Chronic Venous Disorders of the Lower Limbs

A Surgical Approach

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Foreword

This book is a chronicle of an ancient disease, once considered "a poor second cousin" to arterial disease. It starts with a glimpse into the history, portraying the transformation of venous disease into, as the authors write, "if not an emperor, a prince among vascular maladies". The book goes on to a scholarly narration of the basics of venous disease, displaying the gems of anatomy and physiology. It depicts the evolution of the treatment for primary varicose veins from the traditional through contemporary to avant garde. The book intensely dwells on chronic venous insufficiency, the "night of venous diseases". This section on chronic venous disease is a combination of surgeon's micro precision, teacher's passion, researcher's brilliance and storyteller's allure. The book finally has a peek into the pot-pourri of venous disorders. Above all, this book is an autobiography of the authors' immense experience over the years. Valuable Indian data, though much of it unpublished hitherto, given along with international statistics is indeed a breath of fresh air.

Professor Vaidyanathan, undoubtedly the superman of venous diseases in Kerala, has inspired me and taught me. This book is in essence, a collection of his adventures. Dr Riju, once my earnest student, never showed off his artistic talents. All the pictures in the book are conceived and drawn by him, simple, colourful yet demonstrative. Dr Pradeep Jacob and Dr Binni John are "physicians", Hippocrates would have been proud to introduce; they have true and total commitment to the profession and their patients. All these four extraordinary surgeons are known to work in silence; their success is making melodious music though this book. It is there for everyone to hear and relish.

Who is this book meant for? It may perhaps be a bit loud for the postgraduates of surgical training. For the practicing general surgeon, it would be an invaluable guide. The tips and tricks for diagnosing, medically treating and surgically intervening for an assortment of chronic venous disorders are distinctly described. It will help not only in their daily "bread and butter" varicose vein work, but additionally for the occasional complex venous disorder they might encounter. For the venous enthusiasts, this book is a "must-own" classic.

By asking me to write a foreword, I had the opportunity to read this book. As a vascular surgeon, I learnt a lot. My debts to the authors, particularly Prof Vaidyanathan accrue even more. Thank you all.

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Preface

Venous diseases of the lower limbs are extremely common conditions in clinical practice. They are considered trivial but irksome issues and are often neglected. The face of venous diseases has transformed in recent times thanks to the advances made in the diagnosis and treatment of these problems. For a practising surgeon, a huge volume of literature is available on these matters. However, the practitioner has to refer various books and publications to garner information relating to any aspect of the disease. There is no single source to provide comprehensive information, indeed a state of poverty in the midst of plenty! This book was conceived with the idea of providing comprehensive information on common chronic venous problems encountered in surgical practice under one roof. The clinical experience and data for this book were gained by us in two different settings. From 1980 to 2000 some of us (SV, PJ and BJ) were working at Medical College Hospital, Kottayam, Kerala. This is a 1,000 bedded Government sector teaching hospital in the state of Kerala in South India with a huge patient population and providing free treatment for the poor and the needy. From 2000 onwards three of us (SV, RRM and PJ) shifted to Amrita Institute of Medical Sciences, Kochi Kerala. This is a state of the art hospital in the private sector, providing undergraduate, post graduate and super speciality training. This hospital functions under the Amrita Viswa Vidya Peetham, a deemed University in the private sector. Apparently we had the best of both worlds.

This book has basically followed the CEAP classification pattern and is divided into four sections, basics, C2 clinical class, C3–C6 class and an assorted group of venous problems. We have considered only the chronic venous problems affecting the lower limbs. Hence we have not included acute deep vein thrombosis and venous injuries in this work. We must frankly admit that we are novices in the publication field. In fact, this is our first venture as authors of a monogram. Although we have taken lot of pains to present authentic information, there could be omissions and errors in this work. We crave for your indulgence.

The literature on chronic venous problems of lower limbs is voluminous. To pick and choose from this mountain of knowledge has been one of the most difficult tasks for us. The best source of reference for us has been ‘The Handbook of Venous Disorders: Guidelines of the American Venous Forum’ edited by Peter Gloviczki (3rd Edition, Hodder Arnold, London: 2009). We would like to acknowledge this work.

It would be better to say that this book was written through us rather than by us. It is a supreme example of team work in action. Although each chapter was contributed by a specific individual, it was our collective effort that brought it to its final format. A word about the diagrams. The ideas for the different diagrams were conceived by one of us with inspiration from different sources (SV); they were executed by two members from our group (RRM and PJ). They may not look very professional but we have the owner's pride in displaying them.

We would like to acknowledge the following personalities for providing excellent help and assistance:

Dr.B.Rajammal, Professor of Obstetrics and Gynaecology, Amrita Institute, Kochi- for reading and correcting the manuscript of the Chapter, Pelvic Venous Syndromes.

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Dr.PK. Nazar, Associate Professor, Department of Radiology, Amrita Institute of Medical Sciences, Kochi- for providing images of our patients for inclusion in the text.

Dr. Rajashekaran Pillai, Dr.(Brig) K.J.Philipose, Dr.C.Gopalakrishnan Nair (Professors) and Dr. Misha J C. Babu (Associate Professor), our colleagues in the Department of General Surgery, Amrita Institute of Medical Sciences, Kochi, have previewed and corrected the manuscript of the text. We thank all of them.

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We would also like to thank our publishers, the Springer group. Special thanks to Dr Naren Aggarwal, Executive Editor, Clinical Medicine, Springer. The whole concept of publishing this work started with his powerful support for us. Thank you Dr. Naren, especially for putting up with our delay in submitting the manuscript.

To our families, we owe a lot in supporting us when we were busy neglecting them for months together.

We would like to dedicate this book to all our patients with chronic lower limb venous disorders. They have shown us the way!

Kochi, Kerala, India — Subramonium Vaidyanathan
Kochi, Kerala, India — Riju Ramachandran Menon
Kochi, Kerala, India — Pradeep Jacob
Kottayam, Kerala, India — Binni John

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Part I

Basics

Venous Diseases: A Historical Survey

1

Riju Ramachandran Menon

Contents

Introduction

The great Sir Isaac Newton had remarked, "If I have seen further it is by standing on the shoulders of giants." In the field of venous diseases, many giants have made outstanding contribution toward alleviating human suffering from this irksome problem.

Varicose veins and leg ulcers have plagued humanity ever since man assumed erect posture. Phlebology was a neglected area even among vascular surgeons. Venous diseases remained a "poor second cousin" to its arterial counterpart. There is nothing flashy or dramatic about the manifestations of chronic venous disorders (CVD). Both patients and clinicians consider these problems more of a nuisance than something that should be skillfully treated. Not much attention was focused on the evaluation and treatment of these patients. It used to be commented that the patients with varicose veins were relegated to the end of the operation list and delegated to the junior most member of the team. Today, the facade of venous disease has changed dramatically, thanks to the rapid progress in diagnostic technologies and therapeutic interventions. Venous disease has transformed, if not into an Emperor, but at least into a Prince among vascular maladies. This transformation was possible only by the dedicated efforts of several men and women.

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This chapter focuses on the different stages in the evolution and progress of venous diseases.

- *Ancient historical phase*
- *Evolution of treatment for varicose veins*
- *Evolution of diagnostic technologies*
- *Evolution of treatment for venous ulcers*
- *Era of minimally invasive interventions*

This approach is not based on the sequential or chronological order of progression of events but on the focus and stress on different areas of activity.

Historical Vignettes

The word " varicose" is an ancient term and is derived from Greek, meaning "grapelike." It is believed that *Hippocrates* of Cos (460–377 BC), the Father of Medicine, first used this term. He based his theory on the Pythagorean doctrine of the four humors (blood, phlegm, yellow bile, and black bile). According to him, the liver is the "root" of all veins. The veins alone contain blood destined for the body's nourishment. As part of treatment for varicose veins, Hippocrates used bandages. He is also reported to have used the technique of cauterization of varicose veins with a hot iron [1]. He observed the Scythian people and postulated that varicose veins develop from prolonged standing. The women of this race were considered beautiful depending on the length and size of the veins. The people of this race were basically horse riders. Following long rides, they developed dilatation of the lower limb veins along with swelling [1].

Susrutha, the ancient Indian surgeon, described Seera Kautilya or aneurysm of veins. In the Susrutha Samhitha, he has also described superficial thrombophlebitis and its treatment by jalaukavacharan or bloodletting using leech [2].

Ebers Papyrus, during the rule of Amenhotep (1550 BC), has records of this problem [3]. This document clearly forbade any surgery for varicose veins and issued a warning "thou shall not touch something like this" [4]. In ancient Greece, lower limb replicas were offered to the gods in temples to obtain relief of symptoms from this disease [4].

Two great figures, *Aurelius Cornelius Celsus* and *Claudius Galenus*, came into prominence during the Roman Age. Celsus (53 BC to 7 AD) using staggered incisions and employing cauterization removed segments of varicose veins. This was probably the forerunner for the procedure of stripping. He also used bandages for the treatment of leg ulcers. Galenus (130–200 AD) excised segments of veins controlled between ligatures. He employed hooks for this purpose and applied wine to the wounds. The invention of surgical ligation, a crucial milestone in the evolution of surgery, is attributed to Galenus. The great physicians recognized compression therapy as an effective form of treatment. Roman soldiers wrapped their legs in leather straps to minimize leg fatigue during long marches.

In the School of Alexandria, founded by Alexander the Great, ligation was practiced as treatment for many conditions affecting blood vessels. The Byzantine physician *Aëtius of Amida* (502–575 AD) was a pioneer among this group [5]. Details of internal saphenous vein at the thigh were first described by *Paulus Aegineta* (607–690 AD). Compression, marking, ligation, and stripping were practiced by him. The same principles were followed much later by the renowned French surgeon *Ambroise Paré* (1510–1590) [6].

Progress on venous disease was considerably hindered by the Galen's humoral theory of stagnant evils. According to Galen, an ulcer is an attempt by the body to expel these evil forces, and no attempt should be made to make an ulcer heal. The silver lining in this dark cloud of ignorance and superstition was the discovery and postulation of blood circulation by *William Harvey* in 1628. Harvey, in his De Motu Cordis, specifically stressed the importance of venous valves in human circulation [6]. Even before Harvey, *Giovanni Battista Canano* from Ferrara (1540) had described venous valves in renal, azygos, and external iliac veins.

The most comprehensive and complete description of the venous anatomy is attributed to *André Vesalius* in his De humanis corporis fabrica popularly known as Fabrica [6] (1543). He had deep knowledge combined with skill in dissection. His teaching method combined lectures with demonstration of dissection. His

description of the venous anatomy had two glaring omissions. He left out venous valves and the perforating veins.

The theory of valvular incompetence as a cause for varicose veins was put forward by *Hieronymus Fabricius* in 1603. Dilatation of vein as a cause for valvular incompetence was suggested by *Richard Wiseman* (1676). He coined the term varicose ulcer [5].

Gravity as an important factor in venous return was identified following Newton's work. *Petit*, and then *Hunter*, accepting this mechanical theory suggested that patients with varicose veins should be treated in a horizontal position [3].

Sir Astley Paston Cooper identified the role of compression in the treatment of varicose veins in 1824. *John Gay* (1868) identified the importance of deep vein thrombosis (DVT) and changes of post-thrombotic syndrome. He stressed the importance of ankle perforating vein in the genesis of leg ulcers and coined the term venous ulcer [3, 7, 8]. *Virchow* (1846) postulated the theory of thrombosis and stressed the relevance of the triad of risk factors for deep vein thrombosis. He also pointed out the importance of heredity in varicose veins [9].

An important breakthrough in the treatment of venous ulcers was the introduction of the Unna Boot by *Paul Gerson Unna* (1896). He incorporated emollient compounds in a dressing that became increasingly rigid [10]. He was a genius who was responsible for developing dermatology as an independent speciality [11].

Evolution of Treatment for Varicose Veins

In the nineteenth century, significant progress was made in the diagnosis and treatment of varicose veins. This era marked the phase of scientific approach to the study of venous problems. It was *Sir Benjamin Brodie* (1846) who for the first time described a bedside test for the identification of incompetent valves. He did this by making use of constriction and palpation of the limb [3]. *Friedrich Trendelenburg* (*1844–1924*) further refined this method in 1890 [12]. The Brodie-Trendelenburg test as it is currently known is a rich tribute to these two eminent personalities. A clinical method of assessing the patency of the deep veins in venous disorders is attributed to *Georg Perthes* in 1896 [3].

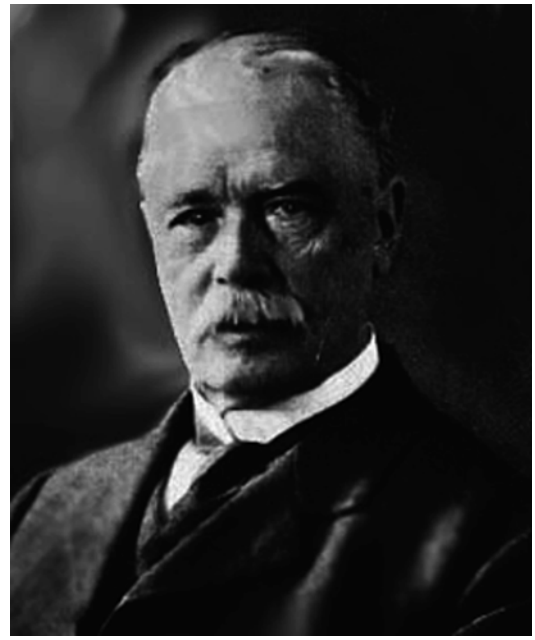

Fig. 1.1 Friedrich Trendelenburg (1844–1924)

Rational principles for surgical treatment of great saphenous vein varicosity were introduced by Friedrich Trendelenburg in 1890 [13] (Fig. 1.1). He was a towering personality with profound wisdom, humility, and modesty. His father was a professor of philosophy. His contributions to the profession apart from varicose vein surgery include the Trendelenburg position [14]. He was interested in the history of surgery especially ancient Indian surgery. He conceived the idea of ligating the saphenous vein as part of treatment for varicose veins. Unfortunately he did not perform the flush tie; instead he ligated the vein at mid thigh level. He was opposed to groin exploration stating that this would create much bleeding. Obviously, Trendelenburg's mid thigh ligation technique did not offer any benefit. Flush ligation was first performed by Perthes, a student of Trendelenburg. Moore, an Australian surgeon in 1896, also is reported to have performed flush

tie [4]. Trendelenburg was such a fast surgeon that no anesthesia was needed for the procedure. Even today, high ligation and stripping are the gold standard in the treatment of varicose veins.

Madelung and *William Moore* were other prominent personalities who contributed to the surgical treatment of varicose veins [15]. William Moore can be credited with outpatient treatment of varicose veins since he popularized the surgery for varicose veins under local anesthesia. The credit for introducing the technique of stripping is shared by *Mayo* (1904), *Keller* (1905), and *Babcock* (1907) [16–18].

One of the most highly disfiguring and horrendous procedures for the treatment of varicose veins practiced in 1908 is called the Rindfleisch-Friedel operation [19]. This consists of cutting a deep spiral gutter to deep fascia that wraps round the leg six times! This spiral gutter brings to view a large number of superficial veins. All of them were ligated. The wound was left open to heal by granulation [20].

Nonsurgical treatment by injecting sclerosing substances was in practice in the mid-1920s. Sclerotherapy almost totally overshadowed surgery till *Linton*, in 1938, introduced the concept of radical varicose vein surgery [21]. This consists of interruption of the points of venous reflux along with stripping of the internal and external saphenous veins. The procedure includes ligation of insufficient perforating veins and staggered resection of varicose tributaries.

Pathophysiology of DVT, post-thrombotic syndrome, and leg ulcers were extensively described by *Homans* in 1917. The role of recanalization of the thrombus with valve destruction was identified by him for the first time. The technique of microphlebectomy was introduced by *Muller* in 1966 [3].

In 1966, *Henschel and Eichenberg* discovered polidocanol [6, 17]. Many other chemicals were used for sclerotherapy till such time with poor results. Polidocanol has revolutionized sclerotherapy. Initially it was used as simple injections. The modern technique of ultrasound-guided foam sclerotherapy has revolutionized varicose veins treatment making it more and more minimally invasive [22].

Conrad Jobst (1930), a successful engineer, who manufactured toothbrushes, had refractory venous ulcers. He understood that the hydrostatic effect of pooled blood in the leg caused symptoms in venous disease. Jobst introduced graduated compression stocking for control of his own disease. At present, graded compression stockings form one of the most effective treatment options for CVD.

Evolution of Diagnostic Procedures

Two major landmark events for diagnosis of venous disorders were the introduction of phlebography and duplex ultrasonography.

The credit of introducing phlebography in human beings for the first time goes to *Berberich and Hirsch*, *Sicard*, *and Forestier* in the 1920s [6, 23]. *Dos Santos* in 1938 described ascending venography for the diagnosis of DVT [23].

The principle of Doppler for the evaluation of venous diseases was introduced by *Sigel and Colleagues* (1967) [6]. Duplex ultrasound, the current gold standard for the assessment of vascular disorders, was introduced by *Szendro*, *Nicolaides*, *Myers*, *Malouf et al.* in 1986 [6].

Other major events in the diagnosis of venous disorders are listed in Table 1.1.

Table 1.1 Landmark events in diagnosis

Year	Scientist	Invention
1948	Pollack and Wood	Dynamic measurement of venous pressure
1953	Whitney	Impedance plethysmography
1960	Hobbs and Davies	Detection of thrombi by radioactive iodium
1968	Dahn	Strain gauge plethysmography
1969	Webber	Detection of thrombi by radioactive technetium
1971	Rosenthal	Radionuclide venography
1973	Norgren and Thulesius	Foot volumetry
1973	Cranley	Phleborheography
1979	Abramovitz	Photoplethysmography
1987	Van Rijn	Air plethysmography

Adapted from *The Vein Book*, Bergan [6]

Evolution of Treatment for Chronic Venous Insufficiency

Bypass surgery for deep venous obstruction was performed for the first time by *Palma* and *Esperon* in 1958. They described the technique of a crossed femoro-femoral graft for iliac vein occlusion [24]. Surgery for incompetent perforators in the treatment of CVI was pioneered by *Robert Linton*. Linton's techniques were further modified by *Cockett* and *Felder*. The subfascial endoscopic perforator surgery (SEPS) introduced in 1985 by *Hauer* and *Sattler* transformed an extensive radical open intervention to a minimally invasive procedure with early recovery [25].

Reconstruction of deep veins as a treatment for CVI was introduced by *Robert Kistner* in 1968. He described the technique of internal valvuloplasty [26]. This opened the floodgate and many more novel procedures were introduced for reconstruction of valves in the deep veins. *Raju* modified the Kistner technique and popularized the supravalvular approach for repair. The technique of external valvuloplasty was also introduced by Kistner and *Ferris. Taheri* and team from Buffalo pioneered the technique of axillary segment transfer. This was a major breakthrough since the technique could be used for post-thrombotic limbs also. *Guarenea* in 1984 published his results of external banding of deep veins using a Dacron sleeve. A modification of this technique using silastic cuff was introduced by *Jessup and Lane* in 1988. *Dalsing* in 1999 tried cryopreserved venous segments for clinical use. Transcommissural valvuloplasty was popularized by Raju in 2000.

Evolution of Minimally Invasive Interventions

Endovenous intervention for treatment of venous disorders was a major breakthrough in converting venous surgery to an office procedure. The major contributions in this field are as follows:

1. *Endovenous chemical ablation* (*sclerotherapy*)
   Ultrasound-guided foam sclerotherapy was introduced by *Orbach* in 1944 and modified further by *Hobbs*, *Tessari*, and *Cabrera* [27–29]. This was a refinement of the technique of liquid sclerotherapy.
2. *Endovenous thermal ablation*
   The use of radiofrequency ablation (RFA) in the treatment of venous disease was described by *Navarro* in 1999 [30]. The application of laser for venous ablation (EVLA) was first performed by *Carlos Bone* in 1999 [31].
3. *Percutaneous endovenous stenting*
   This is used in the treatment of isolated iliac vein obstruction. Raju and colleagues have published extensive data in this field with encouraging results [32].

Current Initiatives

Today several academic forums are actively involved in the study and research on venous diseases. Their activities have far-reaching impact across the world.

- *The American Venous Forum* (*AVF*): This organization was founded in 1987. AVF fosters cutting-edge research and clinical innovations and educates health-care professionals, patients, and policy makers about venous and lymphatic disorders. As their website proclaims, their leadership and membership are recognized internationally as thought leaders, expert investigators, and clinicians in venous and lymphatic diseases. They have evolved multispeciality coalitions for better patient care. They also come out with guidelines for the health-care personnel. www.veinforum.org
- *The European Venous Forum*: The European Venous Forum was founded in Lyon, France, in 2000 to develop "education, scientific knowledge, research and clinical expertise of the highest quality and establish standards in the field of venous disease." www.europeanvenousforum.org
- The Indian scenario is also very bright. Two academic societies are active in the field of venous diseases.
- *Vascular Society of India* (*VSI*): The society was established in the year 1994 and is actively involved in care, treatment, and research on all

areas of vascular pathologies including venous diseases. www.vsi.net.in

- *Venous Association of India* (*VAI*). The forum was established in 2007 to promote research and study of venous diseases. The society maintains healthy collaboration with other sister organizations across the world. www.venous.in

Summary

The history of venous diseases is a long and colorful saga of impressive successes and disappointing failures. The new face of venous disease owes a lot to the untiring efforts of several dedicated men and women.

Several academic organizations are trying to foster excellence in the study of venous diseases at the national and international arenas.

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Lower Limb Venous Anatomy

2

Riju Ramachandran Menon

Contents

Introduction

The venous system of the lower limbs is a well-organized functioning unit promoting unidirectional cephalad flow toward the heart. Altered anatomy and physiology are responsible for the symptoms and signs of chronic venous disorders (CVD) of the lower limbs.

This chapter focuses on the following aspects:

- An outline of the development of veins of lower limb
- Arrangement of veins of the lower limbs
- Anatomy as per ultrasound imaging

The focus would be on the applied aspects which are relevant in clinical practice.

Development of Veins of the Limbs

The limb vasculature commences as a fine capillary network starting from segmental branches of the aorta. During early intrauterine life, the vascular system of the lower limbs consists of ventral and dorsal systems [1]. The primitive femoral artery and vein originate from the ventral system. The dorsal system gives rise to the embryonic sciatic system. In the second month of intrauterine life, the dorsal system regresses almost completely and the ventral system takes over. The primitive sciatic system is represented in the adult by the internal iliac and the inferior gluteal vessels. In the leg, the artery and vein of the sciatic nerve are the remnants of

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the original sciatic system. Persistence of the sciatic system results in the genesis of several types of congenital venous anomalies including Klippel-Trenaunay syndrome [1].

Valves form in the veins early in the course of development and are completed by 6th month [2]. Nerves of the extremities develop before the veins. In fact, some of these nerves stimulate the development of the venous system. The femoral, sciatic, and the posterior femoral cutaneous nerves are examples of such nerves that stimulate embryonic venous development.

Anatomy of Lower Limb Venous System

Variations are the rule rather than the exception in the venous system. It is therefore difficult to define "normal" venous anatomy. But there is some order in this disorder. The nomenclature of the veins of the lower limbs has been updated as per the International Interdisciplinary Consensus Statement [3]. This nomenclature is followed in this book.

The veins of the lower limbs are organized into three systems: superficial, deep, and perforating veins. These veins are located in two compartments:

- The superficial compartment
- The deep compartment

The superficial compartment is the space between the deep fascia and the dermis. Ultrasound has confirmed a separate space in the superficial compartment known as the saphenous compartment [3, 4]. This space is bounded superficially by the saphenous fascia (portion of the membranous layer of the superficial tissue overlying the saphenous vein). The deep boundary of the saphenous compartment is formed by the muscular fascia of the limb. The saphenous compartment contains the great saphenous vein, accompanying arteries, and nerves. Saphenous tributaries and accessory, collateral, and communicating veins lie outside this compartment [3]. *The deep compartment* is bounded by the muscular fascia and contains the deep veins.

