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Varicose Vein Treatment and Its Success Rate

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ABSTRACT

Background: Chronic venous illness is one of the major developing illnesses across the world. Varicose vein leads to major negative consequences, including missed work, pain, discomfort, and a deterioration in quality of life.

Methods: Varicose veins affect people's quality of life and range in incidence from 10% to 30% worldwide Varicose vein treatment options are taken based on a number of factors, including patient preferences, postoperative risk, cost, and the degree of the venous insufficiency.). Varicose vein patients who are asymptomatic are initially treated conservatively with medications, compression therapy, and lifestyle changes. Patients who are symptomatic, on the other hand, are advised to look at surgical options such as radiofrequency ablation(RFA), endovenous laser ablation (EVLA), high ligation and stripping (HL/S) of the incompetent great saphenous vein (GSV), Cure conservatrice et Hemodynamique de Insufficience veineuse en Ambulatoire (CHIVA) , mechanochemical ablation (MOCA) , cyanoacrylate embolization (CAE),etc.

Results: Each treatment is effective in the treatment of each type and each stage of varicose veins and has its pros and cons. This article analysis the varicose vein treatments and discusses the safety, efficacy and success rate of each treatments.

Keywords: Varicose veins, Venous leg ulcers, Great saphenous vein, saphenopopliteal junction, Phlebotonics, Intervention treatment

Introduction

Chronic venous illness was long thought to be a purely aesthetic or psychological issue. However, recent researches indicates that it has major negative consequences, including missed work, pain, discomfort, and a deterioration in quality of life that can be quantified [1]. The blood flow in the veins (calf muscle) prevented from going backward by a network of valves. Blood can flow in both directions in certain persons due to superficial veins, which are veins that reach close to the skin's surface and malfunctioning valves. Varicose veins, also referred to as varicosities, are twisted, protruding veins that can result from this reflux. There are two primary superficial leg veins: the great saphenous vein, which runs from the inner ankle to the inner thigh, and the small saphenous vein, which runs from the outer ankle to the back of the calf [2]. True varicosities, reticular veins, and spider telangiectasias are the various forms of varicose veins that fall under a broad spectrum of chronic venous illness [3]. Family history of venous disease, female sex, advancing age, and persistently elevated intra-abdominal pressure brought on by pregnancy, obesity, persistent constipation, or a tumor are the risk factors. [4]. The CEAP classification categorizes the condition into many stages. The disease first appears as reticular veins and spider veins in stage C1 [5]. In stages C2, simple varicose veins are present. Chronic venous insufficiency is the term used to describe the disease's latter phases. Stage C3 is characterized by oedema without skin alterations. More advanced stages of the condition might result in problems including lipodermato sclerosis or trophic alterations(C4), as well as healed (C5) and active (C6) ulcerations. As such, it may result in the limb being amputated and may even pose a serious risk to life [6]. Less than 1% of people have active venous ulcers, the most serious stage, which affects 3% of patients over 65. Due to the fact that varicose veins are a chronic degenerative condition, their frequency increases with age [7]. The prevalence of varicose vein illness is known to affect 46.7% of women and 27.8% of men, according to an Indian survey. Varicose veins affect people's quality of life and range in incidence from 10% to 30% worldwide [8]. However, 2.6% of women and 1.9% of males are affected each year [9].

Management

Varicose vein treatment options are taken based on a number of factors, including patient preferences, postoperative risk, cost, and the degree of the venous insufficiency [10]. Varicose vein patients who are asymptomatic are initially treated conservatively with medications, compression therapy, and lifestyle changes. Patients who are symptomatic, on the other hand, are advised to look at surgical options such as radiofrequency ablation(RFA), endovenous laser ablation (EVLA), high ligation and stripping (HL/S) of the incompetent great saphenous vein (GSV), Cure conservatrice et Hemodynamique de Insufficience veineuse en Ambulatoire (CHIVA) , mechanochemical ablation (MOCA) , cyanoacrylate embolization (CAE),etc. [11,12].

Venous leg ulcers (VLUs) can form on the distal legs and ankles due to minor trauma or on their own. Individual's health and quality of life, medical expenses, and socioeconomic consequences are all significantly impacted by this cycle of healing and recurrence [13]. Furthermore, global reports indicate that roughly 70% of cases reoccur within three months of healing [14].

