veins.
- Sometimes these veins rupture & leak blood into the subcutaneous tissue and later turn into blackish skin patches.
- This impure blood contains excess fluid and metals like iron, etc, which will be deposited in the subcutaneous tissues, leading to oedema and hyperpigmentation changes.

The Above Abnormalities Cause the Following Features:

- Dilated visible veins.
- Swelling in the legs / feet.
- Blackish/brownish pigmentation / discoloration of skin (due to subcutaneous iron deposition).
- Dragging pain in the legs, especially on prolonged standing / sitting / lying down postures due to
- Venous Stasis.
- Burning sensation / Tingling & numbness in legs.
- Itching in the legs.
- Cramps, especially at night.
- Skin infections / stasis eczema.
- Venous Ulcers.

Life Cries for so Many Years

Venous insufficiency (also called chronic venous insufficiency or chronic venous disease) is a condition in which the leg veins are damaged, preventing normal blood flow to the heart. In normal vein, a series of specialized, one-way valves work together, opening to allow blood to flow upward and then closing to keep the blood from flowing back toward the feet. Venous insufficiency occurs when valves are damaged or not functioning properly. As the valves deteriorate, blood leaks or flows backward and pressure in the vein increases, stretching and dilating the vessel. Blood pools in the veins of the lower legs, increases the blood pressure in the legs and causing chronic inflammation in the veins.

Bacterial Colonization

The physiological microbial flora of healthy skin is very complex and varies strongly among individuals (21)

This normal flora may colonize the wound; however, it may not necessarily influence wound healing. (22)

Various types of bacteria can be found in chronic wounds; however, an active infection should be distinguished from bacterial colonization. (23).

Microscopic analysis of chronic wound specimens revealed that bacteria in this type of wound tend to form colonies coated by biofilms. Such biofilms are common in chronic wounds; however, very rarely present in acute wound specimens (24)

Pathogenic flora, often found in chronic venous ulcers, includes Staphylococcus aureus and Pseudomonas aeruginosa (25).

Bioactivity of Cytokines and Cytokine Receptors

The cytokine and chemokine family consists of many proteins with differing and partly overlapping functions in innate and acquired immunity.

TNF-α, IL-6, IL-8, and IL-10 are key players in innate host defense. Except for IL-8, these proteins are generally not detectable in the plasma of healthy individuals.

TNF-α, IL-6, and IL-8 levels are risk determinants for venous thrombosis.

Cytokines are a large family of small proteins produced by virtually all cells in the body, including immune cells

In general, cytokine concentrations are low under normal physiological conditions but increase sharply in response to different stimuli (26)

Cytokines, by binding to receptors, activate intracellular signaling pathways, eliciting downstream effects. (27,28)

Wounds normally heal through the sequential but overlapping inflammatory, proliferative, and remodelling phases. (29,30)

Most of our knowledge regarding the temporal and spatial variations of cytokines in wound healing derives from acute surgical wounds (31,32)

Wound healing studies in knock-out mice models that have convincingly shown that deficiencies of cytokines severely impair wound healing, which underscores the importance of cytokines in normal wound healing. (33,34)

The development of VLUs is thought to be initiated through venous hypertension, leading to the extravasation of inflammatory cells (35,36)

It has been suggested that a pro-inflammatory wound environment prevents the healing of VLUs (37,38)

Differences in the composition of the immune cell infiltrate between acute wounds and VLUs have implications for the cytokine network (39)

In contrast, other investigators have hypothesized that an initial temporary state of increased inflammation is important for VLUs to heal (40)

The "White Cell Trapping Theory"

The "white cell trapping theory" posits that elevated venous pressure leads to increased leucocyte accumulation in the affected tissues. causing tissue damage. This activation triggers the release of proteolytic enzymes and free radicals, contributing to inflammation and ulceration. Essentially, the theory suggests that white cells become trapped in the smaller vessels of the affected area, leading to an inflammatory response and tissue damage. White blood cell count is an important indicator of an individual's health condition. An abnormal white blood cell count usually results from an infection, cancer, or other conditions that trigger systemic inflammation responses. Currently, white blood cell count is primarily conducted in centralized laboratories, and it requires specialized equipment and dedicated personnel to perform the test and interpret the results.(41)

Varicose Veins May Increase the Risk of Blood Clots

They are also linked to pregnancy as gestation causes the volume of blood in the body to increase, but reduces the flow from the legs to the pelvis. Obesity and a family history of the condition also increase the risk, says the study. Adults with varicose veins, gnarled, enlarged veins, most commonly appearing in the legs and feet, may be at increased risk of suffering from a blood clot that could lead to vascular diseases, a study has found.

Suffering From Varicose Veins?

Varicose veins may sometimes be painful and the physician might, in extreme cases, even need to suggest surgery. Varicose veins occur when the superficial veins in the skin of the legs dilate (enlarge), and appear on the surface as lumpy, purple-coloured cords. This is often due to the incompetence of the function of the valves in the veins. 42)

Subcutaneous Calcifications in the Legs with Chronic Venous Disease

Calcifications in the subcutaneous layer (SCL) have been described by radiographic studies of legs with advanced chronic venous disease (CVD). However, SCL calcifications have rarely been included among the CVD-related changes.(43)

Clinical Implications and Future Directions:

Future research should delve deeper into the specific characteristics and evolution of dermatologic changes in venous ulcers, potentially paving the way for more nuanced and tailored approaches to diagnosis and management. (44)

Factors Prolonging Healing

Acute wounds physiologically heal within 4 weeks; on the other hand, chronic wounds need a longer time to close, with an average healing time of 6–12 months for VLU. Moreover, it has been estimated that recurrence occurs in about 70% of VLU within 5 years of closure (45)

Several events occur to delay wound closure, including ulcer characteristics, concomitant diseases, patient characteristics, diagnostic delays and inaccuracies, therapeutic interventions, and environmental factors.