The term perforating vein is reserved for those veins that pierce the muscular fascia to connect the superficial and deep veins. Communicating veins interconnect with veins of the same system [3]. Bicuspid valves in the veins complete the anatomical arrangement.

Superficial Veins

Great Saphenous Vein (GSV)

The great saphenous vein is the longest vein in the body and runs from the foot to the groin. It extends from the medial aspect of the dorsal venous arch in front of the medial malleolus and then runs upward, lying in a plane between the superficial and deep fascia along the inner side of the leg and thigh. It penetrates the deep fascia of the thigh and passes through the cribriform fascia that covers the fossa ovalis to join the common femoral vein [5]. The normal diameter of the GSV is 5–6 mm in the thigh and 2–3 mm in the calf. There is considerable variation in the size, location, and morphology of the GSV. The GSV is the chief subcutaneous vein of the lower extremity.

The saphenofemoral junction (*SFJ*) is the confluence of the superficial inguinal veins, comprising the GSV and superficial circumflex iliac, superficial epigastric, and the external pudendal veins [6] (Fig. 2.1). One of the landmarks for the location of the SFJ during high ligation is the superficial external pudendal artery as it courses along the free margin of the fossa ovalis. In 90 % of our patients, the vessel was coursing behind the GSV (Fig. 7.2).

The location of the SFJ as per textbooks of anatomy is 4 cm below and lateral to the pubic tubercle [5]. However, during surgery of high ligation, by intraoperative measurement we have localized it to a mean of 2.7 cm below and 3 cm lateral to the pubic tubercle. Any incision used to expose the SFJ should use the pubic tubercle as a landmark. Two valves are located at this point. About 1 cm proximal to the junction, a terminal valve can be found almost consistently. There is another preterminal valve about 3 cm distal to the first one [4]. These valves are bicuspid with the

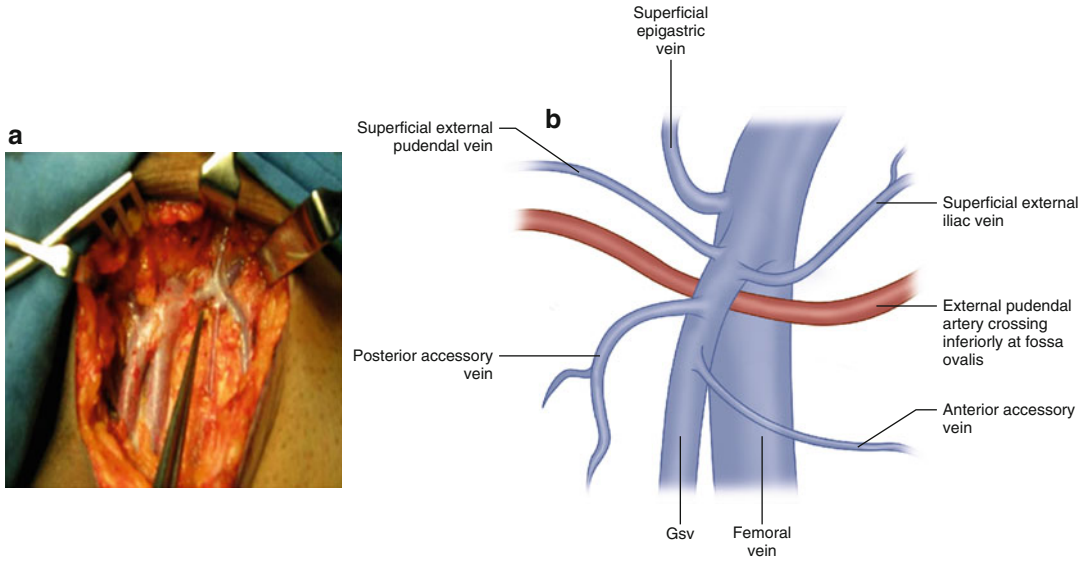

Fig. 2.1 (**a**, **b**) SFJ anatomy

concave leaflets facing upward. Weight of blood coming backward onto the concavity of the leaflets fills them and causes them to fall backward. This prevents further flow and maintains the competence of the valve.

Tributaries of GSV [1]

(a) *Near termination*: The confluence of superficial inguinal veins – formed by superficial circumflex iliac vein, superficial epigastric and external pudendal veins, and the distal GSV.
(b) *At the thigh*: Anterior accessory and posterior accessory GSV of the thigh.
(c) *At the leg*: Anterior accessory and posterior accessory GSV of the leg. The posterior accessory GSV of the leg was known as posterior arch vein or Leonardo's vein.

The accessory veins lie at a slightly anterior plane compared to the GSV outside the saphenous compartment. At the saphenofemoral junction, there could be a variable number of other unnamed tributaries [7].

Saphenous Nerve and Its Relation to the GSV

Saphenous nerve is the largest branch of the femoral nerve and is a purely sensory nerve. It descends along with the femoral artery. It exits the adductor canal at its distal end, pierces the fascia lata, and becomes subcutaneous. In the lower part of the leg, it is in close proximity to the GSV. The nerve can be damaged during surgical stripping and endovenous procedures. The damage is less likely at the upper part of the leg because of the larger gap between the nerve and vein here.

Short Saphenous Vein (SSV)

The SSV originates from the lateral side of the foot and drains into the popliteal vein. The following anatomical facts are important in surgery of SSV:

(a) The SSV pierces the deep fascia of the leg at the mid calf level and runs between the two heads of the gastrocnemius to enter the popliteal vein. The upper one-third of the SSV lies below the deep fascia [8, 9]. Hence, the deep fascia of the popliteal fossa has to be incised to expose the terminal portion of the SSV.
(b) The termination of the SSV can be variable. Three types of terminations have been described – Kosinski's variations [8, 9].
    - Normal termination (57 %) – enters the popliteal vein in the popliteal fossa

- High termination (33 %) – ends in the mid thigh in a muscular vein or the GSV
- Low termination (10 %) – ends in the deep veins of the calf or deep sural muscular veins or GSV in the upper third of the leg

(c) The sural nerve courses along the SSV in the distal part of the calf. In a study on the fascial anatomy of SSV of 20 embalmed human specimens, it has been reported that the distance between the SSV and the sural nerve was less than 5 mm in proximal 1/3 of the lower leg in 70 % of specimens; the deep fascia was present between the SSV and the sural nerve in more than 95 %. In the distal 2/3 of lower leg, the distance between the SSV and the sural nerve was less than 5 mm in 90 % and the deep fascia was present between the two structures in only 15 %. Hence, the sural nerve is at risk of thermal injuries during endovenous thermal ablation in the lower leg [10].

(d) The vein of Giacomini (intersaphenous vein) runs in the posterior part of the thigh and connects the SSV with the GSV. A SSV projection or tributary ascending in the thigh above 12 cm from the popliteal skin crease is designated as the Giacomini vein irrespective of the termination of the SSV (Fig. 7.6b). It is reported in 70.4 % of limbs. In the lower thigh, it is located below the deep fascia. In the middle and upper thigh, it perforates the deep fascia and ends in the superficial or deep veins or in the muscular veins. Its presence does not affect the position of SSV termination; nor does it affect the severity of venous disease [11, 12].

Deep Veins

More than 80 % of the blood flow in the lower limbs is through the deep veins. The deep veins of the lower extremity accompany the arteries and their branches. They possess numerous valves.

In the leg, these include the posterior tibial veins, anterior tibial veins, and peroneal veins. They are all paired structures. *In the thigh*, these include the popliteal vein, femoral vein, profunda vein, and the common femoral veins.

The pelvic veins include the external iliac, internal iliac, and common iliac veins and the inferior vena cava. The gonadal veins draining to IVC on right side and the renal vein on the left side are important vessels in the pathogenesis of pelvic congestion syndrome (PCS).

Perforating Veins [2, 6]

These veins perforate the muscular fascia to connect the superficial veins with the deep veins. Communicating veins connect veins within the same system [3]. There are as many as 150 perforating veins in the lower extremity, although only a few of these are clinically important [13, 14]. The medial calf perforators are probably the most important from the clinical point of view. Most perforators are inactive in the normal state. In the presence of venous hypertension, they open up and reflux blood to superficial veins.

Perforators in the foot: These consist of the dorsal, plantar, medial, and lateral perforators. Between the first and second metatarsal bones, a large perforating vein, connecting the superficial venous arch to the pedal vein, can be identified.

Perforators at the ankle: These are a cluster of vessels arranged as anterior, medial, and lateral groups.

Medial calf perforators: They are arranged in two groups:

(a) *Posterior tibial perforating veins*: They were known as the Cockett perforators. They connect the posterior accessory GSV of the calf (posterior arch vein) with the posterior tibial vein. There are three of them: lower, middle, and upper, located just behind the medial malleolus and at 7–9 cm and 10–12 cm from the lower edge of the medial malleolus respectively. They are at 2–4 cm behind the medial edge of tibia. In perforator surgery, these are the vessels which are mainly targeted (Fig. 2.2).

(b) *Para-tibial perforators* connect the main GSV trunk to the posterior tibial veins.

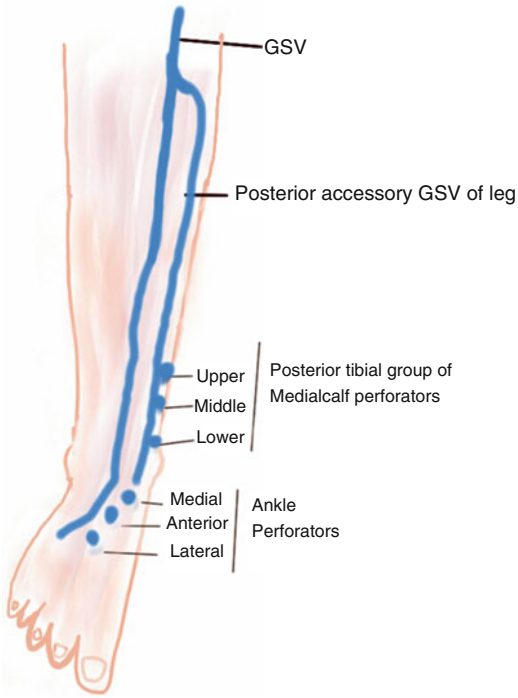

Fig 2.2 Posterior tibial group of medial calf perforators

Below knee perforating veins: These are the anterior, lateral, and gastrocnemius vessels. The gastrocnemius vessels are arranged into medial and lateral groups. Intergemellar and Achillean perforating veins are the other groups of below knee perforators.

The *perforators located around the knee*: These are infra- and suprapatellar and popliteal fossa perforating veins.

Perforators of the femoral canal: In the distal thigh, perforators of the femoral canal connect the femoral vein to the GSV.

Inguinal perforators: These drain into the femoral vein in the proximal thigh.

Valves of the Lower Limb Veins

One of the most important anatomical features of veins from a clinical perspective is the presence of valves. Each of these delicate, but extremely strong, bicuspid structures lies at the base of a segment of the vein that is expanded into a venous sinus. This arrangement permits the valves to open widely without coming into contact with the wall, thus permitting rapid closure when flow begins to reverse.

There are approximately 9–11 valves in the anterior tibial, 9–19 in the posterior tibial, 7 in the peroneal, 1 in the popliteal, and 3 in the femoral vein. In two-thirds of the femoral veins, a valve is present at the upper end within 1 cm of the inguinal ligament. About one-quarter of the external iliac veins have a valve. The common iliac vein usually has no valves. Superficial veins have fewer valves – approximately seven to nine in the greater and lesser saphenous veins.

Electron microscopy of resin-filled veins in cadavers confirmed the presence of valves up to the sixth generation tributaries [15]. Incompetence of these valves is reported to be one of the important causes for the development of skin changes including ulcers in patients with chronic venous disorders.

Venous Sinuses of the Calf Muscle

These are large thin-walled blood-filled spaces located mostly in the soleus (1–18 sinuses) and to a less extent in the gastrocnemius muscle. Venous sinuses of the soleus muscle drain into the posterior tibial vein through multiple large, short, and tortuous soleus veins. Some of these veins may join a perforating vein before entering the deep veins. Gastrocnemius veins drain the two heads of the muscle and empty into the popliteal vein distal to the SP junction. These sinuses are filled from the superficial veins and the reticular venous plexuses. They can hold a large volume of blood and can function as chambers of the peripheral heart [2].

Veins of the Foot

The anatomy of the foot veins has been reported extensively by Uhl and Gillot by their dissection study on 400 cadaveric feet after injecting green

neoprene latex [16]. The summary of their findings is as follows:

Components of the foot veins include the superficial venous network, the deep veins, and the perforating veins.

Superficial venous network consists of plantar network draining into marginal veins, medial and lateral marginal veins connecting the GSV and SSV respectively, and the interdigital veins.

Deep veins are located in two layers: deep bony veins in contact with tarsal bones and large collecting veins – musculotendinous veins. They converge as medial and lateral plantar pedicles.

Perforators. There are several perforating veins in the foot. The named ones are as follows:

- Perforator of the first metatarsal interspace
- Medial marginal perforator vein
- Plantar perforators (malleolar, navicular, and cuneiform)
- Dorsal medial perforator
- Lateral marginal perforator veins

The foot muscle pump has been the subject of extensive studies in recent times. The volume of blood pumped by foot muscle pump is calculated as 25 ml. Two points regarding the foot muscle pump deserve attention [16]:

1. The direction of more than 50 % of valves in the veins of the foot is such that the blood flow is from deep to superficial veins when the foot muscle pump contracts.
2. Impairment of the foot muscle pump by static foot disorder is an important cause of chronic venous disorder.

Ultrasound Anatomy of Lower Limb Veins

Duplex ultrasound imaging of the lower limbs is currently the gold standard for the diagnosis of CVD. Some of the well-described features of US imaging are mentioned below [3, 17–19].

Ultrasonographic eye sign. US visualization of the GSV in the upper thigh gives the classical *Egyptian eye* appearance with the vein sitting between the two fascias. In a transverse imaging, the saphenous fascia is the upper eyelid, muscular fascia the lower eyelid, and the saphenous vein the iris [3, 4] (Fig. 2.3).

The tibiogastrocnemius angle sign has been described to identify the GSV in the leg using a duplex scan, during a difficult cannulation for endovenous ablation. The angle or triangle is made by the tibia laterally, the gastrocnemius muscle medially, and the fascia superficially. Here, the GSV ascends in front of the tibial malleolus and along the medial side of the leg.

The lateral subdermal venous system is a system of small caliber veins extending above and below the knee on the lateral aspect. The direction of flow is downward in this system. This represents the remnant of the embryonic lateral marginal vein [3].

Summary

Sound knowledge of anatomical arrangement of veins of lower limbs is essential for a clinician dedicated to the care of patients with CVD. There is a well-defined pattern of arrangement of the veins, although variations are very common.

The veins are arranged in two compartments – the superficial and deep. A well-defined space in the superficial compartment known as the saphenous compartment houses the GSV and the saphenous nerve.

The veins are arranged in three patterns – superficial veins, deep veins, and perforating veins. The GSV and SSV are the superficial veins. All other terminology for these veins has been abandoned.

With the advent of US in the diagnosis of venous diseases, certain patterns of anatomy are well recognized. Some of these findings are highlighted in this chapter.

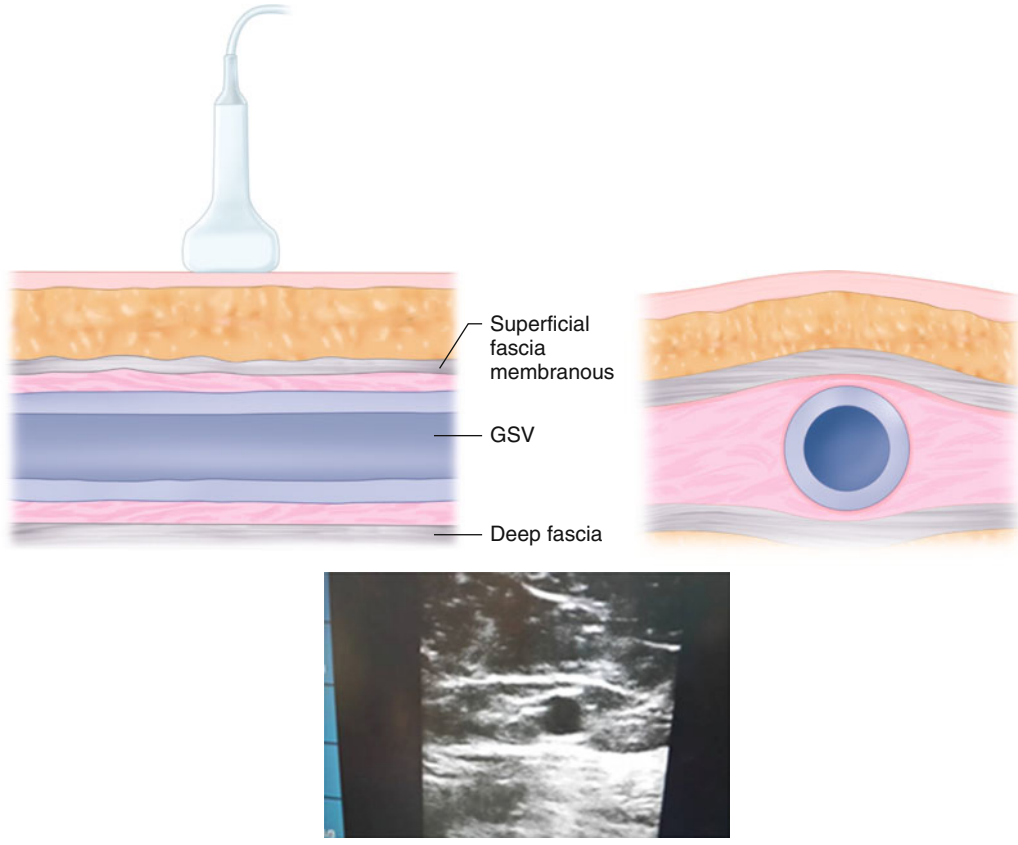

Fig 2.3 US appearance of the GSV in the superficial compartment

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Venous Physiology and Hemodynamics of Lower Limbs

3

Riju Ramachandran Menon

Contents

Introduction

The venous system of the lower limbs is an organized and functional unit. Returning blood to the heart is its primary function. Several factors are involved in the control of this system. These include gravity, the reservoir capacity, venous tone, sympathetic control of smooth muscles, and many other mechanisms. Most of our misunderstanding of venous diseases stems from the inability to appreciate the delicate anatomy and physiology. Details of anatomy were considered in Chap. 2.

This chapter focuses on the physiology of the lower limb venous system. In this section, we plan to discuss the following:

- Physiology of normal venous drainage
- Altered hemodynamics in venous disorders

A simple and effective way to comprehend venous physiology would be to consider the flow and pressure patterns in health and disease. In the clinical setting, this information is obtained by the ambulatory venous pressure (AVP) studies.

Normal Venous Drainage of Lower Limbs

The peripheral venous system functions as a reservoir to store blood and as a conduit to return blood to the heart. In a person in the erect posture, blood entering the lower-extremity venous system must travel against gravity and against

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fluctuating thoracoabdominal pressures to return to the central circulation. Proper functioning of the system depends on the coordinated functioning of several parts.

There are three components of the venous system. These are the veins of the lower limb, the valves in the veins, and the muscle pumps.

The Veins of Lower Limb

The veins of the lower extremity are arranged into the superficial, deep, and perforating systems [1]. Blood flow in these veins is always unidirectional and cephalad. Gravity and hydrostatic pressure oppose venous return in the upright position. A system of valves, an efficient peripheral pump mechanism, and a negative intrathoracic pressure overcome the effects of gravity [2, 3].

The superficial venous system comprising the GSV and SSV and the interconnecting network of veins function as conduits to return blood to the deep venous system [2]. The predominant flow from the saphenous system is through the perforator into the deep veins. This arrangement is especially dominant during activity. Blood seldom travels up along the entire length of the superficial veins except when the deep veins are blocked. Eighty percent of the blood from the lower limb is conveyed to the heart through the deep venous system.

The deep venous system is located below the muscular fascia and serves as collecting veins and the outflow from the extremity. Venous sinuses of the gastrocnemius and soleus muscles are blood-filled spaces with a capacitance function and serve as chambers of the peripheral heart. The venous sinuses drain to the deep veins. The deep veins are surrounded by powerful muscle and the deep fascia of the leg.

The perforating veins connect the deep and the superficial system. Their primary function is as drainage conduits from superficial to the deep system.

Venous Valves

- The superficial, deep, and most perforating veins contain bicuspid valves formed from folds of endothelium, supported by a thin layer of connective tissue. Valves are most numerous in the distal leg and decrease in number in the upper part of the limb [4]. Valves subserve two functions:
- They promote unidirectional cephalad flow toward the heart.
- They break the hydrostatic column of blood into segments.

Normally, at rest, the valves remain open. The valves close during muscular activity. This is a passive event and is initiated by a higher pressure in the supravalvular segment produced by posture and muscle activity. There is a transient phase of retrograde flow lasting for less than 0.5 s. This retrograde flow must be of sufficient velocity to coapt the cusps completely [5] (Fig. 3.1).

In the upright posture, a reflux lasting less than 0.5 s is physiological; if the duration exceeds 0.5 s, it is defined as pathological reflux. The importance of incompetence of a single valve or several valves in genesis of clinical effects is not definitely known [2].

Muscle Pumps

The calf muscle pump is the most powerful force that facilitates venous return from the lower limbs. The thigh and foot muscle pumps also function to some extent toward this purpose.

Contraction of the calf muscle pump increases the pressure within the fascial compartments and forces blood up along the deep venous system (*systole of the muscle pump*). The competent valves prevent reflux distally within the deep venous system or through the perforators into the superficial veins (Fig. 3.2).

When the calf muscles relax, the pressure in the fascial compartment drops. During this phase, blood from the superficial veins and the sinuses

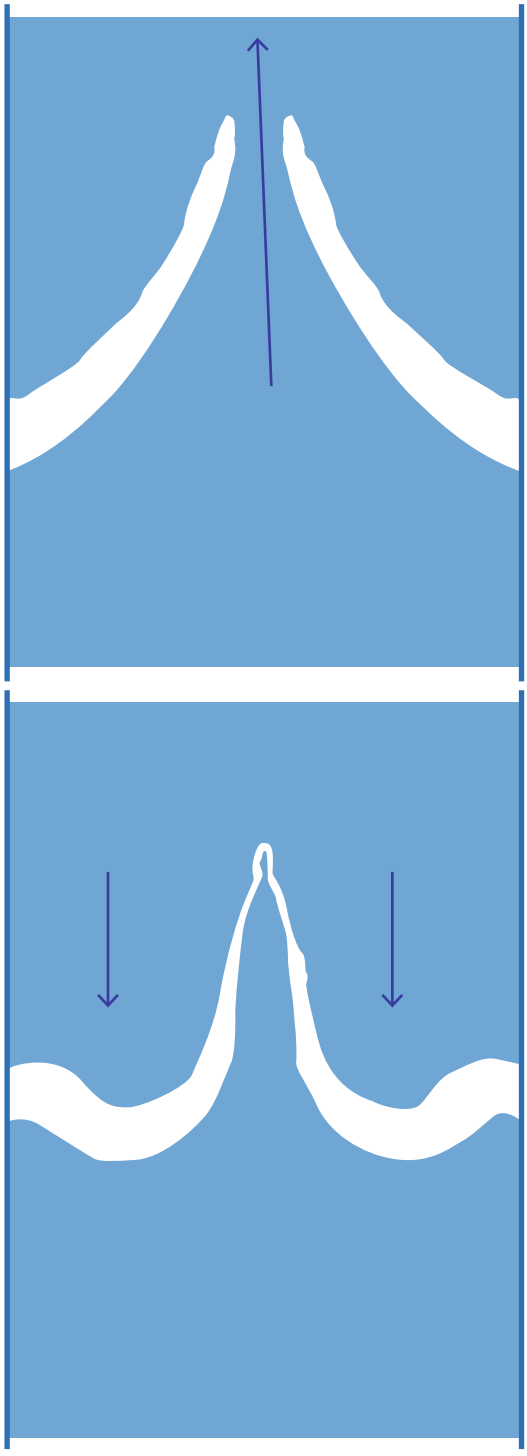

Fig. 3.1 Mechanism of valve closure

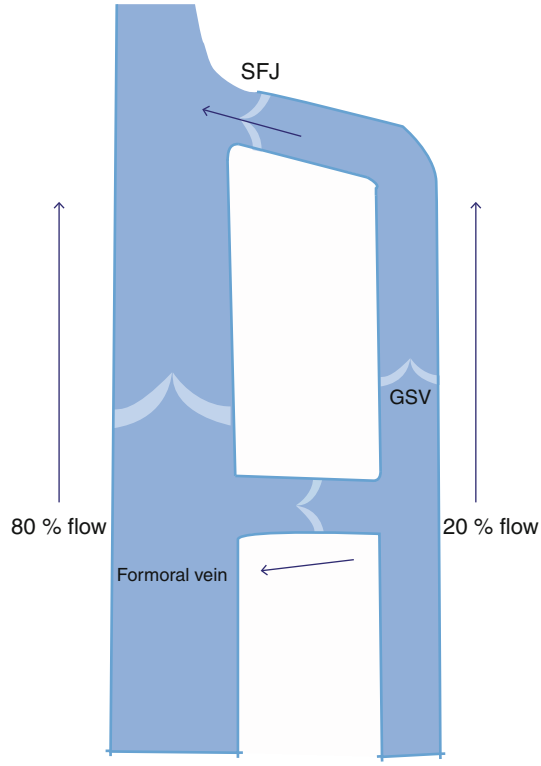

Fig. 3.2 Normal venous drainage of lower limb

fills the deep system through the perforating veins (*diastole of the muscle pump*). The deep fascia of the leg supports the muscle pump considerably. The net effect of a series of contractions of the calf muscle pump would be to promote a streamlined, unidirectional, and cephalad flow toward the heart. This effectively reduces the pressure and volume in the superficial venous system during ambulation [3, 6].