A. Conservative Treatment

Conservative treatment options include weight loss, phlebotonics, elevation of the affected leg, exercise, wearing non-restrictive clothing, modifying cardiovascular risk factors, and avoiding prolonged standing, compression therapy and straining. Patients who are pregnant, do not desire intervention, or are not candidates for endovenous or surgical treatments must consider these precautions prior to receiving treatment [11,15].

COMPRESSION THERAPY

A stiff compression dressing is the primary treatment for a (venous Leg Ulcer) VLU. By lowering venous hypertension, compression helps to improve venous return and lessen peripheral oedema. Studies reveal that compression therapy only has a little impact on healing, with up to 50% of VLUs not healing after two years. In addition to compression therapy, pharmacological intervention that

lowers inflammation and lowers the frequency of VLUs would be quite beneficial [16].

Types of Compression Stocking

Graduated or medical compression stocking

• When wearing graduated compression stockings, the level of compression is highest at the ankle and progressively lowers as the garment is worn up.

• They provide a particular degree of ankle pressure and compression gradation.

Antiembolism stockings

• Antiembolism stockings have been used for deep vein thrombosis.

• They are not technically compatible with being used by ambulatory patients; instead, they have been designed for individuals who are bedridden.

Nonmedical support hosiery

• Elastic support stockings and flight socks are examples of non-medical support hosiery that are typically used to ease sore, heavy and exhausted legs[17].

Strength of The Graduated Compression Stocking

There are multiple standards for classifying the pressure degree in Graduated compression Stockings. However, class 1 pressure is defined as less than 20 mm Hg; class 2 pressure is defined as 20-30 mm Hg; and class 3 pressure is defined as more than mm Hg. [18].

Graduated compression stockings resulted to a considerably larger proportion of healed ulcers than bandages. With the stockings, the average time to ulcer healing was likewise reduced by three weeks. Additionally, graduated compression stockings may be less painfl than bandages [19].

According to reports, between 30% and 65% of people do not wear graded compression stockings [20].

B. **Medical Therapy**

Patients who have varicose veins, ankle edema or venous ulcers are prescribed venoactive medications in order to increase capillary permeability and venous tone. Flavanoids, horse chestnut extract, micronized purified flavonoid fraction (MPFF), Glycosaminoglycans and fibrinolytics enhancers are among the often-utilized medications [16,21].

Pentoxifylline was found to be an adjuvant to compression that results in an overall 21% increase in healing rate. Pentoxifylline should be taken into consideration for the use with patients who are unable to tolerate compression bandaging or who prefer not to use [22].

A RCT on mesoglycan reports, venous leg ulcers healed completely at 24 weeks for 97% after the use of mesoglycans [32]. Mesoglycans has demonstrated effectiveness in lowering plasma fractional breakdown rates levels and recurrence risk in individuals with cerebral artery disease, all while maintaining a favourable safety profile [33].

In a RCT, patients received therapy with sulodoxide for as long as 70days VLU healing increased by 52% to 70% [34, 35].

Defibrotide 400 mg three times a day in conjuction with compression was found to be more effective in repairing VLUs [16]. It is not recommended to take defibrotide along with fibrinolytic treatment or systemic anticoagulants [36].

Oral phlebotonic provides symptomatic treatment for varicose veins, it decreases lower limb edema, and CVI-related signs and symptoms includes trophic abnormalities, cramping, restless legs, swelling, and paraesthesia [37].

In addition, antibiotics to avoid wound infection, Diuretics to treat edema and nutritional supplements such as zinc, magnesium, dihydroergotamine and dihydroergocristine have been given to promote wound healing [16].

C. Intervention Treatemrnt

Most lower limb superficial venous disorders are caused by great saphenous vein (GSV) incompetence, which results in varicose veins and venous insufficiency. Surgery (referred to as high ligation and stripping), laser and radiofrequency ablation and ultrasound guided foam sclerotherapy are among the available treatment for GSV incompetence. Cyanoacrylate glue, mechanochemical ablation and endovenous steam ablation are examples of more recent treatments. In order to make informed decisions on the treatment of varicosities in the GSV, these treatments must to be compared [38].