A well-known risk factor for recalcitrant ulcers is advanced patient age. Elderly patients generally have reduced mobility as well as lower compliance for compression bandages and garment treatments compared to younger patients. (46,47)

Patients with higher body mass index (BMI > 25 kg/m2) and nutritional deficiencies also have a poor healing prognosis (48)

Conflicting results regarding the volume of exudate, the type and amount of wound infection, and the presence of previous ulceration as potential risk factors for prolonged healing may be important factors in delayed VLU healing [49].

Additionally, a history of venous ligation or vein stripping, a history of hip or knee replacement surgery, ankle brachial pressure index < 0.8, and the presence of fibrin covering greater than 50% of the wound area have been associated With prolonged healing (50)

Among the environmental conditions predisposing to delayed wound healing, it has been reported that colder temperature was associated with increased risk of ulcer development (51)

Biochemical and biomolecular markers of wound healing could be assessed both through wound tissue biopsies (52)

Soluble biomarkers circulating in the blood or released within the wound fluid generally represent crucial regulators of tissue remodelling.(53,54)

Complications:

If the above symptoms are neglected, then it may lead to the following complications.

- Chronic uncontrollable skin infections (stasis/ Eczematous dermatitis).
- Cellulitis (infection of subcutaneous tissues).
- Healing ulcers would turn into Non-healing ulcers.
- Wound infections.
- Superficial vein thrombosis.
- Sometimes the clot / thrombus may get dislodged and propagate to other places & cause thromboembolism e.g. Pulmonary embolism .
- LDS (Lipo dermato sclerosis - inflammation, hardening, and discolouration of the skin subcutaneous tissues)
- Varicose bleeds.
- Thrombophlebitis (Inflammation of the vein endothelium)
- Chronic venous insufficiency (CVI)

Diagnostic Tools:

- After clinical examination by endovascular surgeon, colour Doppler test is the main stay of investigation.
- Rarely requires MR venogram of lower limb.

Precautions:

- Not to stand continuously in one position without movements.
- Weight reduction measures if obese.
- Suggested exercises for the legs.
- Not to walk long distance at a stretch without stockings.
- To wear stockings continuously during daytime.
- Elevation of both lower limbs with pillow underneath in lying down posture.
- Not to sit continuously with legs hanging down for long hours.
- If there is necessity to sit for long time, then legs should be rested on the table / chair.
- In case of ulcers, proper wound care should be taken.

Treatment:

Treatment options can be broadly classified as follows :

A. Conservative line of treatment is indicated in patients who may not require immediate interventions, in whom the procedure is contraindicated, and in whom the procedure is not amenable, etc.

B. Conventional surgery, which includes Ligation / Stripping of superficial veins and their tributaries, is an invasive and associated with long admission time and scarring. Moreover, the results are not as expected.

C. Interventional procedures like – Laser (EVLA – Endovenous laser ablation), RFA and Glue methods etc.

Now a days with the advent of laser, the outcome of the treatment is drastically changed.

LASER is the procedure where superficial vein in the leg is punctured with a needle without cuts. Then laser fiber is introduced into the vein through the needle under ultrasound guidance. After assuring its correct position, firing of laser starts from above downwards occluding the vessel. The vessel then starts shrinking with approximation of its walls over next few days resolving the problem of venous stasis.

Sometimes in few cases, a follow up procedure called SCLEROTHERAPY (ablation of veins by using some chemicals) may be needed to treat the residual dilated varicosities.

Advantages of Laser Therapy:

- Painless procedure.
- No cuts / No stitches / No scars / No blood loss.
- Daycare procedure and daily routine can be carried out within 48 hours after the procedure.
- Can also be done under Local Anaesthesia.
- High success rate / Less complications / Low recurrence rate.

Many contemporary studies show that Laser is superior to RFA (Radio Frequency Ablation).

Recent inclusion is the Glue/venoseal(cyanoacrylate) that is used to occlude the vein. But its role is limited when more than 01 to 02 veins need occlusion.

After all practical experiences, it is the endovascular laser ablation that is far superior to its contemporary methods of interventions.

CONCLUSION

Venous ulcers are wounds on the lower legs brought about by chronic venous insufficiency. Due to blood accumulating inside the vein, pressure builds and bursts open fluid into the neighbourhood tissues. The cause of venous ulcers is high pressure in the veins of the lower leg. The excess fluid that annoys the tissue leads to inflammation and, inturn, tissue conks out. Venous ulcers can occur when the veins in a patient's legs do not push blood back up to the heart. Blood backs up in the veins, building up pressure. If not treated, increased pressure and excess fluid in the affected area can cause an open sore to form. Venous leg ulcers (VLUs) often affect patient care, healing time, and quality of life. Now a days with the advent of laser, the outcome of the treatment is drastically changed. Conventional surgery, which includes Ligation / Stripping of superficial veins and their tributaries, is an invasive.

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