The thigh muscle pump is not as powerful as the calf muscle pump in spite of the fact that these muscles are bulkier. Two reasons are attributed for its less powerful action – rapid refill and less compressible intermuscular location of the deep veins in the thigh [2]. The ejection fraction of the calf muscle pump is around 65 %, in comparison with only 15 % for the thigh pump [6].

The foot and lower leg biomechanics also play a major role in venous return. When the sole of

the foot makes contact with the ground, the lateral plantar veins are emptied and blood is forced into the posterior tibial veins. This marks the first but essential step of venous return from the lower limbs. The calf muscle pump then sequentially takes over from the foot muscle pump [7]. When the foot muscle pump contracts, 50 % of the perforators of the foot permit flow from the deep to the superficial veins [2]. The role of the foot muscle pump could be crucial in the genesis of chronic venous disorders. It has been identified that static foot disorders may be associated with impaired venous return from the lower limbs [7].

In an average individual walking 100 steps a minute, the combined stroke volume of the calf muscle pumps of both sides is estimated as 6.0 l/min2.

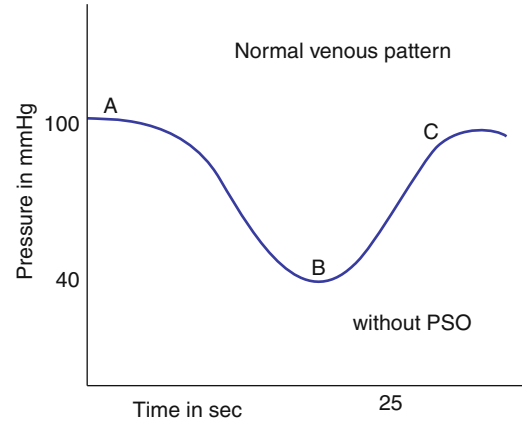

Fig. 3.3 AVP normal venous pattern. Note the prominent drop in PEP. (*A*) Resting pressure at start of exercise. (*B*) Maximum pressure fall with exercise. (*BC*) Recovery time

Correlation with Ambulatory Venous Pressure Studies

In the clinical setting, the function of the calf muscle pump is best demonstrated by recording the ambulatory venous pressure (AVP) in the foot veins. AVP studies are primarily aimed at recording the drop in venous pressure in the superficial veins of the foot following a series of calf muscle contractions such as standing on toes [8].

A foot vein is cannulated and connected to a pressure transducer and a three-channel recorder or a manometer system through a three-way stopcock and a saline reservoir. The pressure in the foot vein with the patient standing upright and at rest is first recorded – *resting pressure* (RP). This will be roughly equivalent to the weight of the column of blood from the right heart to the point of measurement and varies according to the height of the individual. On an average, it is around 100 mm of Hg. The subject is asked to perform a series of standing on toe movements with the cannula in situ. This will produce a powerful contraction of the calf muscle. The pressure after a series of 10–15 contractions drops down by 50–60 % and thereafter remains steady *irrespective of the extent of activity*. The lowest pressure recorded after the series of muscle contractions is designated as the *postexercise pressure* (PEP). On cessation of the exercise, when the subject is at rest, the pressure slowly returns to the original resting value. The time taken for the PEP to return to the RP is designated as the *recovery time* (RT). In normal subjects, this is about 20–30 s. This AVP pattern is known as the normal venous pattern (Fig. 3.3).

In patients with venous disorders, the drop in PEP is very negligible. Also, the recovery time is much faster (0–5 s). Thus the AVP pattern, normal and abnormal, can give an insight into the functioning of the calf muscle pump in health and disease.

Abnormal Hemodynamics in Chronic Venous Disorders

As we have seen in the previous section, the activity of the calf muscle pump reduces the pressure and volume of blood in the superficial venous system. This remarkable ability of the muscle pump is diminished in patients with venous disorders of the lower limbs, resulting in a persistently elevated PEP. In clinical parlance, this is referred to as *ambulatory venous hypertension*. Side by side, the RT is short from rapid reflux refilling. The pathological situations

leading onto development of ambulatory venous hypertension include the following:

- Presence of reflux in the saphenous systems
- Reflux/obstruction in deep veins
- Incompetence of medial calf perforators

In clinical practice, these pathologies exist in combination. But for clarity, they will be considered in isolation.

Reflux in Superficial Veins

An incompetent superficial system permits blood to reflux. If the perforators are normal, the calf muscle pump can cope up with the extra load and reduce the exercise pressure. If there is a large-volume SF/SP junction reflux, the extra load is carried into the deep veins through the next reentry perforator. This establishes a vicious cycle often referred to as private circulation [9]. To accommodate the extra load, two secondary events develop; the volume overload can stretch the deep veins and the perforators can get dilated and become secondarily incompetent. These changes are reversible. Elimination of reflux in the saphenous system can revert both changes.

The cause of valve failure in the saphenous system is not very clear. Till now, primary structural changes in the valve cusp resulting in reflux from above downward were considered to be the sequence of events. This is the traditional *descending valvular incompetence theory* of Friedrich Trendelenburg. Recently it has been suggested that valvular incompetence is secondary to vein wall dilatation. Venous dilatation can develop below the valves. Reflux in saphenous system can proceed in an ascending fashion. This is the *ascending valvular incompetence theory* [10].

Correlation with AVP Studies

AVP studies in this group of patients demonstrated elevated PEP and rapid RT. However, it was observed that this high pressure returned to near normal values when the test was repeated after applying a tourniquet in the thigh below the SFJ to occlude the superficial veins (*proximal saphenous occlusion* – PSO). The RT also normalized after

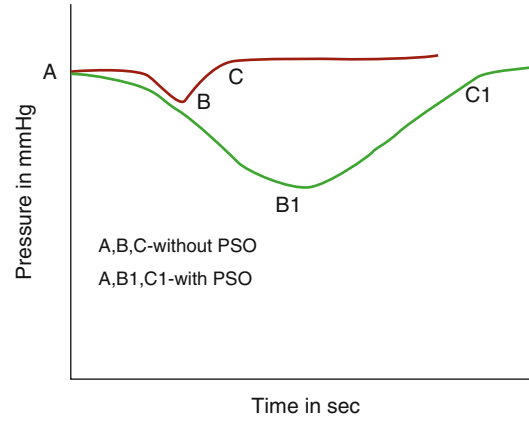

Fig. 3.4 AVP superficial venous pattern. PSO normalizes the AVP pattern. (*A*) Resting pressure at start of exercise. (*B*) Maximum pressure fall with exercise. (*BC*) Recovery time

PSO [8]. This pattern of AVP is known as "superficial venous pattern." These findings indicate that in this subset of patients ambulatory venous hypertension could be easily controlled by correction of reflux in the saphenous system (Fig. 3.4).

Reflux/Obstruction of the Deep Veins

Reflux in the deep veins, axial or segmental, is a common finding in patients with primary chronic venous insufficiency. In patients with post-thrombotic syndrome, there could be reflux, obstruction, or both.

Reflux in deep veins resulting from valvular incompetence from any cause can produce significant alterations of venous return. The normal, streamlined, unidirectional, and cephalad blood flow in deep veins is converted into a turbulent, bidirectional, up-and-down movement, *the "yo-yo" effect* [10] (Fig. 3.5).

There is stagnation and distention of the deep veins which in turn make the perforators and superficial systems secondarily incompetent – "safety valves." Skin changes and ulcerations are very common in such a situation. The effects are more pronounced in the presence of chronic obstruction in the deep veins or when obstruction and reflux coexist as in patients with post-thrombotic syndrome.

Fig. 3.5 Yo-yo effect. Effect of reflux in deep veins. "Safety valve" – incompetent perforator and superficial vein

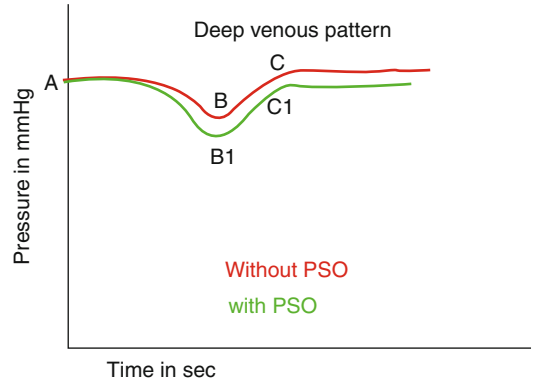

Fig. 3.6 Deep venous pattern. PSO had no effect on PEP. (*A*) Resting pressure. (*B*) Maximum pressure fall with exercise. (*BC*) Recovery time

Correlation with AVP

The PEP remains elevated in this group of patients with reflux/obstruction in deep veins. PSO using above knee tourniquet does not lower the high exercise pressure, unlike in the previous group. This pattern is known as "deep venous pattern" (Fig. 3.6). Such patients may need extensive procedures such as valve reconstruction in the deep veins. When there is an obstruction in the deep veins, the PEP may even rise above the RP. These patients typically experience the symptom of venous claudication. Relieving the obstruction in the deep veins by endovenous stenting of an occluded iliac segment can offer considerable improvement in such patients.

Incompetence of Perforators

The impact of incompetent perforators in venous hemodynamics is very complex. The effect depends on the status of the other systems. As long as the calf muscle pump is functioning normally, the extra load resulting from reflux from the perforators does not create any strain. This is because the volume of blood ejected from these vessels is not very significant. Such a situation is observed when perforator incompetence coexists with saphenous reflux. This is the consequence of the private circulation described earlier. As already mentioned, elimination of reflux in the saphenous system reverts the dilated perforators to normal size.

Incompetent perforators affect lower limb venous physiology only when they are hemodynamically significant. Objective findings of such pathological perforators are outward flow duration more than 500 ms and size equal to or more than 3.5 mm [11]. Such perforators are commonly associated with a pathological deep venous system. Negus named them "Leaking Bellows." They produce large-volume, high-pressure leak of blood from deep to superficial veins during calf muscle contraction – the ankle blowout syndrome [12]. The calf muscle pump cannot cope up with such a situation of high venous pressure. Skin changes and ulceration are very common in such a setting.

Correlation with AVP

When saphenous reflux is the dominant factor along with perforator incompetence, the high PEP drops down with PSO. But the drop in PEP may not be as marked as in a patient with isolated saphenous reflux [8]. In this group of patients, elimination of the saphenous reflux would normalize the venous dynamics significantly. In combined deep and perforator incompetence with or without

superficial reflux, the AVP pattern is similar to the deep venous pattern described earlier.

Multilevel involvement is observed in a large number of patients with venous diseases. Obviously, the alteration in the venous hemodynamics would also be extremely complex. The pattern may not fit in with the oversimplified version described here.

Summary

Lower limb venous drainage is mediated by a very effective functioning unit composed of the veins of the lower limb, the competent valves, and the muscle pumps. The calf muscle pump is the most dominant component of this unit. The net effect of the calf muscle pump activity is to lower the pressure and volume of blood in the lower limb venous system and maintain it at an optimum level. This will achieve the goal of avoiding venous ambulatory hypertension. This delicate mechanism is upset in patients with venous disorders of the lower limb. Ambulatory venous hypertension is the most dominant pathological effect in all these patients. The severity and clinical manifestations of ambulatory venous hypertension would be extreme when there is multisystem involvement.

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Chronic Venous Disorders: Classification, Severity Assessment, and Nomenclature

4

Subramoniam Vaidyanathan

Contents

Introduction

Although chronic venous disorders of the lower limbs are common problems, there were no uniform standards for the assessment of clinical stage and symptom severity. The outcome of treatment strategies was also not standardized. There were considerable variations in the intra- and inter-observer data. In such a setting, comparison of inter-institutional data became a difficult task. The need for uniform reporting standards of venous disorders was a felt need among clinicians interested in the problem. The credit for evolving such standards goes to the American Venous Forum.

This chapter focuses on the following aspects of the problem:

- The system of accurate classification of chronic venous disorder (CVD) – the CEAP classification, both basic and advanced/full CEAP
- Scoring systems for assessment of symptom severity
- Quality of life (QoL) measures
- Definition of terminologies

The CEAP Classification

The CEAP classification is a comprehensive method of classifying chronic venous disorders based on the following:

- **C**linical manifestations
- **E**tiological factors

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- **A**natomical distribution of the disease
- **P**athophysiological processes underlying the disease

CEAP classification has gained universal acceptance and has evolved into a well-organized and meaningful basis for international communication and documentation of CVD.

Evolution of the CEAP Classification

The need for a formally structured classification for CVD was raised in the annual meeting of the American Venous Forum (AVF) in the year 1993. The first consensus CEAP document was formally presented at the next annual meeting of AVF in the year 1994. This document had two parts [1]:

- A classification for CVD based on the clinical, etiological, anatomical, and pathophysiological findings
- A scoring system of the severity of CVD based on the number of segments affected, grading of symptoms and signs, and disability

The need to refine and update the CEAP classification was raised in 2002, and accordingly, in 2004, a revised CEAP document was formally released [1, 2].

The revised CEAP document had recommended the following changes [1]:

- Refinements of several definitions used in describing CVD.
- Refinements of the C classification of the CEAP; identification of subclasses C4a and C4b.
- Addition of the descriptor "n" – (*no venous abnormality identified*). This is under E, A, and P.
- Incorporation of the date of classification and level of clinical investigation (see later).
- Introduction of basic CEAP for routine clinical practice and full/advanced CEAP for research and publication purposes.

CEAP: Clinical Classification [1, 2]

There are seven classes of CVD according to the ascending order of severity (Table 4.1).

Table 4.1 Clinical classification

Clinical class	Description
C0	No visible or palpable signs of venous disease
C1	Telangiectases or reticular veins
C2	Varicose veins
C3	Edema
C4	Changes in the skin and subcutaneous tissue C4a Pigmentation and/or eczema C4b Lipodermatosclerosis and/or atrophie blanche
C5	Healed venous ulcer
C6	Active venous ulcer

Adapted from Kistner and Eklof [2]
Each clinical class is further qualified by a subscript "S" if symptomatic and "A" if asymptomatic
The symptoms include *aching*, *pain*, *tightness*, *skin irritation*, *heaviness*, *muscle cramps*, *and other symptoms* relating to venous disorders

Table 4.2 Etiological classification

E c	Congenital
E p	Primary
E s	Secondary (post-thrombotic)
E n	No venous etiology identified

Adapted from Kistner and Eklof [2]

CEAP: Etiological Classification [1, 2]

Three causes are identified under etiological classification:

- *Congenital* – refers to conditions where the vessels are deformed from birth as, for example, Klippel-Trenaunay syndrome.
- *Primary* – refers to degenerative conditions of the vein wall with reflux as in varicose veins.
- *Secondary* – commonest cause is post-thrombotic syndrome.

The revised CEAP has included a fourth group, "*No venous etiology identified" with the superscript "n"* (Table 4.2).

CEAP: Anatomical Classification [1, 2]

This has primarily three components based on the location of the disease: *superficial veins* (*s*),

Table 4.3 Anatomical classification

A s	Superficial veins
A p	Perforating veins
A d	Deep veins
A n	No venous location identified

Adapted from Kistner and Eklof [2]

Table 4.4 Pathophysiological classification

P r	Reflux
P o	Obstruction
P r,o	Reflux and obstruction
P n	No venous pathology identifiable

Adapted from Kistner and Eklof [2]

perforator veins (*p*), *and deep vein* (*d*). The revised document has incorporated a fourth category, "*n*", *when no venous location could be identified* (Table 4.3).

When an abnormality is identified, to further localize the disease, 18 venous segments from the infradiaphragmatic IVC to the crural veins are recognized (refer later).

CEAP: Pathophysiological Classification [1, 2]

The basic changes here are reflux(r), obstruction (o), and combination of both reflux and obstruction (r,o). The descriptor "n" is employed when no pathology could be identified (Table 4.4).

When reflux or obstruction is detected, further anatomical localization of the pathophysiology can be done by considering venous anatomical segment classification [2] (Table 4.5).

- CVD are progressive and not static problems. Serial CEAP classification is necessary to understand the progression of the disease. The revised document has suggested inclusion of the date of CEAP classification and the level of investigation to make it more dynamic [1]. Three levels of investigations are recognized.
  - Level I Investigation – office visit with history and clinical examination; includes use of handheld Doppler (HHD)
  - Level II Investigations – noninvasive studies (duplex color scanning along with some form of plethysmographic studies if needed)
  - Level III Investigations – invasive studies (Ascending/descending venogram, ambulatory venous pressure studies, CT/MR venograms)

Table 4.5 Venous anatomical segment classification

Superficial veins
1. Telangiectases/reticular veins
2. GSV above knee
3. GSV below knee
4. SSV
5. Nonsaphenous veins
Deep veins
6. Inferior vena cava
7. Common Iliac vein
8. Internal iliac vein
9. External iliac vein
10. Pelvic: gonadal, broad ligament veins, etc.
11. Common femoral vein
12. Deep femoral vein
13. Femoral vein
14. Popliteal vein
15. Crural veins: anterior tibial, posterior tibial, peroneal veins
16. Muscular veins: gastrocnemius, soleus, etc.
Perforating veins
17. Thigh perforating veins
18. Calf perforating veins

Adapted from Kistner and Eklof [2]

Full/Advanced CEAP and Basic CEAP

It is essential that the CEAP classification should be simple enough for routine clinical use. At the same time, it should be comprehensive for research and publication purposes. To achieve these twin goals, the revision committee has recommended a *basic CEAP and an advanced/full CEAP classification*.

For basic CEAP, two simplifications are suggested [1]:

- The single highest descriptor can be used for clinical classification.
- After duplex scan, in basic CEAP, the E, A, and P factors are also to be documented. But the complex 18 venous anatomical segment classification can be avoided.

For advanced CEAP classification, the full spectrum is to be used [1].

- The clinical classification should include the full range of descriptors (see example below).
- Venous anatomical segments are also to be included.

The following example would clarify the issue.

A *patient has varicose veins with pain and lipodermatosclerosis. Duplex scan on 02/02/2014 confirmed primary reflux of GSV and incompetent perforators in the calf*.

The basic CEAP of this patient would be *C4b s*; *E p*; *A s p*; *P r*; *Level II*; *02/02/2014*.

The advanced CEAP for this patient would be *C2,3,4b s*; *Ep*; *A s p*; *P r 2,3,18*; *Level II*; *02/02/2014*.

The advanced CEAP looks a little intimidating, but it is relevant for standardization and cohort study. The revision of the CEAP is an ongoing program of the American Venous Forum and further modifications are likely to emerge.

Outcome Assessment

Venous Severity Scoring (VSS) Systems: Problems and Issues

Any system aimed at evaluating the severity of disease and outcome of therapy should contain objective and quantifiable elements. Further, these elements should reflect positive or negative impact to specific interventions and treatments. Venous diseases, unlike peripheral arterial diseases, do not have well-defined measurable end points. Again, there is no noninvasive test on the venous side, which will provide a quantifiable data on the outcome of therapy. On the arterial side, the ankle brachial pressure index is a very simple noninvasive test, which has all the required criteria for outcome measurement. These issues make severity scoring and outcome assessment more complicated on the venous system [3]. The CEAP is an excellent system for *classifying* CVD. But when it comes to using CEAP for severity and outcome assessment, problems arise. The CEAP in its current form is basically a static system. For example, in C4 lesions, lipodermatosclerosis is unlikely to change with treatment [4]. An ad hoc committee of the American Venous Forum, under the leadership of Dr. Rutherford, arrived at three severity scoring systems based on the elements of the CEAP [4]. The "E" component of the CEAP was not incorporated since it is a fixed entity [3]. The scoring systems evolved are [4] as follows:

- *Venous Clinical Severity Score* (*VCSS*) – basically derived from the clinical classification of CEAP.
- *Venous Segmental Disease Score* (*VSDS*)/ *Anatomical Score* – derived from a combination of the anatomical and pathophysiological components of CEAP.
- *Venous Disability Score* (*VDS*). This is a modification of the original CEAP disability score.

Venous Clinical Severity Score (VCSS)

The present format of the VCSS has nine attributes. Each one of them is assessed by a grading scheme ranging from 0 to 3 (0, absent; 1, mild; 2, moderate; 3, severe) (Table 4.6).

Several validation studies have confirmed the effectiveness of the VCSS in practice [3]. The general criticism is that VCSS is more sensitive in the evaluation of patients with the advanced form of the disease. But Kakkos and group found it useful for early superficial venous disease also [5]. Vasquez and team have revised the VCSS and the new version was published in 2010 [6].

The Venous Segmental Disease Score

This is based on the anatomical and pathophysiological components of CEAP. It is aimed at scoring reflux and obstruction derived from the anatomical segmental studies. Findings of reflux or obstruction on duplex ultrasound scan form the basis of this scoring system [3]. All of the 18 venous anatomical segments are not considered for this scoring. Only the most commonly affected segments are considered. Most of the patients with post-thrombotic disease would have both elements in combination.

The current version of the VSDS is presented in Table 4.7.

Table 4.6 Venous Clinical Severity Score

Attribute	Absent = 0	Mild = 1	Moderate = 2	Severe = 3
Pain	None	Occasional, no activity limitation, no analgesics	Daily, moderate limitation, analgesics infrequent	Daily, severe activity restriction, regular analgesics needed
Varicose veins	None	Scattered, branch VV with competent GSV/SSV	Multiple, single segment GSV/SSV reflux	Extensive, multisegment GSV/SSV reflux
Venous edema	None	Evening ankle edema only	Afternoon edema above ankle	Morning edema above ankle requiring elevation
Skin pigmentation	None	Limited in area	Diffuse over gaiter area	Wide distribution
Inflammation	None	Mild cellulitis, limited to area around ulcer	Moderate cellulitis of gaiter area	Severe cellulitis/venous eczema
Induration	None	Focal, <5 cm	Medial or lateral, < lower 1/3rd	Entire lower 1/3rd or more
Total no ulcers	0	1	2–4	>4
Active ulceration, duration	None	<3 months	>3 months,<1 year	Not healed >1 year
Active ulcer, size	None	<2 cm diameter	2–4 cm diameter	>4 cm diameter
Compression, therapy	Not needed	Intermittent use	Needs stockings most days	Needs full time with elevation

Adapted from Rutherford et al. [3]

Table 4.7 Venous Segmental Disease Score: for reflux and obstruction

Reflux	Obstruction (excised/ligated)
½. small saphenous	
1. Great saphenous	1. GSV (only if from groin to below knee)
½. Perforator, thigh	
1 perforators, calf	
2. Calf veins, multiple (PTV alone = 1)	1. Calf veins multiple
2. Popliteal vein	2. Popliteal vein
1. Femoral vein	1. Femoral vein
1. Profunda femoris vein	1. Profunda femoris vein
1. Common femoral vein and above	2. Common femoral vein
	1. Iliac vein
	1. Inferior vena cava (IVC)
10. Maximum reflux score	10. Maximum obstruction score

Adapted from Rutherford et al. [3]

Venous Disability Score

The original CEAP classification contained a scoring system for the severity of CVD. But the revised document deleted this part. The existing disability score was modified to generate the Venous Disability Score in the present form (Table 4.8).