High Ligation and Stripping Surgery

Vein stripping (HL/S) or high ligation of the saphenopopliteal junction (SFJ) with or without vein stripping has historically been the gold

standard of therapy for varicose veins [39]. The typical procedure for long saphenous vein (LSV) VV is disconnecting the saphenofemoral junction (SFJ), stripping the LSV to just below the knee, and a multiple stab avulsion (MSA) [40]. Because of the concerns about an increase in saphenous vein damage, the stripping is often limited to the knee [41].

Morbidity after surgery can include a variety of consequences, with reports indicating that 18% of patients experience DVT, infection, hematomas, lymph leaks and neurosensory loss [42]. In addition, patients frequently need 2 to 3 weeks to recover from surgery, and significant recurrence rates have persisted despite advances in technology [43]. Ligation by alone is typically linked to a high rate of varicose vein recurrence, which might lead to repeat surgery [44].

Ambulatory Phlebectomy

Another common procedure for VV that is typically carried out in outpatient setting is Ambulatory phlebectomy (PB). During this procedure, many skin incisions are made in order to remove the tributary veins of the saphenous vein by busing phlebectomy hooks. It is also feasible to combine PB therapies with surgical or endovascular procedures like radiofrequency or laser ablation [45].

Ambulatory Phlebectomy has a lower recurrence rate of 2.1% and considered as the successful treatment for the treatment of leg varicose veins [46]. Phlebitis blisters and scars are the possible complications of ambulatory phlebectomy therapy [47].

CHIVA

Claude Franceschi's hemodynamic theories from 1988 provide the foundation for CHIVA, saphenous-sparing treatment strategy for lower limb chronic venous disease (CVD) [48]. This hemodynamic approach to treating the disease is based on the theory that the development of CVD (Chronic venous disease) signs and symptoms, including varicosities, edema, discomfort, itching, dermatitis and ulcers, is caused by elevated transmural pressure (TMP) [49].

The ultimate objective of treatment is to facilitate the saphenous vein and collaterals draining to deep venous system, independently of the direction of the flow [50].

When considering alternative treatment modalities, one of the main benefits of CHIVA is potential to avoid nerve damage [49]. The key benefits of over stripping saphenectomy include local anaesthetic, preservation of saphenous veins, low cost, minimal pain and reduced risks of bruising, nerve injury and recurrence [12].

In an RCT, examined ulcer patients and severe cases says, CHIVA had a better healing rate than compression and a lower rate of ulcer recurrence and also treats venous ulcers greatly and effectively, and its outcomes are greater to those of compression therapy [51].

TIIP [Transilluminated Powered Phlebectomy]

Transilluminated powered phlebectomy (TIPP) is described as a minimally invasive surgery for the treatment of varicose veins that is frequently performed under spinal or general anaesthesia [52]. It was originally considered cosmetics for veins less than 2.5 mm in diameter due to the small number of incisions required. On the other hand, TIPP has been associated with a higher incidence of hematoma, postoperative discomfort and paraesthesia due to injury to tissues and nerve around the veins [53].

TIPP procedure had a higher rate of complications and a greater incidence of hematomas (54). Therefore, it has not be proven to be preferable to other varicose vein removal methods [52].

EVLA [Endovenous Laser Ablation]

Endovenous laser ablation (EVLA) is one of the newer, less invasive surgical method that have been launched in recent years to treat varicose veins. The first report of EVLA was published in the literature in 1999, initially described the administration of endoluminal laser energy forn the therapy of the inadequate GSV using an 810 nm diode laser [55].

The EVLA procedure of venous closure functions by initially inducing collagen to shrink due to heat, followed by causing the vein lumen to fibrose closes. A thermal ablation of the treated vein is achieved using a laser, which is the type of electromagnetic (56). The ideal location for the puncture is immediately below the knee since there is less chance of heat damage to the saphenous nerve and the vein has a larger diameter at this location [57].

DVT is the most anticipated complication, to prevent this low molecular weight heparin

(LMWH) for one week is administrated. Another possible side effect of this surgery is skin burning, to avoid this problem this tumescent solution, can simply be used. The other potential problems are nerve damage, bruising and superficial thrombophlebitis [58].

One week following the surgery, the majority of published studies show a success rate of approximately 100%. Although it gradually decrlines, this success rate is still over 90% in a significant portion in a case series [59, 60, 61]. Two and three years following EVLA, there have been reports of recanalization of a treated vein. Most recurrence happen in the firstbthree months [62].