Table 4.8 Venous Disability Score

0. Asymptomatic
1. Symptomatic, able to carry out usual activities without compressive therapy
2. Can carry out usual activities with compression and/or limb elevation
3. Unable to carry on usual activities even with compression and/or elevation

Adapted from Rutherford et al. [3]
Note: Usual activities – defined as activities before onset of disability from venous disease

The validation study of Kakkos and group has concluded that the VCSS and the original CEAP severity scoring system are superior for outcome measurement than the CEAP classification alone [5].

Quality of Life (QoL) Instruments

QoL measures are mostly patient-reported outcome measures. The instruments, usually in the form of questionnaires, may be generic or venous disease specific. *Generic QoL instruments* permit comparison with population norms and other disease states. They also measure any ill effects of treatment. For CVD, Short Form 36-Item Health

Survey (SF-36) has been used with success [7]. *Venous disease-specific QoL instruments* bring out patient-reported outcomes (PROs) in relation to disease progression and treatment results. The commonly used disease-specific tools for CVD are as follows [7]:

1. *Venous Insufficiency Epidemiologic and Economic Study of Quality of Life* (*VEINES-QoL/Sym*) *questionnaire scale*. This has 35 items in two categories and generates two summary scores. It is mostly focused on physical symptoms and not so much on psychological and social aspects.
2. *Chronic Venous Insufficiency Questionnaire* (*CIVIQ*). This measures physical, psychological, social, and pain factors and consists of 20 questions.
3. *The Aberdeen Varicose Vein Questionnaire* (*AVVQ*). This has 13 questions and covers all aspects of the disease.
4. *The Charing Cross Venous Ulceration Questionnaire* (*CXVUQ*). This was designed to measure QoL issues specifically for venous ulcers.

Formulation of Guidelines and Recommendations: The GRADE System

Professional and academic societies periodically come out with practical guidelines for the clinicians. AVF has been in the forefront in formulating such guidelines in the field of phlebology. This is a balancing act between benefits of an intervention on the one hand and its risks and fiscal implications on the other. Grading of Recommendations Assessment, Development, and Evaluation (GRADE) is a comprehensive system for this purpose [8]. For each guideline, the letter A, B, or C marks the level of current evidence (A, high quality; B, moderate quality; C, low or very low quality). The grade of recommendation for a guideline can be [7]:

I. Strong recommendation: if benefits outweigh risks and burden
II. Weak recommendation: when benefits are closely balanced with risks and burdens

Some of the guidelines of the AVF are cited in this work.

Definition of Terminologies

Use of imprecise and non uniform terminologies has brought in a lot of confusion in CVD. Hence, it is appropriate that some clarity be brought into this area. The following is a list of the accepted terminologies and their definition in venous diseases of the lower limbs. The other terminologies are considered in the respective chapters.

- *Chronic venous disorder* (*CVD*) [1, 2, 9]
  This term includes the full spectrum of morphological and functional abnormalities of the venous system from telangiectasia to venous ulcer, C1 to C6 clinical classes (Fig. 4.1a and b).
- *Chronic venous disease* [9]
  Any morphological and functional abnormality of the venous system of long duration manifested either by symptoms and/or signs indicating the need for investigation and/or care.
- *Chronic venous insufficiency* (*CVI*)
  This is a term reserved for advanced CVD. This is applied to functional abnormalities of the venous system producing edema, skin changes, or venous ulcer, C3–C6 clinical classes [9] (Fig. 4.1b). In CVI, ambulatory venous hypertension is responsible for the structural and functional anomalies [7]. CVI can be of the primary or secondary type. *Primary chronic venous insufficiency* is a degenerative condition of the vein wall and valves. It commences as a reflux in the superficial veins and subsequently involves the perforators. Involvement of the deep venous system is late [2]. Superficial venous involvement is the dominant pathology here.

  Secondary chronic venous insufficiency is otherwise known as *post-thrombotic syndrome* [2]. It is a late sequela of acute DVT. It is an acquired inflammatory process commencing as an obstruction to the deep veins first, following an acute DVT.

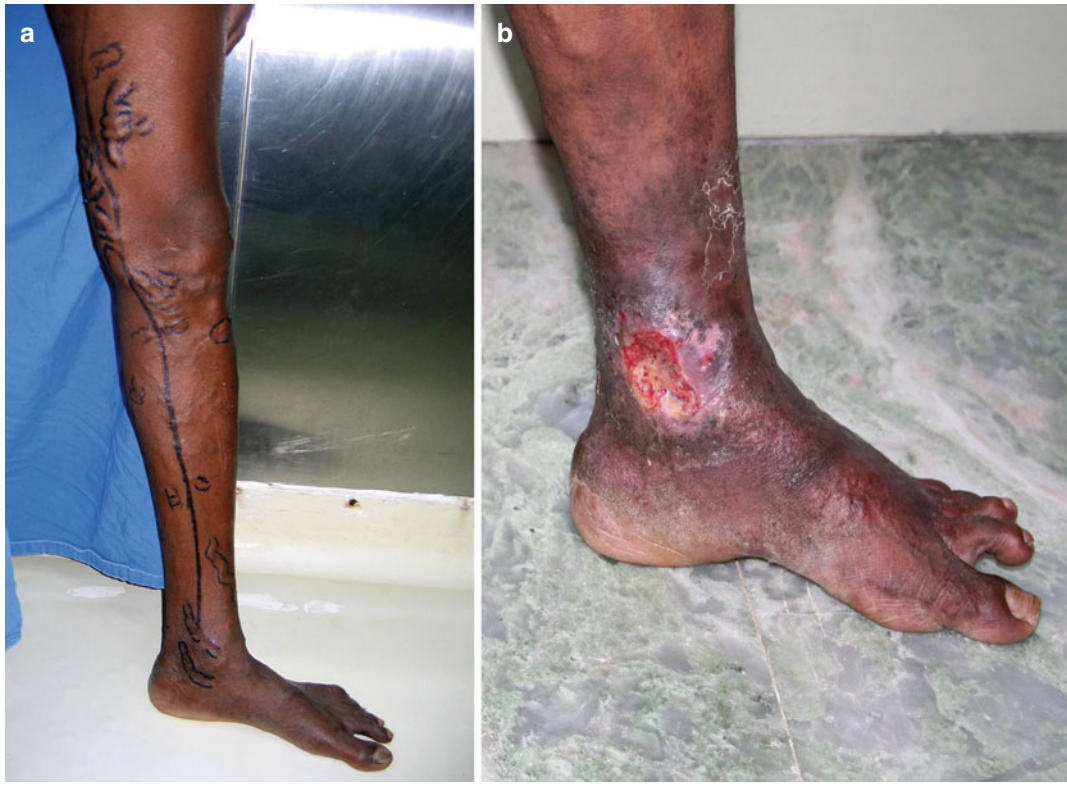

Fig. 4.1 (**a**) and (**b**) CVD. (**b**) CVI

Components of CVD

(a) *Varicose veins*: *Dilated*, *tortuous*, *and elongated veins in the subcutaneous plane*, *3 mm in size or larger*, *measured in the upright position* [2]. According to Bradbury and Ruckley, the cutoff size is 4 mm or larger [10]. They may be palpable and do not discolor the overlying skin [10]. They involve the saphenous veins and tributaries or nonsaphenous superficial leg veins [2]. Synonyms include varix, varices, and varicosities. Varicose veins are usually tortuous but tubular saphenous veins with demonstrable reflux may be classified as varicose veins [2].

(b) *Reticular veins. Dilated bluish subdermal veins*, *1–3 mm in size*. They are not palpable and render the overlying skin dark blue. They may or may not be associated with trunk varices. Synonyms include blue veins, subdermal varices, and venulectases [2, 10].

(c) *Telangiectasia. Confluence of dilated intradermal venules less than 1 mm in caliber*. They are not palpable and render the overlying skin purple or bright red. They can be associated with trunk and reticular veins. Synonyms include spider veins, hyphen webs, and thread veins [2, 10].

The AVF recommendations for identifying the various subdivisions of veins based on the caliber of the veins have not been strictly adhered to. This can create a lot of ambiguity and lack of clarity. *It is recommended that this system of classification is followed as far as possible*.

Summary

This chapter has focused on the basic aspects of venous disorders of the lower limbs pertaining to classification, assessment of symptom severity, and outcome measures.

The CEAP classification is now the universally accepted system of classification of CVD. However, CEAP is not very useful for severity assessment and outcome measurement. For this purpose, the Venous Clinical Severity Score (VCSS), Venous Segmental Disease Score (VSDS), and Venous Disability Score are suggested. Patient-reported outcomes can be measured by generic and venous disease-specific QoL instruments.

For the information of practicing clinicians, the AVF has come out with guidelines following the GRADE recommendations.

This chapter tries to highlight the difference between chronic venous disorders, chronic venous disease, and chronic venous insufficiency. The components of CVD like varicose veins, reticular veins, and telangiectasia are defined.

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Part II

Primary Varicose Veins -C2 Clinical Class

Epidemiology and Risk Factors

5

Pradeep Jacob

Contents

Introduction

Venous diseases of the lower limbs are common problems in clinical practice. The disease has a global prevalence and has been extensively studied and reported. But there is a paucity of literature pertaining to the prevalence of the disease in the Indian subcontinent.

This chapter would focus on the following aspects:

- To highlight the prevalence of chronic venous disorders (CVD) based on the available literature
- To enumerate the risk factors for the development of CVD
- To highlight some of the current concepts regarding the pathogenesis of CVD

Prevalence of the Disease

The exact prevalence of the disease is not precisely defined since there are very few community-based studies. The paucity is glaring in the Indian scenario. The incidence varies based on the criteria used and the geographical region studied. In early studies, the reported prevalence for varicose veins varies from 1 to 73 % in women and from 2 to 56 % in men. The incidence for chronic venous insufficiency (CVI) varies from 1 to 40 % in women and 1 to 17 % in men [1].

One of the widely quoted work is the Edinburgh vein study, reported by Evans and

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team. This is a cross-sectional study based on the analysis of data from 1,566 subjects (867 women and 699 men) [2]. Approximately 1/3 of men and women of the age group of 18–64 years had truncal varices.

In a study of 1,500 subjects of the age group of 15–64 years from Athens, Dimakakose and group have identified CVD in 224 subjects (14.9 %) [3].

CEAP-based epidemiologic studies reported that the prevalence of varicose veins in the adult western population was more than 20 % (21.8–29.4 %) and those with skin changes and venous ulcer was less than 10 % (3.6–8.6 %) [4–6].

Risk Factors

Age

As age increases, the prevalence of varicose veins increases [7, 8]. The Framingham study showed an increase in prevalence from 1 % in men less than 30–57 % in men over 70. Similarly, there was an increase of prevalence from 10 % in women below 30–77 % in women over 70 [9].

Several other studies have corroborated this finding.

Gender

Most studies demonstrate an increased prevalence of varicose veins in women (2–56 % in men, 1–73 % in women) [7]. In the San Diego study, the odds ratio for female gender as a risk factor for varicose veins was 2.18 [6].

The Edinburgh vein study reported a higher incidence of CVI (C3–6 class) in men [8].

Pregnancy and Hormones

Chiesa et al. demonstrated an odds ratio of 1.11 in parous women compared to an Odds ratio of 0.75 in nulliparous women [5]. The Bonn vein study also showed an increase in the odds ratio with increasing number of pregnancies [10]. Raised intra-abdominal pressure and increase in the levels of hormones like relaxin, progesterone, and estrogen, which cause venous relaxation and increased venous capacitance, are postulated as the cause for varicose veins in pregnancy.

Hormone replacement therapy and oral contraceptive pills are not risk factors for the development of varicose veins [11].

Positive Family History

Positive family history for varicose veins among first-degree relatives is associated with higher risk [4, 12]. It has been reported that the risk of developing varicose veins was 90 % when both parents were affected. When only one parent was affected, the risk is 20 % for males and 62 % for females. The risk is 20 % when both parents were unaffected. The chromosome and the related proteins associated with the disease are not fully known now [13].

Genetic Associations

Varicose veins are seen associated with certain genetic disorders. Seventy-two percent of patients with Klippel-Trenaunay syndrome developed varicose veins [14]. Mutations in the von Hippel-Lindau gene, *FOXC2,* and *NOTCH3* are also associated with varicose veins [15–17].

Others

Obesity, smoking, hypertension, and decreased physical activity as risk factors for varicose veins have not been conclusively established.

Pathogenesis of Chronic Venous Disorders

A normal venous system depends on the integrity of valves, vein wall, and the hemodynamics of venous blood flow [18]. Normally the venous flow is a unidirectional and cephalad flow from the superficial veins through the perforators and

into the deep system. In varicose veins, this flow is disrupted resulting in stasis and venous hypertension. Chronic venous hypertension causes ischemia and inflammation of the vein wall. The initiating event is considered to be an inflammatory process resulting from the increased venous pressure. Several structural and functional changes have been observed in the vein wall and the valve cusp. [13]

Changes in the Vein Wall

The structural changes in the vein wall can affect the larger macrovessels (axial and tributary veins) and the microcirculation.

At the *macrocirculation*, the changes observed include dedifferentiation of the smooth muscle cells (SMC) in the media and adventitia from a contractile to secretory phenotype [13]. There is an imbalance in the connective tissue matrix regulation as evidenced by net increase in the collagen/elastin ratio. The matrix metalloproteinase activation leads to wall fibrosis and dilatations.

Microcirculation responds to these events. The endothelial cells of the dermal microcirculation become edematous with widened interendothelial gaps. This increases capillary permeability leading on to exudation and edema formation. Persistent venous hypertension acts on the end organ, the dermal tissues over the gaiter area. Dermal fibroblasts over the gaiter area show several histological changes. Biopsy from venous ulcer edge demonstrated aberrant phenotypic behavior of fibroblasts compared to biopsies of normal skin from the thigh in the same patients. This may be a factor for the nonhealing nature of the venous ulcer. The cellular events are described in more detail in Chap. 11

Changes in Valve Function

Changes in the valve function can result from two reasons: from primary valvular dysfunction or secondary to changes in the vein wall [18–20].

Primary valvular dysfunction has been reported by several workers. Absence, deformities (scarring, splitting etc.), or hypotrophy of valves has been demonstrated in varicose veins [19, 20]. At the molecular level, these valves have less collagen and show increased inflammatory activity as evidenced by monocyte and macrophage infiltration of valvular sinuses [21].

Valvular dysfunction initiates the vicious circle of venous hypertension, inflammation, and further wall damage.

Valve Dysfunction Can Also Arise from Primary Changes in Vein Wall It is believed that the valvular incompetence is due to structural and biochemical changes in the vein wall [22, 23]. Several theories have been postulated for explaining these changes, including extracellular matrix (ECM) degradation, the role of matrix metalloproteinases, endothelial cell activation, smooth muscle proliferation, dedifferentiation, and dysregulation of smooth muscle apoptosis, etc.

Extracellular Matrix Degradation and Matrix Metalloproteinases

Extracellular matrix (ECM) in normal veins is composed of collagen, proteoglycans, glycoproteins, elastin, and fibronectin [24]. In varicose veins, the total elastin content is reduced [25, 26], and there is downregulation of type III collagen and upregulation of type I collagen [27]. It has been postulated that alteration in the balance of elastin and collagen may lead to weakening of the vein wall and subsequent varicosity [28]. The ECM is a dynamic structure and homeostasis is maintained by the zinc-dependent matrix metalloproteinases (MMPs) and its endogenous tissue inhibitor (TIMPs) [22, 24, 29].

MMPs are endopeptidases that cleave most of the constituents of extracellular matrix. There are 26 identified MMPs. They are subdivided into four major subgroups – gelatinases, interstitial collagenases, stromelysins, and membrane-type MMPs. They have a role in embryogenesis, acute tissue healing, remodeling, neoplastic invasion, aging, and chronic wounds. MMPs are regulated by cytokines, growth factors, and the activation of TIMPs.

Studies by Raffetto et al. showed that venous hypertension was associated with increased levels of MMP-2 and MMP-9 which causes ECM degradation and venous relaxation [30].

At the final analysis, the major cellular event responsible for the development of varicose veins may be related to an imbalance of MMPs and TIMPs [18]. Pharmacologic modulation of this factor might be a therapeutic option in future.

Class Progression in CVD

It is well known that the distressing events like edema, lipodermatosclerosis, and ulceration (C3, 4, 5, 6) are not a necessary progression for all C2 class patients. In fact, in a large number of patients, this progression seldom happens. Incidence of progression from C3 to C6 class was 2 % per year. The triggering factor for the initiation and maintenance of such factors are unknown. Identification of such factors would be a major step in preventing venous ulcers [31].

Summary

Varicose veins and its related problems are extremely common problems in clinical practice. There are no accurate data regarding the prevalence of CVD in the Indian community. Several risk factors such as advancing age, influence of gender, pregnancy, and positive family history have been identified in several studies.

The pathophysiology and cellular events in CVD and CVI are complex. Primarily, it is an inflammatory process involving the wall and the valves of the large axial and tributary veins. In turn, these changes affect the microcirculation and the dermal fibroblasts resulting in ulceration.

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Primary Varicose Veins: Symptoms and Diagnosis

6

Pradeep Jacob

Contents

Introduction

Varicose veins are a common problem in clinical practice. The condition is so common that many clinicians brush it aside as a "mundane" problem not deserving serious attention. However, it is now realized that varicose veins and its complications can impose considerable fiscal and social burden on the individual and community. Many newer developments in the field of phlebology like newer diagnostic technologies and minimally invasive interventions have all changed the face of care for venous disease.

This chapter would address the following issues:

1. The definition of varicose veins
2. The three types of varicose veins – primary, secondary, and congenital
3. The common symptoms and complications of primary varicose veins
4. Steps in the clinical evaluation including handheld Doppler studies (HHD)
5. The investigations to be undertaken and level of investigations

Varicose Veins: Definition and Types

Varicose vein is a chronic venous disorder (CVD) characterized by dilated, tortuous, and elongated veins of the lower limbs and located in the subcutaneous plane, 3 mm or more in size, measured in the erect posture and with demonstrable reflux

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[1, 2]. The cutoff size is defined as 4 mm or more by Bradbury and Ruckley [3].

Varicose veins may be of three types based on the basic etiology – primary, secondary, and congenital type [4].

Primary varicose veins result from valvular reflux in superficial venous system commonly in the saphenofemoral (SFJ)/saphenopopliteal junctions (SPJ). It could also result from reflux from nonsaphenous sites. It is not the manifestation of other pathological process. The basic defect is an inherent weakness in the vein wall or the valves.

Secondary varicose veins are the manifestation of another pathological process. The commonest cause for the same is post-thrombotic syndrome (PTS). This is discussed in Chap. 14. Secondary varicose veins can also develop in traumatic AV fistulae.

Congenital varicose veins are seen in certain anomalies such as congenital AV malformations and Klippel-Trenaunay syndrome.

Primary Varicose Veins: Symptoms

On the basis of presenting symptoms, two groups of patients with primary varicose veins are recognized – symptomatic group and asymptomatic group [5].

The common symptoms reported include [3, 5] the following:

1. Aching, pain, and heaviness worse on hanging down and relieved on limb elevation and with compression stockings. This pain is different from venous claudication observed in patients with the PTS.
2. Ankle swelling and tiredness.
3. Itching.
4. Nocturnal cramps.
5. Restless legs.
6. Patients with bulging vein with poor circulation experience localized pain, whereas those with axial venous reflux have diffuse pain [6].
7. Cosmetic disfigurement.

These symptoms are aggravated on standing or sitting and relieved by limb elevation and compression stockings. In women, there is aggravation of pain during the premenstrual phase. All these are very nonspecific symptoms shared by a lot of other musculoskeletal conditions. Sometimes, it is extremely difficult to assess the contribution of varicose veins in the genesis of these symptoms. This is especially true for the symptom of lower limb pain. It is important to rule out other vascular, neurological, and musculoskeletal causes of lower limb pain before recommending interventions for varicose veins.

Studies have confirmed that the severity of symptoms is unrelated to either extent of varices or the severity of reflux on duplex scan [3, 5, 6].

Complications of Primary Varicose Veins

Three important complications are identified – hemorrhage, superficial vein thrombosis (SVT), and progression to chronic venous insufficiency.

Hemorrhage from Varicose Veins [5]

This is a common complication. Bleeding can be spontaneous or traumatic.

Traumatic bleeding is rare and can occur from any injury involving the trunk or tributaries of the saphenous system. It is common in the leg.

Spontaneous bleeding is more common. This can develop from the tributaries and reticular veins around the ankle. Bleeding results from progressive enlargement of the localized blow outs with thinning and rupture of the overlying skin and can be precipitated by the dermatitis and itching around the ankle. It is a painless bleed and often occurs when the patient is in the upright position. Surprisingly large volume of blood can be lost before the patient becomes aware of it.

Bleeding can be controlled by bed rest and limb elevation. Once the bleeding is controlled, the patient should be evaluated and advised some form of intervention at an early date, since the problem can recur. Sclerotherapy of bleeding segment of vein is a method of buying time in the event of recurrent bleed from the same site, before elective interventions can be carried out.

Superficial Vein Thrombosis (SVT)

This can develop under two circumstances:

In normal veins, SVT usually follows IV cannulation. This is an infective pathology. Migratory SVT may arise in association with occult malignancy.

In varicose veins, it is believed to result from the sluggish flow in the distended veins and is common during pregnancy. It is a sterile thrombus. There is intense pain over the affected segment which becomes red and indurated. The clot can extend along a junctional perforator to involve the deep veins. Incidence of deep vein thrombosis (DVT) along with SVT in patients with varicose veins is 3–20 % [7]. The affected segment undergoes a cordlike thickening. Treatment is usually by conservative therapy with warm compresses and nonsteroidal anti-inflammatory agents. For SVT within 1 cm of SFJ, two therapeutic options have been suggested – high ligation with or without stripping or heparinization followed by 6 weeks of warfarin therapy [7].

In all varicose vein patients with superficial vein thrombosis, duplex scan must be performed to rule out DVT.

Progression to Chronic Venous Insufficiency

This is the most distressing outcome of primary varicose veins. The triggering event and risk factors for this change over is not clearly understood. Only a small subset of patients progress to this stage. Incidence of progression from C3 to C6 class was 2 % per year [8]. Surgery of varicose veins of C2 class is not known to prevent class progression.

Varicose Veins: Clinical Evaluation

In the curricula of many medical schools, recording the history of a patient with varicose veins and making a detailed clinical examination with all the tests have received considerable attention. However, the sensitivity of the clinical evaluation is reported to be extremely low. There are recommendations to the effect that courses and text books should abandon this part of clinical training [9]. While this is an extreme step, a balanced approach is the right strategy. *It is recommended that no decision on treatment for varicose veins be made on clinical evaluation alone*.

Clinical evaluation is helpful in fulfilling the following objectives:

1. To assess the extent and severity of the problem and to arrive at the CEAP classification.
2. To locate major sites of reflux in the saphenous and perforator systems.
3. To locate any sites of nonsaphenous reflux.
4. To gain information about the status of the calf muscle pump and deep veins. This is the area where clinical evaluation has the least sensitivity.