RFA [Radio Frequency Ablation]

RFA is minimally invasive procedure guided by ultrasonography that uses thermal energy injected through a radiofrequency catheter to ablate the refluxing venous segment. Heat inducing methods up to 120°C can be used in RFA [63].

In RFA, 98.2% had complete GSV destruction at a median follow-up of 11 months. It provides a high quality of life score and satisfaction rate. Even while the RFA procedure took far longer to complete than a surgery, patients recovered from the procedure much more quickly, going back to their regular activities and jobs in just one week and experiencing less serious side effects [64]. Compression therapy has been used in order to reduce the risk of venous thrombosis, discomfort and postoperative bruising. Following RFA, patients are advised to walk immediately following it [63].

Sclerotherapy

Sclerotherapy is a minimal invasive percutaneous method of injecting sclerosants into the desired veins, which would thereafter close under immediate external pressure. In general sclerotherapy doesn't require anaesthesia [65]. For veins less than 2.5 mm in diameter and for all for all other causes, sclerosing is considered cosmetic. This is recommended to treat varicose tributaries or the incompetent saphenous vein [11].

Foam sclerotherapy (FS) is a technique that uses a mixture of sclerosant and air (often a 1:4) in place of sclerosant as liquid. It can be used alone or in conjunction with other procedures, and it can be utilized either way. After 12-month follow-up, the closure rate of veins treated with FS found to be higher (68%) compared to liquid sclerotherapy (17.5%) [66].

UGFS (Ultrasound guided foam sclerotherapy) is linked to a quicker recovery and reduced pain following surgery. Still, during a one-year follow-up, the UGFS group had the highest rate of GSV recanalization (51%) [66]. It is important to note that UGFS may need to be done multiple times in cases of recurrences because it cannot entirely seal inadequately GSV segments [67].

The most frequent sclerotherapy related complications are subacute venous thromboembolism telangiectasia matting, hyperpigmentation, recurrence and other issues. Patients frequently report just nodular or linear hardness in their varicose veins, along with pain. After FS, especially when liquid sodium morrhuate is used DVT, tissue necrosis, even arterial thrombosis has been reported [66]. Following sclerotherapy, bandages or compression stockings should be put on immediately to minimize the risk of sclerotherapy related complications [65].

Sclerotherapy alone has not shown to be helpful in the treatment of saphenopopliteal junction reflux, Patients should be treated with EVLA or HL/S to limit the risk of recurrence [11].

MOCA [Mechanochemical Ablations]

The MOCA is a non-thermal, non-tumescent (NTNT) alternative that shows equivalent efficacy to stab avulsions, yet avoids the possible risk of nerve damage. The ClariVein device was implanted for MOCA in 2010. In order to mechanically remove the initial layer of the venous wall from the targeted veins, a wire tip is inserted and rotated at a speed of 3500 revolutions per minute. In concurrently, a liquid sclerosant is injected to the damaged venous wall beneath the catheter tip in order to close the veins. [68]

When comparing MOCA with RFA for truncal vein reflux MOCA causes significantly less pain than RFA. Compared to GSVs >5.9 mm (84.3% vs. 59.5%). The total closure rate for GSV<5.9 mm was greater. The total success rate of MOCA is significantly less than of EVLA, RFA and HL/S regardless of sclerosant concentration. [68]

CAE [Cyanoacrylate Embolization]

Since CAE was initially used in 2013, numerous research has demonstrated its efficacy. CAE is a new endovascular non-traumatic NT&NT

ablation procedure that uses n-butyl-2-cyanoacrylate (NBCA) glue to treat defective truncal veins. The VariCloseR vein sealing system and the VenaSealTM Closure System are the two methods now in practice. [69]

After examining NBCA cases, Bissacco et al. reported that 96.8% of the veins had been occluded at 12 months (70). Compared to other endothermal modalities, NBCA requires kless time to complete occlusion. [71]

Phlebitis, cellulitis and DVT are the complications of CAE treatment. The adhesive probably doesn't breakdown and stays in the vein for a long time and results in long-term foreign body reactions that require surgery [72].

Methods

A review article on meropenem antibiotic compared with cephalosporins/cephalosporin siderophores for hospital-acquired or nosocomial pneumonia, namely Cochrane. Based on the main topic of the article, terms such as "hospital-acquired pneumonia," or "nosocomial pneumonia," "cephalosporin", and "meropenem" were selected as search keywords. Inclusion criteria were patients with HAP who were given meropenem therapy, cephalosporins/cephalosporin siderophores used as empirical therapy, adult and elderly patients published within the last ten years, and documents could be accessed in full. Exclusion criteria included articles that did not address HAP or nosocomial pneumonia and used cephalosporins/cephalosporin siderophores and meropenem as definitive antibiotics. The PRISMA flowchart was used as a model in the article selection process (Figure 1).

Result and Discussion

A search through Cochrane and PubMed identified 598 studies. After removing articles that did not evaluate antibiotic treatment for HAP or nosocomial pneumonia, 53 relevant studies remained, and only seven studies met the predefined inclusion criteria. There were three evaluation comparison groups: cefiderocol versus meropenem, ceftazidime-avibactam versus meropenem, and ceftolozane-tazobactam versus meropenem.The seven articles were randomized controlled trials comparing meropenem with cephalosporin/ cephalosporin hydrophore agents (Table 1). Of the seven studies, five were double-blind, one was open-label, and one did not report the randomized procedure.

Table 1. Drugs used in treatment of varicose veins [22 – 31]

DRUG	DESCRIPTION	INDICATIONS	SIDE EFFECTS
PENTOXYFYLLINE	Xanthine derivatives	Increases micro-circulatory blood flow, decreases whole blood viscosity	Gastrointestinal symptoms
GLYCOSAMINOGLYCANS			
Sulodexide (SDX)	A sulfated polysaccharide complex extracted from porcine intestinal mucosa (80% of fast-moving heparin fraction and 20% of dermatan sulfate component)	Inhibitions of microvasclar inflammatory and proliferative changes	Cutaneos rash, diarrhea, headache, abdominal pain
Mesoglycans	Composed of 52% heparin sulfate, 35% dermatan sulfate, 8% slow-moving heparin and about 5% chondroitin	Profibrinolytic action, microrheoloic benefits, It enhances the process of wound healing	Not known major effects
Defibrotide	Anti thrombic and profibrinolytic drug	Increase plasmin activity, inhibition of tissue factor pathway, increase concentraions of	hypotension, diarrhea, vomitting, nausea, epistasis

		prostaglandins, modulate thrombomodulin, platelets and fibrinolysis.	
FLAVANOIDS			
Diosmin	Originates from Citrus spp	Reduce venous tissue inflammatory responses, increase limb drainage.	not known major side effects
MPFF [Micronised purified Flavanoids Fractions]	90% diosmin and 10% supplementary flavonoids, including hesperidin.	Decreases the inflammatory cascade, protecting microcirculations	not known major side effects

Cefiderocol is a novel cephalosporin siderophore with broad activity against gram-negative bacteria, susceptible or non-susceptible to carbapenems, including Extended Spectrum Beta-Lactamase (ESBL)-producing Enterobacter, P aeruginosa, and A baumannii. The inhibitory power of cefiderocol is also excellent, with a low MIC value that can inhibit the growth of up to 90% of organisms. [7] In addition, cefiderocol has a safety profile with high doses compared to the cephalosporin group [8].

Using cefiderocol and meropenem antibiotics for 14 days (plus or minus 2-3 days), cefiderocol. (2g administered by infusion every 8 hours) had no lower effectiveness than meropenem (2 g every 8 hours extended by infusion for 3 hours). [9]. Clinical improvement results showed 65% in patients with meropenem intervention and 67% in patients with comparator cefiderocol. The microbiological response in both meropenem and cefiderocol groups was at the same percentage of 48%. The mortality rate of cefiderocol was 7% and meropenem 9%. Monitoring mortality at day 14 was the primary outcome of interest, and the secondary outcome of interest was clinical improvement and microbiological response to the antibiotics. From the results of the analysis of the two groups, it was found that meropenem and cefiderocol were adequate for all groups tested both in terms of patient characteristics, namely age, renal function, clinical diagnosis, ventilation status, severity of illness, APACHE II score, and pathogen. In a study conducted by Wunderink et al (2021), the patient population tested were high-risk and critically ill patients representing the current epidemiology and etiology of nosocomial pneumonia. Almost half of the patients had an APACHE II score of 16, required mechanical ventilation in 60%, and 70% were in the ICU [11]. From the culture results obtained, almost 85% of patients had gram-negative pneumonia [12].