History and General Examination

Detailed history of the patient, focusing on symptoms and complications if any, should be documented. Risk factors such as profession involving prolonged standing and family history of varicose veins are important. In a female patient, menstrual and obstetric history along with symptoms of pelvic congestion syndrome is of relevance. Past history of any major surgical interventions and history of DVT should be enquired into. In the event of DVT, history suggestive of thrombophilia in relevant cases is essential. Finally, any therapy for the CVD such as compression stockings, sclerotherapy, surgical/endovenous interventions should be documented. Any comorbidities such as diabetes, hypertension, and any other systemic illness should be considered in detail.

General survey should focus on body mass index and presence of any other systemic illness. An important step is to rule out any associated lower limb ischemia. Abdominal examination and pelvic examination should never be neglected.

Local Examination and Clinical Tests

Certain basic tenets are to be observed while examining a patient with varicose veins. They include the following:

1. Patients should be examined in a well-illuminated room preferably with natural sunlight. Artificial illumination can cast a shadow and can obscure proper evaluation.
2. The patient should be evaluated initially in the upright position and then supine if needed.
3. The exposure is from umbilicus to both feet.
4. Both lower extremities have to be assessed even though patient may complain of symptoms only on one side.
5. The extremity being examined should be relaxed with the weight being borne on the opposite side.

Inspection of Extremity with Varicose Veins

The following findings are to be systematically noted:

1. Are there any dilated veins over the lower limb?
2. Is it unilateral/bilateral?
3. Which system is involved? GSV/SSV?
4. Which segments are involved? Foot/leg/thigh?
5. Thigh varices are not usually visible especially in an obese patient. Exceptions are saphena varix and incompetent thigh perforators.
6. Pattern of involvement: truncal/tributary/reticular/telangiectasia.
7. Any limb enlargement with predominantly lateral varices – Klippel-Trenaunay syndrome.
8. Any complications? Superficial thrombosis/features of CVI: corona phlebectatica, lipodermatosclerosis, atrophie blanche, and venous ulcers active/healed.
9. Scars of previous surgery if any.
10. Ankle joint stiffness.
11. Are there any dilated veins over the lower abdomen? This indicates an obstruction to the iliac veins or inferior vena cava (Fig. 14.1).

Steps of Palpation

Main goals of palpation are to identify sites of reflux from deep to superficial veins and also to assess the status of the deep veins and calf muscle pump by performing the various tests. Preliminary palpation along the entire course of the GSV and SSV is done by gently running the hand without exerting much pressure, with the patient in the upright posture. This is important for the following reasons:

1. Varicose veins are often palpable even when not visible, especially in obese individuals. This is especially true in the thigh segment.
2. One may be able feel the tender induration of acute SVT or the cordlike thickening of the late cases.

Tests to Identify Deep to Superficial Junctional Reflux

Brodie Trendeleburg Test

This test is useful in identifying competence of the valve at the saphenofemoral junction (SFJ). The steps of the test are as follows:

1. The veins are emptied by placing the patient supine, raising the legs to 45°, and milking the veins proximally.
2. The SFJ is located 2–4 cm below and lateral to the pubic tubercle. It is compressed and controlled with the thumb of the clinician. Alternatively, it can be controlled by applying a tourniquet just below the SFJ. This is a better option since it is easier to sustain the pressure, especially when the patient stands up.
3. The patient is then made to stand and the compression is released. Incompetence of Valve at SF junction is confirmed if there is immediate, rapid filling of the thigh and leg veins from above downward – "the cascade effect."
4. While performing the test, the pressure at the SFJ is maintained when the patient stands up. If there is rapid filling from below upward, it indicates perforator incompetence.

The test is positive when both or only one of the above findings is present. Traditionally the first part of the test is called *Trendelenburg Test I* and the second component *Trendelenburg Test II*. Some authors recommend performing the second component of the test initially, i.e., observing the extremity with the tourniquet/digital pressure in place and noting for the perforator response. Then the tourniquet is released to observe for the presence or absence of the cascade effect. The

advantage of this strategy is that, in one maneuver, both responses can be assessed.

Assessment of Saphenopopliteal Incompetence

The same principles can be applied to evaluate the short saphenous vein (SSV) and the SPJ.

In isolated SSV disease, a tourniquet is applied below the popliteal fossa after emptying the distended veins.

In combined GSV and SSV reflux, it is important to first control SFJ reflux with a tourniquet in the thigh. The SPJ is controlled by the tourniquet in the infra-popliteal region. When the patient stands up, the thigh tourniquets are retained to prevent reflux along incompetent SF junction. The infra-popliteal tourniquet is then released, and the response noted in terms of rapid filling of leg veins especially on the posterolateral aspect.

Morrissey's Cough Impulse Test

This test is also for assessment of the valve at the SFJ. With the patient standing, place a finger without exerting pressure over the saphenous opening in the upper part of thigh. The patient is asked to cough. If the valve is incompetent, an expansile impulse is felt at the saphenous opening. According to Dodd and Cockett, this test is very sensitive for confirming SF incompetence [5]. Other workers have not supported this [9].

Tests to Locate Incompetent Perforators

Multiple Tourniquet Test

If the Brodie Trendelenburg test indicates incompetent perforators, the site of these perforators can be localized by the multiple tourniquet test. The veins are emptied, and multiple tourniquet (usually three) are applied with the patient in the supine position. The first tourniquet is applied just above the ankle; the second, just below knee; and the third, in the upper thigh, below SFJ. With the tourniquet in position, the patient is asked to stand up. Note the limb below the ankle tourniquet and the segments between the other tourniquets. Distended veins below the ankle tourniquet indicate incompetent ankle perforators. If it is between ankle and below-knee tourniquets, it is usually due to incompetent medial calf perforators. And if it is between the thigh and below knee, it is due to thigh perforator incompetence.

Serially releasing the tourniquet starting from the lower most can produce the cascade effect.

Fegan's Method

This test also identifies the site of incompetent perforators. With the patient standing, the clinician marks the varicosities with a skin marker. The patient is then made to lie down and the affected limb is elevated to empty the veins. Palpate along the line of marked varicosities for gaps or pits in the deep fascia. This corresponds to the location of incompetent perforators. An incompetent perforator is larger in size compared to a normal one. It stretches the opening in the deep fascia as it makes its exit. This is the anatomical basis for this test.

Assessment of the Deep Venous System

This is the area where clinical evaluation is least sensitive. The original Perthes' test is mostly of historical importance.

Modified Perthes' Test

This is to establish the patency of the deep veins. Without emptying the veins, a tourniquet is tied below the SFJ, tight enough to occlude the superficial veins without obstructing the deep veins (selective saphenous occlusion). The patient is instructed to walk briskly for five minutes or perform ten standing on toe movements with the tourniquet in position. If the deep veins are occluded, the patient will complain of bursting pain in the leg and the superficial veins become more prominent. The test is observer dependent and hence not very sensitive.

Percussion in the Evaluation of Varicose Veins

Schwartz Percussion Test/Tap Test

With the patient standing, tap the GSV with the right middle finger, while the fingers of the left hand are placed over the distal varicosities. When the valves are incompetent, there is an uninterrupted column of blood, and the thrill will be felt over the distal vein. Distal palpation and proximal percussion of the saphenous vein are useful tests to suggest valvular incompetence [6].

Auscultation in the Evaluation of Varicose Veins

A continuous machinery murmur may be heard in cases of varicose veins secondary to arteriovenous fistula.

Palpation of the Peripheral Pulses and Recording Ankle Brachial Pressure Index (ABPI)

This is to rule out coexisting ischemia and is relevant in deciding treatment priorities in patients with combined arterial and venous problems. Correction of arterial insufficiency should receive priority over venous problems in such situations. Graded compression stockings used in CVD can aggravate ischemia and may be harmful in the presence of arterial insufficiency.

Examination of Abdomen

Large pelvic or abdominal mass (pregnant uterus, tumors, ovarian cyst, carcinoma rectum) may compress the external iliac vein and cause secondary varicose veins

Pelvic Examination

This is relevant especially in patients with the pelvic congestion syndrome.

The objective of clinical examination of a patient with varicose veins is not only to assess the extent and severity of the venous problem but also to rule out other coexisting local or systemic pathologies.

Validation of Clinical Examination in Varicose Veins

Kim and team conducted a prospective validation study on 44 patients to assess the sensitivity and specificity of Trendelenburg test, cough impulse test, tap test, and the Perthes' test using duplex US as the gold standard. They also included handheld Doppler (HHD) in this validation study. Their findings are interesting [9].

1. Trendelenburg test – high sensitivity (0.91), low specificity (0.15)
2. Cough test – low sensitivity (0.59), low specificity (0.67)
3. Perthes' test – high sensitivity (0.97), low specificity (0.20)
4. Percussion test – low sensitivity (0.18), high specificity (0.92)

These workers have also identified that HHD has a high sensitivity and specificity in the evaluation of reflux in the GSV and SSV. They have concluded that clinical tests used in the examination of varicose veins are inaccurate and that assessment using HHD is more accurate [9].

Handheld Doppler (HHD) in Evaluation of Varicose Veins

An HHD is a simple, inexpensive equipment, based on continuous wave Doppler ultrasonography. The study can be carried out by the bedside of the patient. In fact, HHD study is only an extended clinical examination. Clinicians involved in the treatment of vascular diseases, both arterial and venous, should be familiar with this equipment. A standard HHD basically consists of the following components (Fig. 6.1):

1. Transmitting Piezo crystal that emits ultrasound waves when agitated by passing an electric current.
2. Receiving crystal, which collects the reflected waves.
3. Processor that converts the reflected waves to an audible signal or records in a strip chart.
4. Coupling aqueous gel is required to conduct the waves to tissues.

The penetration of the ultrasound waves is inversely proportional to the frequency of the probe. The greater the frequency, the lesser the depth of penetration; the lesser the frequency, the greater the penetration. This means that deeper vessels such as the common femoral vein (CFV) and popliteal veins are evaluated with a probe frequency of 5 MHz and superficial vessels such as posterior tibial and ankle perforators with a probe of 8 MHz.

The normal venous velocity signal is a low pitched, nonpulsatile signal like a "wind storm." It exhibits spontaneity, phasicity (signal varies with respiratory phase), competence, augmentation, and is nonpulsatile [10].

The instrument can be used to study all the three components of the venous system – the superficial veins, deep veins, and the perforators. Both obstruction and reflux can be evaluated by an experienced

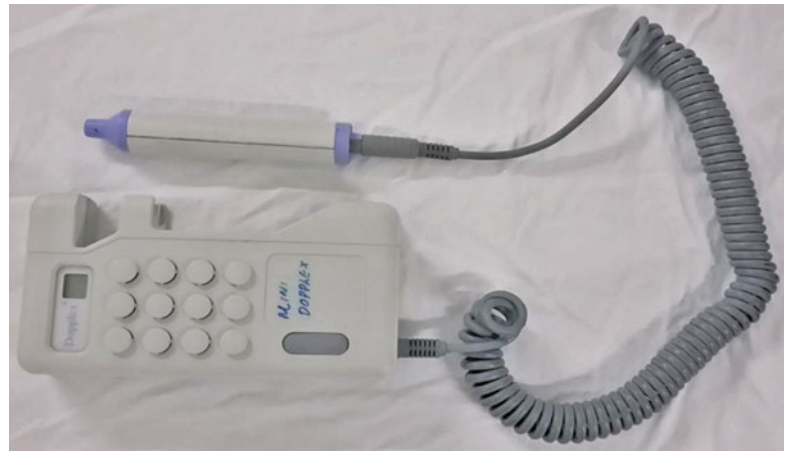

Fig. 6.1 Handheld Doppler unit

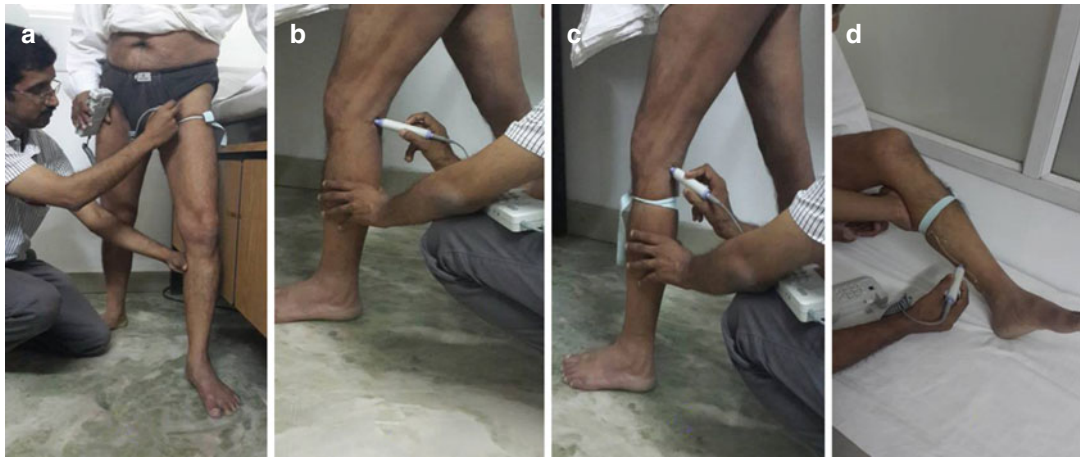

Fig. 6.2 Reflux evaluation by HHD. (**a**) SF junction. (**b**, **c**) SP junction. (**d**) Medial calf perforator

clinician. However, the evaluation of the deep veins is not very sensitive especially in acute DVT. The most useful application is to assess reflux at the SF and SP junctions. It has limited application in the diagnosis of incompetent perforators.

The diagnosis of reflux is established by the presence of bidirectional flow on the release of distal compression. Normally, only a forward flow signal is observed on distal compression due to augmentation effect. As long as the valves are competent, release of distal compression will not produce any signal.

HHD-Saphenofemoral Junction

The patient is evaluated in the upright posture. The extremity to be evaluated is kept slightly forward with the knee and hip slightly flexed. The other limb is held back and the knee extended; the entire weight is borne on the contralateral leg. It is better that the patient supports himself on a table stationed in front to ensure non-weight-bearing. The common femoral vein in the groin is insonated with a 5 MHz probe. Locating the femoral artery signal first and shifting the probe slightly medially is the key to locating the CFV. With the probe in position, the examiner applies thigh/calf muscle compression and release. Bidirectional flow is diagnostic of incompetence. The test is repeated after applying a tourniquet in the upper thigh. If the bidirectional flow disappears or diminishes in intensity, it confirms SF reflux (Fig. 6.2a)

HHD-Saphenopopliteal Junction

The patient is in the upright position. The limb to be tested is relaxed and kept a little forward with the knee slightly flexed. The examiner is comfortably seated behind the patient. The popliteal vein is insonated with a 5 MHz probe. The response to calf compression and release is observed. A bidirectional flow may indicate either SPJ incompetence or reflux in the popliteal vein. The test is repeated after applying a tourniquet below the probe. If the bidirectional flow is abolished or is reduced significantly, it indicates SP reflux. If it persists even after tourniquet, it is due to reflux in the popliteal vein. HHD evaluation of SPJ is not as sensitive as SFJ (Fig. 6.2b, c).

HHD-Incompetent Medial Calf Perforators

The technique of confirming perforator incompetence using continuous wave Doppler was initially documented by Folse and Alexander. The evaluation of incompetent perforators using HHD is not very sensitive. A competent perforator allows blood to flow from superficial to deep veins during relaxation of calf muscle pump (diastolic phase.). The volume of inward flow of blood may not be sufficient enough to generate a signal. The competent perforator does not permit an outward flow of blood from deep to superficial veins during contraction (systole) of the muscle pump. If this happens, it indicates a dilated and incompetent perforator. Hence, the HHD finding in the presence of an incompetent perforator would be an abnormal signal on calf muscle compression or sometimes a bidirectional flow, if the inward flow is of large volume.

The test can be carried out with the patient in the supine or erect position. We prefer the supine position. The patient lies flat on an examination couch with the knee on the side to be tested flexed at 45–60° and the foot flat on the bed. The other knee is kept straight. A tourniquet is applied over the middle of the leg to prevent any reflux through an incompetent saphenous system. Generous quantity of aqueous gel is applied over a large area on the medial aspect of the leg. A probe of 8 MHz is insonated first over the medial aspect starting just below the medial malleolus and shifting progressively upward along a line 2 cm behind and parallel to the posterior border of tibia (the line of the medial calf perforators). Concurrently, the calf muscle above the tourniquet is compressed and released. The sites of incompetent perforator are indicated at the points where a prominent signal is heard on compression of the calf muscle [11] (Fig. 6.2d).

The deep venous system can be evaluated for patency and reflux using HHD, but the results are not sensitive. Duplex scan would be more appropriate for this purpose.

The limitations of HHD are that the results are observer dependent and are only qualitative. Clinical examination combined with HHD can miss up to 30 % of important connections between deep and superficial veins [2].

Primary Varicose Veins: Investigations

The diagnostic studies used for primary varicose veins broadly falls under two groups: noninvasive studies and invasive studies.

Noninvasive Studies

Duplex Scan

The test of choice for the evaluation of chronic venous disease is duplex scan. This employs a pulse wave Doppler in which the energy of the returning echoes is displayed as an assigned color; by convention, echoes representing flow toward the transducer are seen as shades of red, and those representing flow away from the transducer are seen as shades of blue. The color display is superimposed on the B-mode image, thus allowing simultaneous visualization of anatomy and flow dynamics. It is safe, noninvasive, and cost-effective. The evaluation is objective and quantifiable unlike HHD. It can be repeated for follow-up. Portable units are available for bedside evaluation. It provides simultaneous anatomic and hemodynamic information.

A linear transducer of 5–10 MHz range is ideal for the evaluation of most veins. Higher-frequency probes are used for superficial veins,

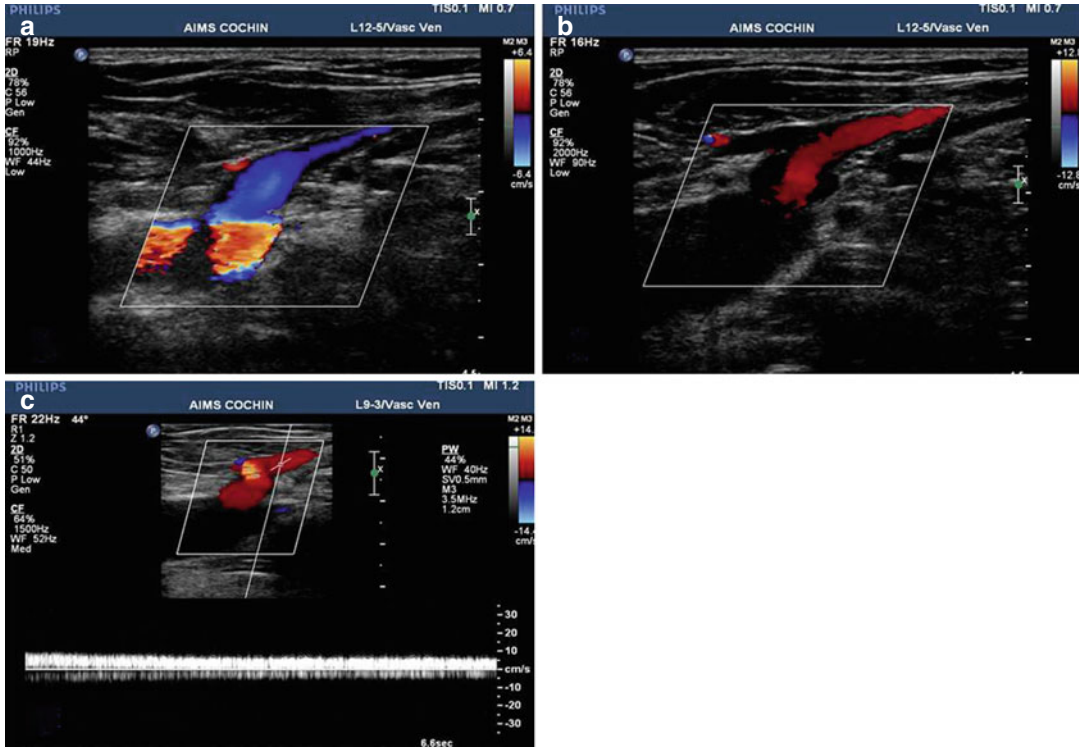

Fig. 6.3 Duplex scan demonstrating gross SFJ reflux. (**a**) Normal flow, no provocation maneuver, (**b**) Reflux following provocation. (**c**) Demonstrating duration of reflux

and lower-frequency probes for evaluation of vena cava and iliac veins. All venous duplex examination includes four components – visualization, compressibility, flow, and augmentation. Duplex ultrasound can be used to demonstrate obstruction and/or reflux. Color coding enables rapid evaluation (Fig. 6.3).

Duplex scan evaluation of a primary varicose vein patient has the following objectives [2]:

1. To assess the competence of the SF/SP junctions
2. The extent and severity of reflux in the axial saphenous veins and also to determine the dimensions of the vein
3. The site and location of the incompetent perforators
4. Any nonsaphenous source of reflux
5. Patency, competence, and any other structural changes in the deep veins

Reflux is the dominant finding in primary varicose veins. It can be elicited by different methods [12].

1. Response to Valsalva; useful for groin veins
2. Compression and release distal to point of examination
3. Rapid inflation and deflation of a cuff

It is important to follow a standard pattern of evaluation. Evaluation is recommended in an upright position, especially for superficial veins. This is to standardize the measurement of size and duration of reflux. The test commences from the common femoral vein and proceeds down toward the deep veins. The GSV, SFJ, SSV, and SPJ follow in sequence. The vessels are evaluated at 3–5 cm intervals. The perforators are studied last.

In the short saphenous system, two areas deserve special mention: posterior thigh extension of the SSV – the vein of Giacomini [2] and gastrocnemius vein reflux as a cause for recurrence. If detected, it should be surgically corrected [13].

Nonsaphenous reflux (vulval, gluteal, posterolateral thigh, etc.) has been reported in 10 % of limbs [12].

The general consensus is that a reflux of 0.5 s or more is considered pathological. Abai and Labropoulos have suggested the following values for duration of pathological reflux:

1. CFV, femoral vein, and popliteal vein: 1,000 ms or more.
2. Superficial veins, deep femoral vein, deep calf axial, and muscular veins: 500 ms.
3. Perforating veins: 350 ms. A cutoff of 500 ms is also suggested for perforators.

Common Duplex Scan Findings in Varicose Veins

Abai and Labropoulos have summarized their common observations of duplex scan findings in varicose vein patients:

1. In C 1 and C 2 classes, the common finding was reflux in the superficial system only.
2. C 3–C 6 had incompetence of the perforators and deep system.
3. Most common site of reflux in the superficial system was in the GSV (70–80 %). SSV reflux was noted in 15–20 %.
4. Nonsaphenous reflux – 10 %.
5. Perforator reflux – 20 %.
6. Deep vein reflux – 30 %.

In conclusion, duplex scan is a simple and noninvasive method of evaluating primary varicose veins. However, there is no uniform pattern of evaluation. One of the urgent needs is to evolve "standardized duplex scan for venous evaluation" to bring in uniform reporting standards [8].

Plethysmography

1. Photoplethysmography (PPG) & Light reflection rheography
   These techniques calculate changes in tissue blood density by measuring the intensity of reflected light. The PPG probe consists of an infrared-emitting diode. This is positioned on the skin. Some of the infrared rays are absorbed by the moving RBCs in the dermal veins and the rest are reflected. The backscattered rays are picked up by a receiving probe. The output signals are DC coupled to make a recording on a strip chart. The probe is usually taped around ankle to get a baseline at rest. Then the patient actively performs plantar and dorsiflexion of the ankle to produce emptying of superficial veins. The time taken for the veins to refill (refill time) is documented. In patients with reflux in the superficial veins, the refill time is short. The test is repeated with a tourniquet. This can normalize the refill time in patients with reflux in the superficial veins. Failure to normalize the refill time with tourniquet indicates pathology of the deep veins. The test is somewhat similar to the ambulatory venous pressure studies [14]. The technique is found to have poor sensitivity. Calibration is difficult. Currently, it has found little application in the evaluation of chronic venous diseases [15].
2. Air plethysmography and Strain gauge plethysmography
   These are two indirect noninvasive tests for the evaluation of chronic venous disease. The change in size of the limb in response to exercise, postural change, and tourniquet application is measured. The assumption is that the change in volume of the limb in response to these maneuvers is due to filling and emptying of veins.

   Air plethysmography is one of the noninvasive tests that can detect reflux reliably. It is recommended in patients with advanced CVD in whom information on duplex scan is inconclusive [6]. Although they provide quantitative measure of the impact of CVD on venous and muscle pump function, these techniques are cumbersome and requires patient cooperation. Results may be affected by external mechanical and pharmacological stimuli. They can identify obstruction and reflux but cannot localize the affected segment.

Invasive Studies

Phlebography

Two types of phlebographic techniques are used in the study of venous diseases – ascending venogram and descending venogram.

Ascending venography is performed by cannulating one of the dorsal veins of the foot and injecting a contrast medium. A tourniquet applied around the ankle would force the

contrast into the deep system. This is basically an anatomical study providing a road map of the venous system of the lower limbs. It can visualize the deep and superficial veins and the perforators. Currently duplex scan has almost totally replaced the need for ascending venogram. Moreover complications like contrast-induced anaphylaxis, thrombosis at the site of injection and sometimes DVT can be induced by this study. At present, ascending venogram is considered to rule out post-thrombotic changes in patients with previous history of DVT.

Iliac venogram is sometimes performed by directly injecting the contrast into the common femoral vein for better visualization of the iliac veins and IVC. Dilution of the contrast in a standard ascending venogram would make visualization of these segments difficult.

Descending venogram, originally introduced by Kistner, is practically abandoned now. It was used to assess the extent of reflux in the deep veins in patients with CVI. Some workers still undertake this prior to valvuloplasty of the deep veins.

CT and MR Venography

These studies are not done for the evaluation of varicose veins. They are useful in the evaluation of congenital venous malformations and complex venous problems. MR venogram is especially useful in delineating pelvic venous anatomy. Unlike CT venogram, there is no risk of radiation exposure in MRV.

Venous Pressure Studies

Ambulatory Venous Pressure Studies (AVP Studies)

This is a method of evaluating the functional status of the veins of the lower limbs. It is aimed at measuring the ability of the calf muscle pump to lower the pressure in the superficial veins of the foot during a series of contractions of the calf muscle pump. In primary varicose veins, the AVP is usually of the superficial venous pattern. Elimination of the reflux in the saphenous system normalizes the high resting pressure in this group of patients. The details are presented in Chap. 3. Although the test is sensitive, it is cumbersome to carry out and is labor intensive. It causes considerable discomfort to the patients. Hence, it is not very popular in routine practice. It is mostly used as a research tool and in patients with complex problems [16].

Elevation of resting foot pressure with Valsalva maneuver: Raju has recommended this as a test to quantify reflux in the venous system [17].

Foot arm pressure differential with reactive hyperemia was considered to be very sensitive in differentiating obstruction from reflux, but currently it is abandoned since it is not very sensitive. These two techniques are not very sensitive since a normal study may not rule out a significant venous pathology [17].

Femoral venous pressure studies: The technique is not needed in primary varicose veins. It is used in patients with iliofemoral venous obstructions prior to stenting.

Intravascular Ultrasound (IVUS)

IVUS is more sensitive than venogram, CT or MR venogram, in the diagnosis of iliac vein occlusion and is performed pre- and post-venous stenting (details are discussed in Chaps. 19 and 22).

Levels of Investigations in CVD

Overinvestigating simple clinical problems is one of the unwelcome tendencies in current medical practice. Obviously, it is not feasible to undertake all these tests in all patients with varicose veins, nor is it necessary. To streamline these issues, Eklof and team have suggested a selective policy of investigations in patients with CVD. Such an approach would curtail unnecessary invasive studies in patients with CVD [1]. They have defined three levels of investigations.

Level I investigations: History, clinical examination, and HHD. This would be sufficient for patients to be managed conservatively.

Level II investigations: Noninvasive investigations. The mainstay is duplex scan evaluation. Plethysmographic studies may be added if needed. This is recommended in patients needing saphenous vein surgery (HL and S), US-guided foam sclerotherapy, or endovenous procedures.

Level III investigations: Invasive studies: venography, computed tomography or magnetic resonance imaging, intravascular ultrasound, and ambulatory venous pressure studies. These tests are to be considered in patients requiring complex reconstructions such as valvuloplasty or endovenous stenting.

Classification of the Disease and Assessment of Severity of the Disease

The disease should be classified on the basis of clinical examination and lab studies. For routine clinical purposes, the basic CEAP classification would be sufficient. It is important to indicate the date and level of investigation along with the CEAP classification. There are many systems for assessing the severity of symptoms. The details are presented in Chap. 4.

Summary

Varicose veins are dilated tortuous and elongated veins in the subcutaneous plane, 3 mm or more, measured in the erect posture and associated with valvular incompetence. Primary varicose veins are not the manifestation of any other pathology, unlike secondary and congenital varicose veins.

The common symptoms of primary varicose veins are aching pain and discomfort along with swelling around the ankle. Cosmetic disfigurement is an important indication for seeking treatment in a large number of patients. A subset of patients may be totally asymptomatic. The severity of symptoms is unrelated to the extent of the visible varices, nor does it correlate with the duplex scan findings. The common complications include SVT and bleeding. A small percentage of patients with primary varicose veins may progress to chronic venous insufficiency. The exact factors responsible for this progression are not clear.

An elaborate protocol for clinical examination of varicose veins is taught in medical schools. Validation studies of the clinical examination with duplex scan have revealed the poor sensitivity and specificity of these tests. Handheld Doppler is an extended clinical examination that is carried out at the outpatient clinics and bedside of patient. While it is useful in the evaluation of reflux in the SFJ and SPJ and to some extent incompetent perforators, it is not very sensitive in the study of the deep veins. Many diagnostic tests are described. But the gold standard is the duplex scan. The most widely practiced system of classification is the CEAP classification.

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Open Surgery for Primary Varicose Veins

7

Pradeep Jacob

Contents

Introduction

High ligation and stripping [HL/S] is still the standard of care for patients with primary varicose veins. Historically, Friedrich Trendelenburg in 1891, advocated ligation of great saphenous vein (GSV) at the mid thigh. Tavel in the early twentieth century recommended high ligation. Keller and Mayo recommended the procedure of stripping. These were the major milestones in the evolution of surgical treatment of varicose veins.

Open surgery is even now the "gold standard" in the care of a patient with varicose veins. However, its role is being increasingly threatened with advent of the "endovenous revolution." Flush ligation is being challenged by several workers since groin dissection is the stimulus for neovascularization, a major cause for recurrent varicose veins after surgery (REVAS).

This chapter would address the following issues:

1. The indications for investigations and care in a patient with chronic venous disorder (CVD)
2. The indications for open surgery
3. The components of open surgery for GSV varices: High ligation, stripping, and stab phlebectomy
4. Saphenous preserving surgery
5. Special problems in surgery of short saphenous vein (SSV)

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6. Complications of open surgery
7. Treatment outcome

This chapter focuses mainly on the C2 class. Open surgery is also an essential step in the treatment of C3–C6 class patients.

Treatment Options for CVD: General Considerations

The therapeutic options for CVD fall into the following categories:

1. Conservative management
2. Nonoperative interventions – US-guided foam sclerotherapy
3. Open surgical procedures
4. Minimally invasive surgical interventions – radiofrequency/laser ablation

Not all patients with chronic venous disorder (CVD) need detailed evaluation and care. Only those who are symptomatic and are categorized as chronic venous disease are to be subjected to this policy [1]. The common indications for intervention in a patient with varicose veins include [2]:

1. Symptomatic patients. Pain is an important concern. But it is important to rule out other causes of pain in the lower limb such as musculoskeletal, orthopedic conditions, and neurological causes before planning any intervention for varicose veins.
2. Patients with recurrent bleeding and superficial vein thrombosis.
3. Prevention of progression of C2 disease. This is a controversial area. There is no evidence to indicate that compression therapy, pharmacotherapy, open/endovenous interventions in C2 stage would prevent the progression of the disease. It has been reported that 100 symptomatic patients with C2 disease should be operated to prevent one ulcer. In limbs with C4 disease, this number reduces to ten [3].

In patients with chronic venous insufficiency (CVI – C3, C4, C5, and C6), correction of the superficial reflux is carried out either in isolation or in combination with surgery of the perforator and/or the deep venous system.

Conservative management consists of lifestyle advice relating to leg elevation, weight and diet, therapeutic exercise program, and the use of compression hosiery.

Endovenous thermal ablation of the saphenous vein is a relatively new and minimally invasive procedure which can be carried out under local tumescent anesthesia as an outpatient procedure. This can be carried out using radiofrequency waves or laser.

Sclerotherapy by injecting a sclerosant into the vein to produce fibrosis and obliteration of the vein has been in use for almost a century. Ultrasound-guided foam sclerotherapy is widely practiced currently for the control of varicose veins as an outpatient procedure.

Open surgery still remains the gold standard in the treatment of venous disease. This chapter will focus on this procedure.

Open Surgery in the Treatment of Varicose Veins

With the advent of endovenous interventions, the indications for open surgery is restricted to those patients with largely distended truncal varices with marked local blow outs and saphena varix and veins that cannot be pushed to a depth of 1 cm below the skin surface after tumescence (risk of skin burns) [4, 5]. There is a transition from long incisions and extensive exposure to short incisions and optimum exposure. The greatest criticism of open surgery is the need for longer hospital stay and the incidence of more severe postoperative pain. At present, even open surgery is scheduled as a day case procedure.

Surgery for GSV Varicose Veins

The correction of GSV varicosities would require the following steps:

1. *High ligation*
2. *Stripping of the trunk of the GSV*
3. *Stab/hook phlebectomy*

The first two steps correct the hemodynamic defects and are crucial in the treatment. Hence, very often, the open surgery for GSV varicose veins is known as high ligation and stripping (HL/S). Stab phlebectomy basically improves the

cosmetic appearance of the extremity. It also contributes to the improved functional outcome.

HL/S can be performed under GA, spinal, epidural anesthesia or regional block. Tumescent local anesthesia is preferred by some surgeons for stripping and stab avulsion. The entire procedure can be planned as a day case or short-stay procedure.

Role of Preoperative Compression Therapy in C2 Disease

There are several trials of preliminary compression therapy (CT) with below-knee (BK) stockings (ankle pressure 20–25 mmHg) in patients with C2 disease. No extra benefit was reported by including preoperative CT. The current guidelines of the American Venous Forum strongly recommend against the use of pretreatment CT in patients with C2 disease [4]. Despite this, preoperative CT still remains an enticing but redundant option.

Hospital Admission/Day Case Surgery

One of the important changes in the mindset of both clinicians and patients is to undertake varicose vein surgery as a day case procedure. The procedure can be carried out comfortably under local anesthesia. In very apprehensive patients, a short general anesthesia (GA) or epidural or spinal anesthesia can be considered. Except in very elderly patients with comorbidities and occasionally for bilateral varicose vein surgery, admission as an inpatient is seldom needed. But in the Indian scenario, many patients would prefer to get admitted and operated as an inpatient.

Open Surgery for Bilateral Varicose Veins: Single Sitting or Staged Procedure?

In several studies comparing bilateral and unilateral varicose vein surgery, it was established that there was no statistically significant difference between the two procedures in terms of postoperative pain, hospital stay, and return to work [6, 7].

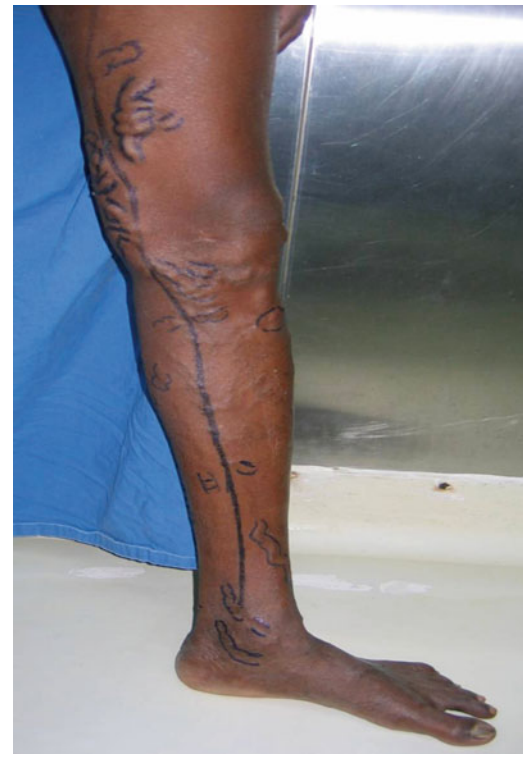

Fig. 7.1 Preoperative mapping of the veins

A study among surgeons in the UK, 73 % performed open surgery for bilateral varicose veins on inpatients and 37 % as day case. General health of the patient, extent of varices, and availability of a second surgeon were factors which influenced decision making [8].

Preoperative Measures

The following steps carried out before surgery would greatly improve the final outcome:

1. Duplex ultrasound (US) scan is necessary to locate reflux at saphenofemoral junction (SFJ), trunk of GSV, perforators, and also deep veins. Some workers have suggested a clinical examination and handheld Doppler (HHD) for this purpose, but duplex US is certainly more sensitive than HHD.
2. Mapping the position of SFJ. This is done with the patient in the standing position (Fig. 7.1).
3. Mapping the local varices and blow outs in the extremity. This is again done with the patient in the standing position. Total extirpation of

the marked varices would improve the final cosmetic appearance of the limb.
4. Documenting the ankle brachial index to rule out ischemia.

Perioperative thrombosis prophylaxis is not recommended by the American Venous Forum guidelines for patients who do not have additional thromboembolic risk factors. Early and frequent ambulation is suggested. Low-molecular-weight heparin as prophylaxis is recommended for patients with extra risk factors [4].

High Ligation: The Actual Procedure

The term indicates ligation and division of the GSV at its confluence with the common femoral vein (CFV) along with ligation and division of all upper GSV tributaries [1]. The patient is positioned on the table with a Trendelenburg tilt. The limb to be operated is slightly abducted and externally rotated and the knee joint slightly flexed and supported on a roll.

Siting the incision at the appropriate level is a crucial step. One of the common errors is to site the incision too low. According to textbooks of anatomy, the SFJ is located 4 cm below and lateral to the pubic tubercle [9]. During surgery, it is found to be much higher. We make a transverse incision of sufficient length, with its center located 2 cm below and lateral to the pubic tubercle. This incision is cosmetically pleasing and gives a good exposure of the SFJ and all the terminal tributaries. The hockey stick incision described by Dodd and Cockett gives an excellent exposure, but such extensive exposure is not really needed.

There are three basic steps involved in the surgery:
1. Exposure of the terminal 7–10 cm of the trunk of the GSV and exposure of the SFJ
2. Control of the terminal tributaries
3. Making the high ligation

The location of the SFJ is confirmed by displaying the anterior surface of the common femoral vein. Another useful landmark is the superficial external pudendal artery. It runs along the curved lower border of the fossa ovalis, usually posterior to the trunk of the GSV. In a small subset of patients, this vessel runs anterior to the GSV. Its pulsation can be made out and this is a useful pointer to the position of SFJ (Fig. 7.2).

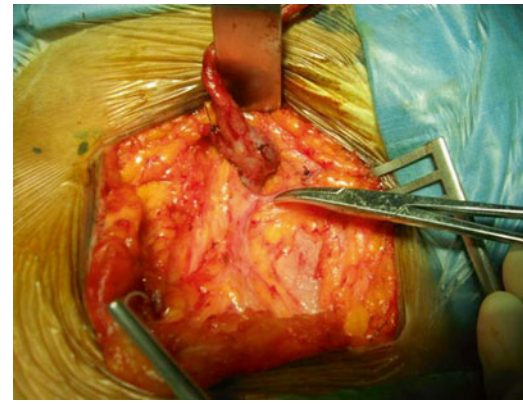

Fig. 7.2 SFJ location. Note the position of the superficial external pudendal artery and the CFV

The tributaries to be controlled include the named terminal tributaries – superficial circumflex iliac, superficial epigastric, and external pudendal veins (Fig. 7.3).

The anterior accessory saphenous vein and posterior accessory saphenous vein in the thigh are also controlled. Hidden tributaries entering on the posterior aspect of the GSV may be evident by transecting the GSV at a point 7–10 cm from the SFJ and turning the proximal stump upward. The deep external pudendal vein may join the GSV on its posterior aspect close to the femoral vein. Sometimes this vessel can enter the femoral vein also [2]. The tributaries are ideally controlled beyond their secondary branch [10].

Confirming Reflux at SFJ: We always confirm reflux at the SFJ by the intraoperative test for SF incompetence. For this, the GSV is divided about 7–10 cm from the SFJ between two bulldog clamps. The bulldog clamp controlling the proximal end is released under control. If the SFJ is incompetent, there is a brisk bleed back from the divided proximal stump even as an arterial flow [11] (Fig. 7.4).

The SFJ is ligated with double ties with non-absorbable sutures. The second tie may be a transfixing ligature. The stump should be about 1–2 cm long. Too short a stump has a risk of slipping of ligature. Too long a stump can produce a cul-de-sac. Covering the stump with a patch of PTFE graft is recommended by some to prevent neovascularization. This is not recommended in

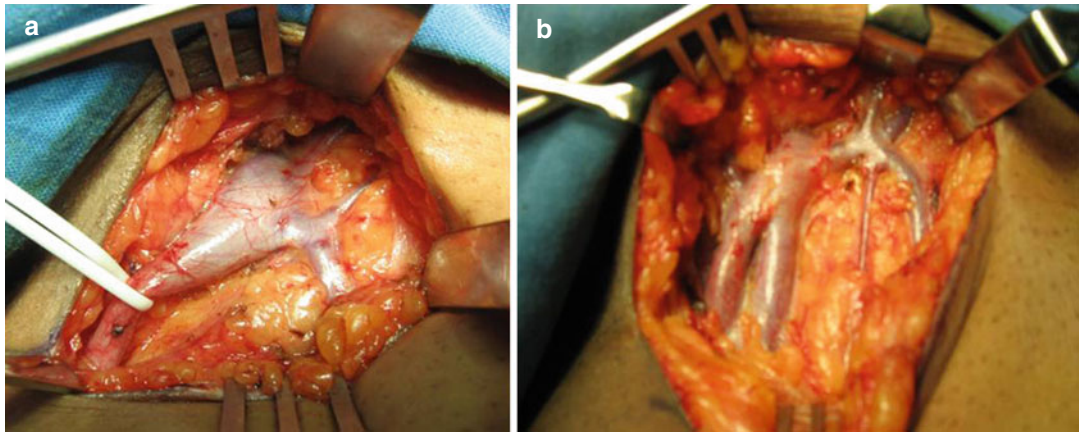

Fig. 7.3 Anatomy of SFJ displayed during high ligation. Note the variations in the position and distribution of tributaries. (**a**) Distribution of tributaries are displayed. (**b**) Bifid GSV with a different pattern of tributaries

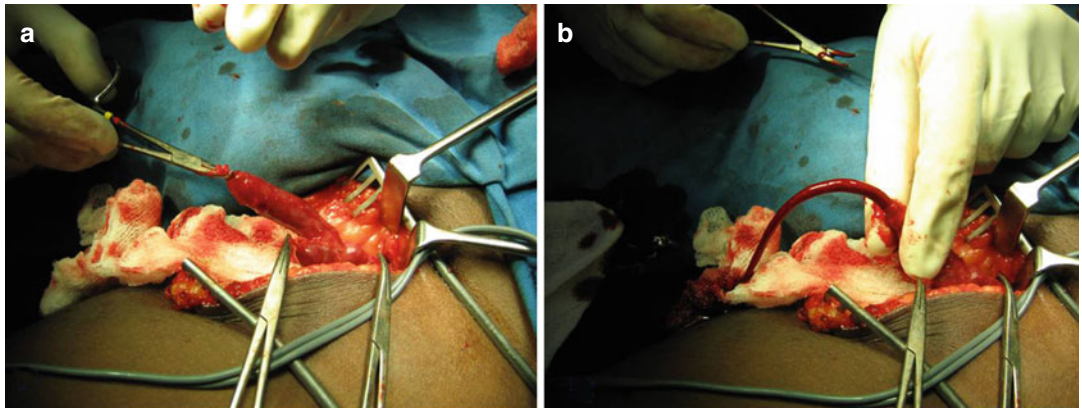

Fig. 7.4 Intraoperative test for SFJ incompetence. (**a**) Transected stump of GSV controlled with a clamp. (**b**) Clamp released. Note the brisk bleed back

the guidelines of the American Venous Forum [4]. The distal end is removed along with stripping. The wound is closed with a suction drain after completing the stripping procedure.

Two problems can add on to the technical difficulties:

Saphena varix: This is a localized, circumferential, or anterior wall dilatation of the terminal portion of the GSV. It results from reflux at SFJ. During straining and coughing, a jet of refluxing blood from the femoral vein strikes the anterior wall of the GSV at a point 7–10 cm from the junction. This is the reason why saphena varix is seldom located at the exact SFJ. The varix is thin walled and when torn can bleed profusely (Fig. 7.5)

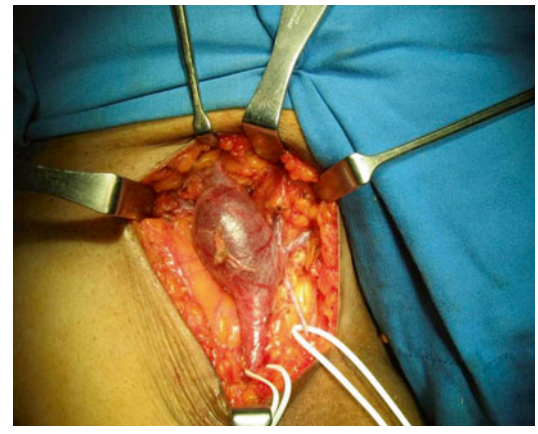

Fig. 7.5 Saphena varix

Enlarged inguinal lymph nodes: May be a difficult problem especially in an ulcerated limb. The dissection of the vein should be kept away from the nodes. Injury to the nodes can cause bleeding and postoperative lymphatic leak.

Our Observations During High Ligation

In a series of 80 dissections in the groin for high ligation of the groin, we made the following observations:

1. SFJ was on average situated 2.6 cm below and 3 cm lateral to the pubic tubercle.
2. The number of tributaries varied from 2 to 7.
3. Superficial external pudendal artery could be identified in 90 % of the limb. The vessel was coursing anterior to the GSV in only two limbs.
4. Saphena varix was seen in 25 % of the limbs, 6.25 cm (mean) from the termination.

Stripping of the Trunk of GSV

The term stripping indicates removal of a large segment of the vein, the GSV or SSV, by means of a device. This is an essential step in the surgery of GSV varicose veins. It is recognized that the recurrence rate can be minimized by including this procedure [4]. One of the important causes of REVAS is presence of refluxing channels [12].

Total stripping from groin to ankle is not practiced currently because of the risk of damage to the saphenous nerve in the leg and the high incidence of postoperative saphenous neuralgia [4, 10]. Moreover, even total stripping does not disconnect incompetent ankle perforators [2].

Short-segment stripping from the groin to below-knee level is the recommended option now. This procedure removes the incompetent thigh segment of the GSV (the below-knee segment of the GSV is usually competent in the majority of patients); at the same time, it avoids injury to the saphenous nerve.

Perforate-invaginate stripping (*PIN stripping*) minimizes these events and is the preferred option. In conventional intraluminal stripping, the stripped vein gets rolled over and wrapped around the acorn-shaped stripper head to form a thick hard "plug." The tissue trauma along the stripped tract can be considerable. Again, a large exit wound is needed. The PIN stripping uses an instrument with a miniscule head and flat neck. It is a minimally invasive procedure and can be carried out even in an office setting under local anesthesia. The technique was introduced by Oesch in 1993, initially for short saphenous varicosity [13]. A flexible Codman disposable stripper without the removable acorn can also be used for invagination stripping [4].