Ceftazidime-avibactam combines a third-generation cephalosporin with avibactam as a beta-lactamase inhibitor, making it a broad-spectrum antibiotic that can inhibit ESBL bacteria, Klebsiella pneumonia, P. aeruginosa which are classified as severe threats to public health. [13]. In a study conducted by Torres (2018), [15] the main point in monitoring is 28 days of death after administration of ceftazidime-avibactam therapy. The results of clinical cure and microbiological response are the second goal of this study.

The use of ceftazidime-avibactam (ceftazidime 2 g and avibactam 0.5 g given every 8 hours for 2 hours by intravenous infusion) and meropenem (1 g every 8 hours by intravenous infusion for 30 minutes) showed that meropenem required an MIC greater than and equal to 4-fold to overcome P. aeruginosa so that it was feared that it would lead to potential resistance that emerged in treatment [16]. In some studies, using meropenem often has a lower mortality rate, less than 15% (Zhuang et al., 2022) [17].

The effectiveness of ceftazidime-avibactam was not affected by baseline renal status, previous antibiotic use, type of infection (ventilated or unventilated), or APACHE II score category [18]. In patients with impaired renal function, there is a fluctuating decrease in the dose of ceftazidime-avibactam, so it is necessary to increase the dose by 50% to achieve maximum effectiveness in pharmacokinetic and pharmacodynamic analyses done in previous studies.

Ceftazidime-avibactam had no lower efficacy than meropenem concerning patient mortality caused by HAP over 28 days. The results of the

ceftazidime-avibactam research study support FDA approval of it as an antibiotic therapy for HAP. Thus, ceftazidime-avibactam is the first new gram-negative antibiotic approved in the United States to indicate HAP in over 15 years.

In previous studies, trials of new antibiotics (tigecycline, doripenem, and ceftobiprole) showed that the new antibiotics were not better than existing therapy. Under-dosing of new antibiotics may contribute to therapeutic failure. Ceftolozane-tazobactam is an antibacterial combination consisting of ceftolozane (a cephalosporin) and tazobactam, a beta-lactamase inhibitor approved for complex urinary tract and intra-abdominal infections at a dose of 1.5 g (ceftolozane 1 g and 0.5 g tazobactam) every 8 hours [19,20]. Drug concentrations in the lungs are often lower than in plasma, and the pathogens that cause nosocomial pneumonia often have lower antibacterial susceptibility (Zhang et al., 2021) [21]. These factors lead to insufficient drug concentrations at the site of infection, so dosing regimens in nosocomial pneumonia patients must be carefully optimized [22,21].

Several studies have been conducted to determine the effectiveness of ceftolozane-tazobactam using high doses (ceftolozane 2 g and tazobactam 1 g) given every 8 hours. The safety of high-dose ceftolozane-tazobactam in critical and at-risk populations was found to be safe. High-dose ceftolozane-tazobactam compared with meropenem at a dose of 1 g given every 8 hours gave microbiological responses that were not clinically significant, and the comparison showed that the initial susceptibility of P. aeruginosa to ceftolozane-tazobactam was higher than meropenem. This was also true for Enterobacter. Mortality was lower in patients with pathogenic P aeruginosa who were given meropenem at baseline. Meanwhile, mortality was lower in participants with Enterobacter pathogens and ESBL-producing Enterobacter who received ceftolozane-tazobactam therapy [23]. This trial showed no difference between ceftolozane-tazobactam and meropenem on the assessment until day 28. Both are mortality, clinical cure, and microbiological response [24].

Conclusion

In early-stage treatment of varicose veins compression therapy and conservative therapy play a major role in treatment of varicose vein either by alone or in combination. In drug therapy pentoxifiline proves to be effective. But in severe stages the use of drugs and compression therapy became less effective. In this part the role of surgeries plays a vital role in treatment of varicose veins.

Many surgeries have been used to treat varicose veins. Each treatment is effective in the treatment of each type and each stage of varicose veins and has its pros and cons. High ligation and stripping surgery, EVLA, RFA and Sclerotherapy are most widely used surgical procedure for varicose veins. CHIVA has proved to be more effective and safest surgical procedure among all surgeries.

Conclusion

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