To reduce bleeding during stripping, the limb is elevated and as the stripping progresses, compression bandages are applied. Infiltration of the perivenous space by tumescent anesthesia is recommended by Gloviczki et al. to reduce bleeding [4].

Cryostripping of the GSV: This is recommended to decrease hemorrhage from the stripped tract. The procedure needs the use of a cryosurgical system. After high ligation, the cryoprobe is passed down to the desired level around knee and freezing initiated. The saphenous vein is invaginated by pulling the vein with force. The incidence of post stripping bruising and complications were less compared to standard stripping [14].

Phlebectomy

This procedure is aimed at excising local blowouts and bulging veins. It improves the cosmetic appearance of the limb, an important goal of treatment of varicose veins. Meticulous preoperative mapping of the veins is essential to achieve optimum outcome.

Cosmetic phlebectomy: The procedure was described by Dodd and Cockett. Through 1–2 cm long vertical incisions, large segments of the veins are excised. It is compared to birds picking out worms from burrows and hence is also called "worming." The wounds are sutured. Vertical incisions in the extremities are preferred between joints since they fall in the natural Langer's line. The resultant scars are cosmetically acceptable [2].

Ambulatory phlebectomy: The procedure is also known as stab or hook or mini phlebectomy. It involves the avulsion or removal of varicose

veins through small 1–2 mm stab wounds made by a number 11 blade. Avulsion of varicose veins is performed with hooks (Muller or Oesch) or forceps. The procedure can be performed under tumescent local anesthesia. The skin wounds are approximated with steristrips. Thigh-length compression stockings/bandages are applied on completion of the procedure [4].

Light assisted stab phlebectomy: Lawrence and Vardanian have reported a newer technique stab phlebectomy. It combines transillumination, tumescent anesthesia, and stab phlebectomy using special surgical instruments. It provides better visualization and more rapid and complete removal of veins [15].

Transilluminated powered phlebectomy (*TIPP*): This is a useful technique for the removal of larger clusters of varicosities. The procedure is done under spinal, epidural, or general anesthesia. Tumescent anesthesia is added with infusion of dilute lidocaine with epinephrine. Transillumination is achieved by a specially designed cannula. Vein extraction is done using a resector [16]. The procedure is combined with HL/S. The advantages claimed include a decrease in the number of incisions and much faster removal of a large amount of varicose vein tissue [4].

Preservation of the GSV

The CHIVA Technique: Ambulatory Conservative Hemodynamic Management of Varicose Veins

Basically this technique preserves the GSV to facilitate venous drainage into the deep veins. The tributaries are controlled by phlebectomy. This is to reduce the hydrostatic pressure in the GSV and tributaries. The drainage function of the superficial veins is maintained by a reversed flow [4]. CHIVA is an example of duplex-controlled surgery. The aim of CHIVA is to treat varicose veins by preserving the GSV and utilizing its drainage function by eliminating reflux points. A basic requirement is to make a detailed study by duplex scan and determine the sites of reflux [17].

The surgical approach is planned on the basis of duplex finding. A common CHIVA technique includes ligation of the incompetent saphenous vein; ligation, division, and avulsion of only the incompetent tributaries; maintaining patency of the saphenous trunk and the competent saphenous tributaries; and maintaining venous drainage through reentry perforators [18]. In contrast, the conventional procedure of HL/S disconnects competent tributaries and also removes the re entry perforating veins [17].

The ASVAL Technique: Ambulatory Selective Varices Ablation Under Local Anesthesia

The procedure was described by Pitaluga and colleagues and tries to control the disease by eliminating the varicose reservoirs and preserving the incompetent and refluxing saphenous vein. Traditionally it was believed that in primary varicose veins, reflux starts at the confluence of the SFJ and descends progressively downward. This descending hemodynamic concept has been questioned, and it is believed that it can happen the other way round, in an ascending manner. The encouraging results of endovenous techniques where the SF junction is spared tend to support this theory.

A careful preoperative mapping of the reservoir filling sources is carried out by duplex scanning. For this, each segment of the limb is divided into four surfaces, anterior, medial, lateral, and posterior. A total of 32 zones are identified. The areas to be controlled are selected from this on the basis of the scan. The stab avulsion of the tributaries is carried out under local anesthesia. The procedure is recommended for the less evolved form of the disease. Follow-up at 32.4 months revealed reduction of SF reflux with a significant diminution in the diameter of the superficial veins [19].

Surgery of Short Saphenous Vein

Surgery of the short saphenous vein (SSV) is often a demanding procedure. The following anatomical facts are important in SSV surgery:

1. The SSV pierces the deep fascia of the leg at the mid calf level. The upper one third of the

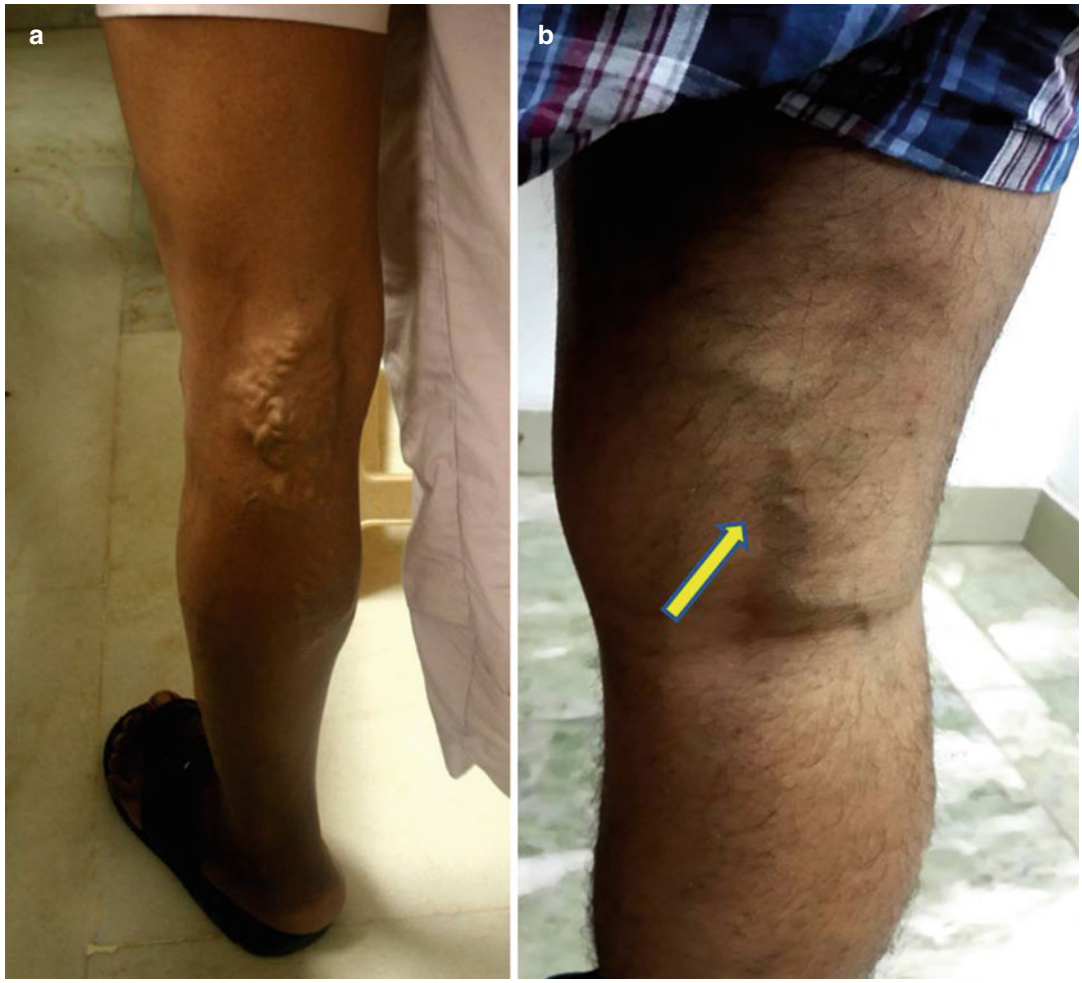

Fig. 7.6 (**a**) Short saphenous vein. (**b**) Vein of Giacomini

SSV lies underneath the deep facia [2, 9]. Hence, the deep fascia of the popliteal fossa has to be incised to expose the terminal portion of the SSV. The termination of the SSV can be very variable. Three types of terminations have been described – Kosinski's variation [2]

Normal termination (57 %) – enters popliteal vein in popliteal fossa.

High termination (33 %) – ends in the center of thigh in a muscular vein or the GSV.

Low termination (10 %) – ends in the deep veins of calf or GSV in upper third of leg.

2. The exploration of popliteal fossa can be technically more difficult because of the crowded space and presence of vital structures.
3. The terminal portion of the SSV can occasionally be enormously dilated at its junction with the popliteal vein (Fig. 7.6a).
4. The vein of Giacomini (intersaphenous vein) runs in the posterior part of the thigh and connects the SSV with the GSV. An SSV projection or tributary ascending in the thigh above 12 cm from popliteal skin crease is designated as Giacomini vein irrespective of the termination of SSV (Fig. 7.6b). It is reported in 70.4 % of limbs. In the lower thigh, it is located subfascially. In the middle and upper thigh, it perforates the deep fascia and ends in the superficial or deep veins or in the muscular veins. Its presence does not affect the position

of SSV termination, nor does it affect the severity of CVD. Reflux in the Giacomini vein is not very common probably because of its subfascial course in the lower thigh. In combined GSV and SSV reflux, Giacomini vein incompetence is observed in 4.7 %. In view of these findings, a routine duplex evaluation for Giacomini vein is not recommended. It could be considered in patients with SSV or combined GSV and SSV incompetence [20].

Surgical Interventions

The most crucial step is to map the course and termination of SSV. Duplex US is currently the most sensitive method for this [21]. Another option recommended is an on-table venography [22]. Handheld Doppler has an accuracy of only 70 % [23]. The most optimum position of the patient for SP ligation is the prone position. Some surgeons prefer a lateral position. A transverse incision is made in the popliteal crease over the located position of the SP junction. A large "S"-shaped incision gives a better exposure especially in re-explorations [2].

Flush Tie

For this, the incision is deepened and the deep fascia of the leg is incised along the same line. The terminal 1/3 of SSV lies below the deep fascia. The SSV is located in the groove between the two heads of gastrocnemius (Fig. 7.7).

It is traced down to the SP junction exposing the popliteal vein. Flexion of the knee joint can aid the dissection. If the terminal part of the SSV is considerably dilated, it would be safer to expose the popliteal vein and control it first before proceeding to the SP junction. Diathermy should be used with care since it can produce damage to common peroneal and sural nerve. Flush ligation has the advantage that it does not leave behind a stump of SSV which is a cause of recurrence.

Low Tie

The SSV is ligated 3–5 cm distal to the SP junction by making a small incision. This avoids the need for deep dissection in the popliteal fossa. There is no evidence that flush ligation is better than simple ligation [4].

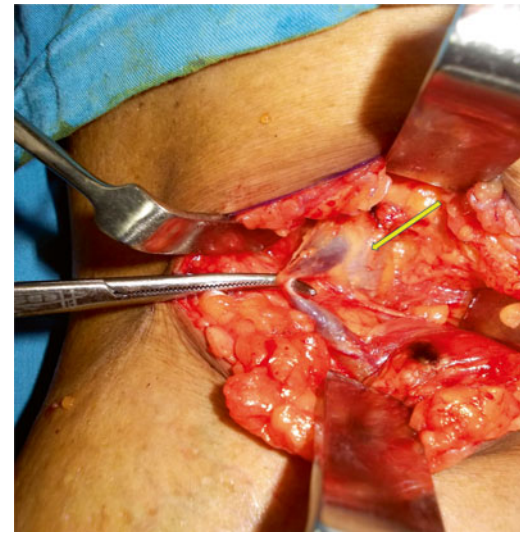

Fig. 7.7 Exposure of SP junction. Note deep fascia has been incised, SSV identified between two heads of the gastrocnemius. *Arrow* points to the popliteal vein

Stripping of SSV

Complete stripping of the SSV is seldom performed now because of the associated sural nerve injury. The alternative options available are SP ligation and limited invagination stripping up to mid calf [4], resection of proximal 10 cm of the SSV [10, 23, 24], and multiple phlebectomies and sclerotherapy [23].

Complications of Open Surgery for Primary Varicose Veins

The complications may be general complications or specific complications.

General Complications

1. Complications relating to anesthesia and metabolic dysfunctions due to comorbidities.
2. Thromboembolic complications. This is not very common in patients with no extra risk

factors. The reported incidence is approximately 0.5 % following varicose vein surgery [24]. It is important to assess risk factors in individual patients and use pharmacoprophylaxis whenever needed.

Specific Complications

These may be related to either the groin exploration or to the stripping procedure.

Groin Wound Complications

1. *Bleeding*, *seroma, and hematoma*. Are not uncommon complications. Usually result from slippage of the ligated tributaries. Proper techniques and the use of a groin drain can minimize these.
2. *Lymph leak and collection*. Can occur when the lymph nodes and lymphatics are disrupted. This is more common after re-exploration.
3. *Wound infections*. The reported incidence of groin wound infection following varicose vein surgery varies from 1.5 to 16 %. Recent RCTs have shown that the incidence of wound infection can be minimized with the use of a single dose of perioperative antibiotic prophylaxis [4].
4. *Injury to femoral artery* and *vein*. This is a potential complication during groin exploration but the incidence is rare. A publication by Rudstrom et al., based on a systematic search of Medline and Pubmed for papers on vascular injuries during varicose vein surgery published after 1945, has identified 44 arterial and 43 deep vein injuries. Most of them were avoidable complications. Bleeding was the common symptom. Laceration or division of the femoral vein was the most common type of venous injury. Partial stripping of the femoral vein can occur if the stripper head passes into the femoral vein. Accidental arterial stripping dominated the arterial injury. These injuries are very serious leading on to loss of limb, life, or other serious morbidities. Anatomical knowledge and awareness of the possibility of vascular injuries are preventive. Routine checking of arterial circulation during surgery and in the postoperative period is important [25].
5. *Recurrence of varicose veins*. This is a late complication. The exact cause may not be clear in every case. The most widely accepted cause is neovascularization which is well known to develop after extensive groin clearance. Other causes include faulty techniques and progression of the disease.

Stripping-Related Complications

1. *Discomfort*, *bruising*, *and bleeding from the stripped tract*. Bruising is a frequent complication following stripping and clears usually in 3 weeks time. These events can be minimized by bandaging in the immediate postoperative period.
2. *Nerve Injuries*. They can vary from transient numb patches to permanent neuropraxia. The nerves commonly involved are the saphenous and sural nerves. Seven percent of patients who had undergone stripping up to knee had saphenous nerve injury; the injury rate hikes up to 39 % in patients who had stripping up to ankle level [4]. The incidence of sural nerve injury in short saphenous vein surgery varies from 2 to 4 %. The figures for common peroneal nerve injury ranged from 4.7 to 6.7 % [4].
3. *Stripped tract revascularization*. A study reported by Munasinghe and team has documented that in a series of 70 patients, complete stripped tract revascularization with duplex-proven reflux was observed in 4 patients (6 %); 12 patients (17 %) had partial revascularization. All these patients had a postoperative hematoma in the stripped tract 1 week after surgery. Revascularization of the stripped tract is a recently identified complication of stripping [26].

Postoperative Compression Therapy

The role of postoperative CT in patients who have undergone open surgical treatment for C 2–3 disease to improve postoperative pain, to reduce the incidence of complications, and to facilitate early return to work is controversial. RCTs have shown no extra benefit for the use of CT worn beyond 1 week after uncomplicated H L/S of the GSV [4].

Outcome of Open Surgery for Varicose Veins

The results of surgery have steadily improved over the years. The following observations are pertinent [4]:

1. RCTs have reported marked improvement in QoL after open surgery.
2. In comparison to conservative treatment, surgery provided marked symptomatic relief at 2 years.
3. The need for reoperation was 6 % in patients who have undergone HL/S compared to 20 % in those who had HL alone. This is because patients who had HL alone have recurrent reflux in the residual GSV.
4. Selected trials have found CHIVA superior to HL/S. But CHIVA is a complex approach and has a long learning curve.
5. ASVAL is currently used for early disease. (GSV diameter less than 8 mm; SSV less than 6 mm). Hence, the outcome cannot be compared with HL/S.

A comparative study of 580 limbs in 500 patients comparing the outcome of EVLA, RFA, US-guided foam sclerotherapy and open surgery for GSV varicose veins has concluded that all treatment modalities were effective and efficient. But more recanalization and reoperations were seen after US-guided foam sclerotherapy [27].

High Ligation: A Bane or a Boon?

A lot of debate is going on about the role of HL. The endovenous revolution has almost totally marginalized HL/S. The traditional approach of high ligation with control of tributaries beyond the secondary tributary was the sacred rule even from Trendelenburg's time. This concept is being strongly challenged now. The arguments to avoid high ligation include the following:

1. Groin exploration is known to promote neovascularization.
2. Following RFA and EVLA, it was identified that the SFJ remains closed with no or very little reflux and the tributaries exhibit only normal flow [28, 29].
3. In the technique of ASVAL wherein an incompetent GSV is deliberately left intact with control of distal reflux, posttreatment duplex scan demonstrated a significant reduction in size of GSV and abolishment of reflux [19].

These evidences suggest that groin exploration with high ligation may be a redundant procedure in the treatment of GSV varices. In fact, it may be positively harmful by promoting neovascularization. Only future studies can confirm these facts.

Summary

Varicose veins are common problems in clinical practice. For a patient presenting with C2 disease, several treatment options are available. But open surgery still remains the gold standard. Preoperative CT is not recommended for C2 patients.

The standard procedure for GSV varicose veins is high ligation, stripping, and stab avulsion. The surgery of high ligation needs precise attention on the siting of the incision, control of tributaries, and technique of flush tie.

Stripping to a point below knee improves outcome without increasing the hazard of saphenous nerve injury. Total stripping up to the ankle is seldom practiced. Stab avulsion using hooks improves cosmetic and functional outcome. Transilluminated powered phlebectomy is a good option for the removal of clusters of veins in a more rapid and complete manner.

Two emerging procedures are the CHIVA and ASVAL techniques. But they are more complex and need lot of input for proper execution.

Surgery of SSV is more demanding because of the varying anatomy and limited space. Outcome with flush tie and low tie (3–5 cm below SPJ) is reported to be equally effective. Stripping is preferably avoided in SSV. Instead, the proximal 10 cm of the vein is excised.

The complications are generally avoided by proper attention to details. Nerve injuries and recurrence are the most common problems.

RCTs have shown that the outcome of open surgery and endovenous interventions are

comparable. The latter procedures are less invasive and are not known to produce neovascularization since no groin dissection is involved.

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Endovenous Thermal Ablation

8

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Contents

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Introduction

Man constantly strives for excellence and perfection. Patients with varicose veins can seldom be offered a complete cure. The aim of treatment is adequate control of the disease process. Chronic venous disorders can be controlled by conservative measures or by the use of interventions. The interventions in turn can be open surgical or endovenous procedures.

This chapter focuses on endovenous thermal ablation and would consider the following aspects:

1. Endovenous options for CVD
2. Types of endovenous thermal procedures
3. Endovenous laser ablation (EVLA); our experience and brief review of literature
4. Radiofrequency ablation (RFA); our experience and review of literature
5. Comparison of open surgery with EVLA, RFA, and ultrasound-guided foam sclerotherapy (USFS) for CVD
6. Current status of endovenous interventions in the treatment of CVD

This chapter focuses on the role of endovenous thermal procedures in ablating the truncal and tributary varices of C2 class of patients. The technique can be used to eliminate the superficial reflux in C3–C6 classes also. Recently these techniques have been extended for the percutaneous ablation of perforators (PAPs).

Endovenous interventions are less invasive intraluminal techniques for ablating the vein in

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situ. These procedures aim at delivering a chemical or thermal energy to inflict permanent structural damage to the venous endothelium. Ultimately the veins are converted to a fibrous cord and become nonfunctional. Endovenous procedure in general has gained approval due to their minimally invasive nature, excellent outcome, good long-term results, early ambulation, and return to work. USFS is a widely practiced technique of endovenous chemical ablation. This chapter focuses on endovenous thermal ablation.

Radiofrequency and Laser: A Comparison

Endovenous thermal ablation can be performed using RFA or EVLA. Both procedures are safe and effective. RFA and laser differ in their technique of delivering thermal energy to the vein wall. Laser energy is delivered endovenously from the fiber tip. It is highly focused with temperature of over 100 °C close to the fiber tip. RFA operates by resistive heating of the vein wall in its whole circumference causing endovenous temperatures of 85–90°C [1].

Each procedure has its proponents. Supporters of EVLT cite higher recanalization rates with RFA [2]. Proponents of RFA cite greater patient discomfort with EVLA. Based on our experience with both RFA and laser, we feel that for veins with larger diameter and fewer dilated tributaries, the RFA procedure is superior. EVLA is better when the tributaries and branches are more, and the truncal vein is smaller in diameter [3]. Cosmesis is definitely superior with EVLA [4]. It is difficult to cannulate and treat small veins using the RFA probe. EVLA is a more versatile technique since the fiber and sheath have smaller dimension (Fig. 8.1).

Other advantages of EVLA include ease of use, speed of pull back, and decreased cost of the disposables. Because of the focused nature of the laser beam and higher temperatures, EVLA unlike RFA is associated with higher vein wall perforations. This is one of the reasons why EVLA is associated with more treatment-related pain and induration during the patient recovery phase, compared to RFA [1]. Postoperative complications

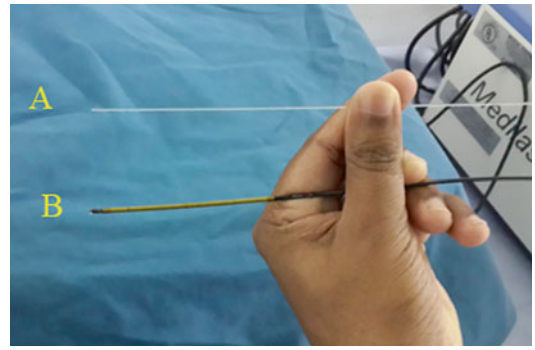

Fig. 8.1 Laser (**a**) and RFA (**b**) probes. Note the larger size of the RFA probe and the 7 cm working end

such as bruising and pain were significantly less with RFA ablation with second-generation catheters than ELT in two RCT trials [5].

RFA produces uniform heating of only the endothelium. It is unlikely to produce perforation of the vein. Gibson et al. have expressed identical views in the choice between RFA and Laser [6].

Endovenous Laser Ablation

Endovenous laser ablation (EVLA) was first described by Carlos Bone in 1999. The procedure was then published by Navarro et al. [7].

The Mechanism of Action

Although the exact mechanism is not known, the widely accepted view is that endovenous laser produces a nonthrombotic occlusion of the vein by the delivery of laser energy. Heat bubbles are produced in the endothelial cells that eventually lead to their damage. Once destroyed the vessel contracts, fibrosis follows, leaving behind a cord-like structure [7, 8].

Physical Properties

Monochromatic (single wavelength) light emitted from both diode and neodymium-doped yttrium aluminum garnet [Nd:YAG] are used for EVLA [9]. Lasers used for EVLA work in the infrared wavelengths. Lasers of wavelength

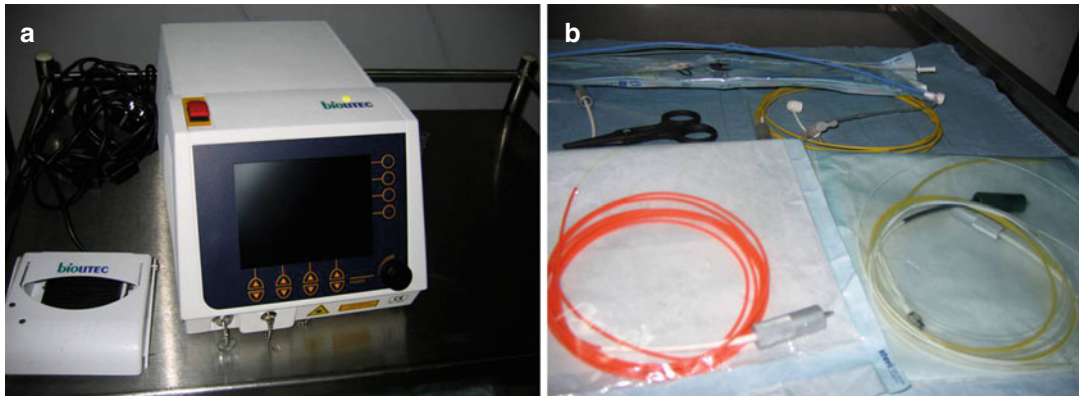

Fig. 8.2 Endovenous laser ablation equipment. (**a**) Laser generator and foot pedal. (**b**) Laser fibers

ranging from 810 to 1,470 nm have been used [8–10]. All wavelengths of EVLT are safe and effective. There are conflicting reports of the action of the lasers based on the different wavelengths. Studies comparing lasers of 940 and 1,320 nm have shown significantly less pain and bruising in the longer wavelength group [11, 12]. The main chromophore of 1,320 nm laser is water, while other wavelengths used for EVLA primarily target hemoglobin [11]. In our center, we have used a diode laser with a wavelength of 980 nm (Fig. 8.2).

The "dose" of laser energy delivered can be expressed as joules (J)/cm of vein. A minimum laser energy of 60 J/cm is required to achieve optimum ablation [13]. The energy so delivered depends upon the diameter of the vein. A vein with a larger diameter requires more energy to be closed [14, 15]. It is pointed out that high power along with a short application time tends to have an evaporating effect, and low power along with a longer application time has a coagulating and shrinking effect [14].

Most surgeons prefer to set the power between 12 and 15 W; higher power is required when the diameter of the vein increases. A withdrawal rate of 2 mm/s at 14 W delivers 70 J/cm [13]. The laser delivery is by pulsed or continuous pullback [14]. The laser unit can give feedback regarding the dosage of energy delivered.

The laser energy is commonly delivered endovenously. But for non-cannulable veins, it can be delivered by perivenous or transcutaneous methods.

Indications and Contraindications for EVLA

Any vein that is sufficiently large (3 mm or more), relatively straight, and which can be pushed down after tumescence to a depth of 1 cm below the skin surface (to minimize risk of skin burns) is amenable to endovenous laser ablation.

The veins treated by endovenous laser include GSV and its tributaries, including incompetent anterior accessory GSV of thigh and leg, SSV and its tributaries. The inclusion criteria for treating such veins would be the presence of superficial venous insufficiency only, duplex scan reflux of over 0.5 s, patent deep venous system, cannulable veins, and ambulant patient [9, 14, 16].

EVLA is contraindicated in AV malformation, obstructive pathology of the deep veins, and patients with restricted mobility. Relative contraindications include deep vein reflux, prior treatment for varices, extremely tortuous veins, large caliber veins, patients on oral anticoagulant and hormone replacement therapy, and aneurysmal veins segments [8, 9, 16].

Technique

Preoperative Assessment

A thorough patient history is recorded and an informed consent is obtained. The high expectation of the patient regarding the outcome of the surgery needs to be tempered. The possibility of recurrence and other complications should be informed.

The limb to be treated is mapped using a 7.5 MHz Doppler probe. Deep vein is assessed to rule out deep vein incompetence or obstruction.

Anesthesia

Local anesthesia with instillation of tumescence in the perivenous plane is preferred for this procedure.

An occasional patient may need sedation or regional block (femoral nerve block). In very apprehensive patients, general anesthesia or regional anesthesia may be appropriate [17].

EVLA is an office procedure. Many of our patients prefer an overnight stay post procedure.

Tumescence

The term literally means "a swollen condition" or a "swollen part of an organ."

Tumescent saline – Depending on the requirement, a tumescent anesthetic contains a 5–20-fold dilution of local anesthetic (15 ml of xylocaine or 15 ml of bupivacaine), epinephrine 1:100,000, with sodium bicarbonate ($NaHCO_3$) (10 mEq/l) and diluted with physiological saline solution [18].

The tumescent saline is injected in the perivenous plane, deep to the fascia covering GSV, under ultrasound guidance along the entire length of the vein to be treated. The injection can be made by multiple punctures or by pressure flow apparatus. We prefer the multiple puncture using a long 23G spinal needle inserted into the perivenous plane under USG guidance (Fig. 8.3).

Benefits of Tumesence. Tumescent saline has the following beneficial effects [14]:

1. It acts as a heat sump to absorb the heat escaping from the treated vein and thus protects the overlying skin from thermal injury.
2. It compresses the vein in its circumference and gives better proximity of endothelium with the laser tip.
3. It pushes the vein away from the skin.
4. Local anesthetic effect.

EVLA: Steps

All the routine precautions for the use of laser fibers are to be observed. The procedure is done under US guidance. The procedure starts with painting and draping the affected limb. A local block is given at the site of cannulation of the vein, in the lower part of the thigh, or the just below the knee. Here the saphenous nerve is away from the vein. A second more proximal site should be identified and kept in reserve in the event of difficult cannulation. In case of difficulty in identifying the vein, the medial border of the shin of the tibia is identified and the vein is then located about 1 cm medial to this. The GSV is cannulated using a 16G cannula. A guide wire is then passed through the cannula and positioned so that the tip of the guide wire is at or just across the SF junction (Fig. 8.4).

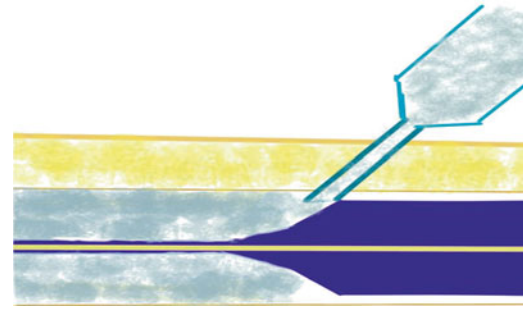

Fig. 8.3 Instillation of tumescence in the saphenous compartment. Note the proximal vein collapsed and approximated to the laser fiber

A large 8 F cannula with a two-way stopcock is passed over the guide wire after dilatation of the entry point. Laser probe with its covering sheath is passed through the cannula. The bare tip of the laser fiber is kept about 1 cm outside the covering sheath so that the sheath does not get inadvertently burnt during pull back.

Diode laser of 980 nm is used. The tip of the laser fiber emits a red color of the 980 nm wavelength which is visible through the skin (Fig. 8.5).

The laser tip is positioned about 1 cm proximal to the SF junction using the USG probe [10, 13]. Care should be taken that this is proximal to the first tributary of the GSV – the superficial epigastric vein [16] (Fig. 8.6a). Tumescent saline is injected in the perivenous plane.

A Trendelenburg tilt is given to empty the veins. The vein is then treated by activating the

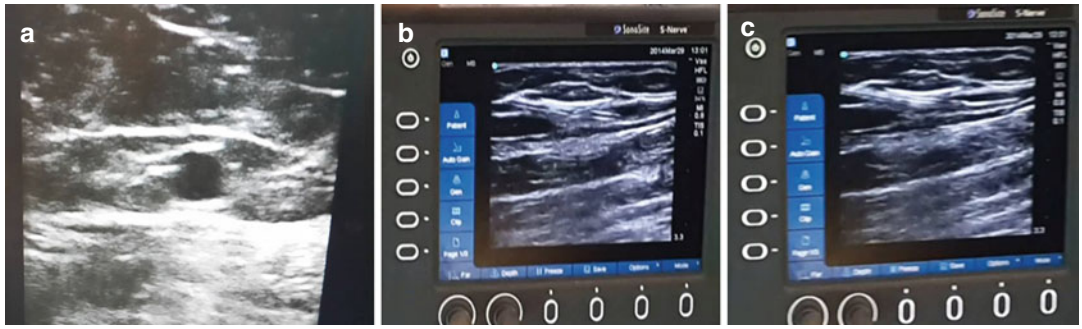

Fig. 8.4 (**a**) Identification of GSV – Egyptian eye. (**b**) Cannulation under guidance. (**c**) Guide wire inside GSV

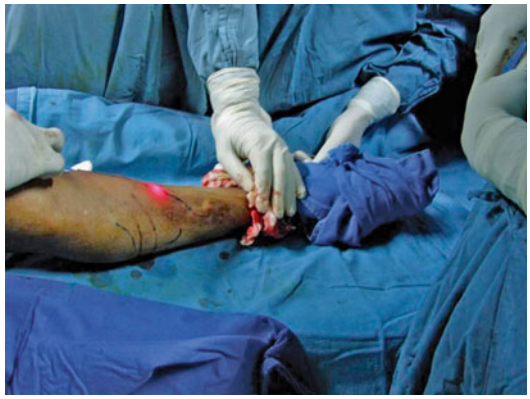

Fig. 8.5 Laser tip emitting a red glow

laser generator. We use the pulse mode pullback with one pulse lasting 1 s given at each point. The power is kept between 12 and 15 W depending on the size of the vein. If the GSV is more than 1 cm in diameter, higher wattages are given.

The entire length of the vein from the SFJ to the point of cannulation is treated by a "pullback technique" with the fiber being pulled backward from the SF junction by 2 mm after each 1 s pulse (Fig. 8.6). Below-knee segment is usually not treated to avoid injury to the saphenous nerve.

A check completion duplex scan is always undertaken to confirm closure of GSV.

The telangiectatic veins are treated by transdermal ablation of the veins as most often these veins are too small to be cannulated. Thigh-length compression hosiery is applied. Patient is encouraged to walk at the earliest. Patients are discharged same day or the next day morning. Duration of postoperative compression is for 7–10 days in C2 class patients. Normal activity is encouraged soon after the procedure.

Perforators can also be treated by the technique of percutaneous ablation of perforating veins (PAP). This is a day case procedure performed under local anesthesia. Under US guidance, the perforators are cannulated and the catheter is placed at or just below the deep fascia. The veins can be ablated using laser, RFA, or sclerotherapy. Newer RFA and laser fibers are available for this purpose.

Technical Difficulties and Complications

Technical difficulties one may encounter during EVLA are difficulty in cannulation, difficulty in advancement of the fiber, and equipment failures.

Complications may be classified as early and late.

Intraoperatively patient may experience syncopal attacks, saphenous neuralgia, and sensation of transient heat due to inadequate tumescence. In the immediate postoperative period, patient may experience pain, paresthesia, bruising, skin burns, superficial vein thrombosis (SVT), and DVT [8, 14, 16]. The reported incidence of DVT in various published data varies from 0.2 to 2.2 % [14]. Most other complications are mild and only require supportive care.

Late complication is recurrence. Patients who develop SVT due to inadequate obliteration can

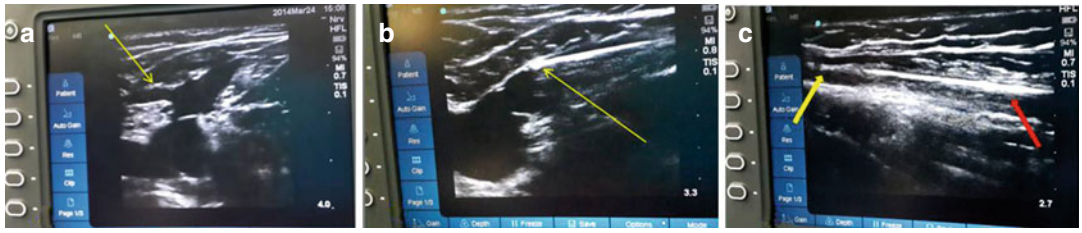

Fig. 8.6 (**a**) Superficial epigastric vein. Landmark for positioning tip of fiber. (**b**) Laser fiber tip at optimal site. (**c**) *Yellow arrow* showing treated collapsed segment of vein and *red arrow* the untreated segment during pull back

develop recurrence due to recanalization. Three patterns of recurrence – types I, II, and III are described for RFA. This will be considered later.

Outcome of Treatment

EVLA has a high success rate. In the first three months, the ablation rate is almost 100 % [9, 10]. But with time, the success rate drops. Serial duplex scan between 1 and 3 years follow-up have shown truncal vein ablation rates of 93–99 % [16] (Table 8.1). The lower success rate has been attributed to the following:

- Inadequate treatment
- Failure to address the tributaries at the SFJ
- Lower power used to ablate the vein

From 2004 May to 2009 May, a total number of 343 limbs were treated in our center with EVLA. Our ablation rate at the end of 36 months was 89.6 %. The complications observed include superficial thrombophlebitis 8/343, cordlike feel in the leg, infected thrombus in the treated vein segment in three patients, one case of DVT, one case where a small segment of covering sheath left behind due to fiber being pulled inadvertently and burning the covering sheath. Forty-four patients had minor skin burns and 36 recurrences at 3-year follow-up.

Neovascularization is uncommon following EVLA. This is because there is no groin dissection and specifically the superficial epigastric vein is preserved [16].

The procedure can be combined with other surgical interventions. EVLA has been performed with ambulatory phlebectomy [19]. Combined EVLA and endovenous iliac vein stenting has been reported by Raju et al. [20]. The procedure can be extended to treat patient with more advanced CEAP classes also.

Table 8.1 EVLA comparison of different series

Author	Number of veins treated	Follow-up (months)	Successful ablation (%)
Navarro	40	4.2	100
Chang and Chua	252	19	96.8
Timperman et al.	111	7	77.5
Huang et al.	230	6	100
Almeida and Raines	819	5.3	98.3
Disselhof	93	29	84
Min et al.	121	24	93.4
Meyers et al.	404	36	80

Adapted from Morrison [16]

Recurrence rate at 1 year following EVLA is much lower than the 10–20 % figures following HL/S. In an analysis of 280 patients comparing EVLA with conventional surgery of high ligation and stripping (HL/S), Carradice et al. reported that EVLA had lower rates of clinical recurrence compared to HL/S in short term [21].

Disselhoff et al. comparing EVLA with cryostripping observed no significant differences in outcome between the two procedures [22].

One of the concerns for the widespread use of EVLA is its cost-effectiveness. Gohel et al. have analyzed this aspect of the problem with reference to surgery, foam sclerotherapy, EVLA, and RFA. Ultrasound-guided foam sclerotherapy had the lowest initial cost but needed further interventions. EVLA and RFA performed as an office

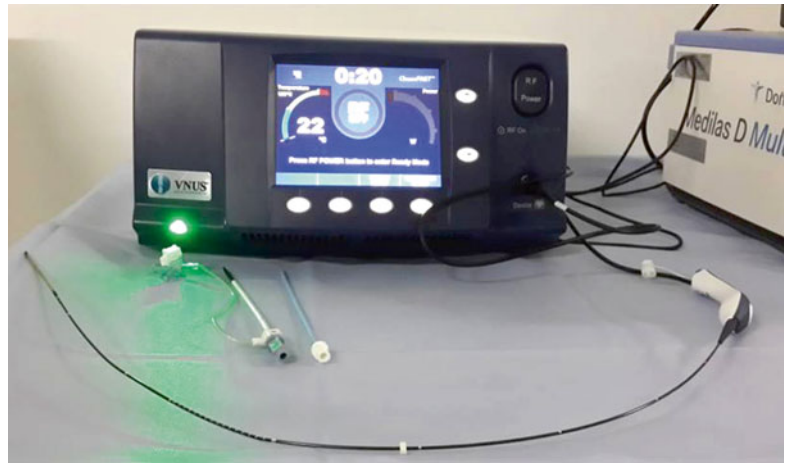

Fig. 8.7 Equipment for VNUS segmental closure

procedure and day case surgery are all found to be equally cost-effective strategies [23].

In conclusion, a properly evaluated and counselled patient, EVLA offers an excellent cosmetic and symptomatic treatment of varicose veins with very low failure and recurrence rates.

Radiofrequency Ablation

The reports of this modality of treatment for varicose veins were cited as early as in the 1950s. But the technique fell into disrepute because of the complications related to positioning of the catheter. There was a resurgence of interest for this modality of treatment in the twenty-first century. This resulted from the use of USG in the operation suite which provided better visualization of the veins and proper catheter positioning.

Two types of RFA are used presently [24]. Segmental RFA and radiofrequency-induced thermotherapy (RFITT). Segmental RFA is currently the most popular method.

Principles of Radiofrequency Ablation

The initial RF systems used RF current which heats up and destroys the venous endothelium like a diathermy. The radiofrequency heats local tissue up to 85–90 °C at the site of direct contact. The heat causes collagen shrinkage, denudation of endothelium, and obliteration of the venous lumen [25].

The new generation units has a radiofrequency powered catheter which works on the principle of radiofrequency segmental thermal ablation (VNUS closure fast devices). Segmental RFA (closure fast) has a 7 cm therapeutic distal segment that heats to 120 °C. It relies on oscillation by the probe to generate heat by activating the heating element for 20-s cycles. The tip of the probe has a 7 cm working end. During treatment, the probe is withdrawn by 7 cm each time. The heat is then automatically shut off, and the catheter is repositioned to the next treatment zone indicated by marking on the catheter.

The older-generation models of the VNUS system had only probes to address the major truncal veins. The newer-generation of RFITT probes can be used to treat smaller veins and the perforators (Fig. 8.7).

Procedure

The procedure of RFA is essentially similar to EVLA. Since the RFA probe is slightly larger in circumference, an occasional stab incision may be required to introduce the RFA probe and sheath through the skin. Pullback of the catheter is in 7 cm segments. Positioning of the catheter and instillation of tumescence is the same as in EVLA.

Table 8.2 RFA: comparison of different series

Author	Technique	Number of limbs	Closure rate (%)	Follow-up in years
Proebstle et al. (2008) [1]	Segmental	252	99.6	6 months
Kapoor et al. (2010) [27]	Segmental	100	97	1 year
Weiss et al. (2002) [26]	First-generation RFA	140	90	2 years
Merchant et al. (2005) [26]	First-generation RFA	1,222	87	5 years
Authors' series	Segmental	42	97.6	2 years

The proximal section of the vein near the SFJ is treated by two 20-s cycles. The catheter is then withdrawn by 7 cm. The rest of the vein is treated by a single 20-s cycle for each segment. It should be ensured that the temperature of the catheter tip should be 120 °C at the time of treatment. The process is repeated until the entire vein is treated. Duplex scan is routinely carried out post procedure.

A class II (30- to 40-mmHg gradient) compression stocking is effective in reducing postoperative bruising and tenderness, and it can also reduce the risk of venous thromboembolism. Patients are encouraged to walk immediately following the procedure and are asked to resume their normal activities within a day.

The patient is reevaluated 3–7 days after the procedure, by clinical examination and duplex scan. Duplex ultrasonography at this time should demonstrate a closed GSV. DVT should also be ruled out. Clinical examination at 6 weeks should reveal resolution of truncal varices.

Complications

The complications reported by the VNUS closure study group include DVT, skin burn, phlebitis, and paresthesia. The most serious complication reported for RFA is DVT with a reported incidence of 1 % [26]. Nerve injury can be avoided if the procedure is limited to the above-knee segment. Proper tumescent anesthesia will minimize skin burns.

Treatment Outcome

Published results show a high early success rate with a very low subsequent recurrence rate up to 10 years after treatment. Early and midrange results are comparable to those obtained with other endovenous ablation techniques. Proebstle et al. in a study of 194 patients (252 GSV) treated by radiofrequency-powered thermal segmental ablation have reported high occlusion rates at early follow-up. On 3 days, 3 months, and 6 months follow-up, their occlusion rate was 99.6 % [1]. Kapoor et al. reported a complete closure of 97 % at the end of 1 year in a series of 100 consecutive patients. They have also reported one case of neovascularization [27] (Table 8.2).

Recurrence Rates Described in Literature

Merchant and Kistner [26] have categorized recurrence patterns following RFA. They have identified three anatomical patterns.

Type I (nonocclusion) – initial and long-term failure of occlusion

Type II (recanalization) – early occlusion with late recanalization

Type III (groin reflux) – truncal occlusion with persistent groin reflux

Our experience with RFA in 42 patients over a 3-year study period has been extremely encouraging with a closure rate of 97.62 % at 3 months and no major complications.

RFA is more effective in treating larger veins as compared to the EVLA. However, it carries a higher recanalization rate. There is a failure rate of 5–10 % at 1 year follow-up. The risk of developing deep vein thrombosis (DVT) or a pulmonary embolism, while rare, is higher than endovenous laser therapy [28].

Comparison of RFA, EVL, USFS, and HL/S

Ramussen et al. [25] in a randomized clinical trial have made the following observations:

1. All treatments are effective.
2. Technical failure rate is higher after USFS.

3. RFA and USFS – faster recovery and less pain compared to EVL and HL/S.

The same group at 3-year follow-up has concluded that all modalities were efficacious and resulted in a similar improvement in VCSS and QOL. However, more recanalization and reoperations were seen with USFS [29] (Table 8.3).

Endovenous Steam Ablation

Endovenous steam ablation (EVSA) is a new method of thermal ablation [30]. It works by heating the vein wall with steam at 120 °C. The procedure is very similar to EVLA and is performed under local tumescent anesthesia in an outpatient setting. Under ultrasound guidance, the vein is punctured using 16-gauge cannula. The GSV access is usually done at or just above-knee level because cannulation is easy at this site and the risk of nerve injury is low. The SSV is usually punctured in the distal third of the calf or mid calf, depending on vein diameter and extent of reflux. After puncturing the vein, the steam catheter, which is about 1.2 mm diameter, is passed into the vein and the echo-dense tip of the catheter is positioned 3 cm from the SFJ, under ultrasound guidance. This is the most important requirement for the procedure. Depending on the length of vein treated, about 250–500 ml of tumescent anesthesia is administered into the perivenous space under ultrasound guidance. On activation, the catheter releases small "puffs" of steam. As in other endovenous procedures, catheter is pulled back in a stepwise fashion. At the first activation, 3 cm below the saphenofemoral or saphenopopliteal junction, four puffs of steam should be administered, while exerting gentle manual pressure on the junction. As we come lower in the vein, two or three puffs of steam can be administered at 1 cm intervals depending on vein diameter. As the steam can reach several centimeters beyond the catheter tip, manual compression of the junction should be applied for the first 4 cm of vein during treatment. After the procedure, patients are advised to wear thigh-length medical elastic compression stockings (pressure range 25–35 mmHg) for 1 week and to mobilize immediately after the treatment.

Fate of SFJ and Tributaries Following Thermal Ablation

Following endovenous thermal ablation, the GSV remains as a cordlike structure without any flow. In a few patients, it may recanalize and allow flow which may not produce any clinical symptoms. Patent tributaries were present, even when the SFJ was occluded. Again these were of no clinical significance [31]. The frequency of recurrent varicosities 2 years after surgery and EVLA was similar. Neovascularization was less common following endovenous thermal ablation [32]. Further, current recommendations on modifications of energy delivery in laser and RFA should ensure foolproof closure of the SF junction [33].

Gold Standard: HL/S or Endovenous Procedure

The Trendelenburg doctrine of reflux control at the groin, by high ligation and control of all the terminal tributaries, is considered to be an essential and unalterable step for successful surgical outcome. The endovenous procedures constitute a conceptual and ideological opposite to this approach. Critics point out that leaving behind a refluxing GSV in the groin along with uncontrolled tributaries is a certain way to court failure. The excellent early and intermediate clinical outcome along with posttreatment duplex imaging of the groin has disproved the traditional Trendelenburg concept. Theivacumar et al. on duplex scan 12 months after EVLA could not identify SF reflux in any of the treated limbs ($n=81$). Patent tributaries were present but these were of no clinical significance because they were all competent. Pichot et al. in a similar study 2 years after RFA had similar findings [34]. Coupled with the high incidence of neovascularization following high ligation, this traditional concept is being strongly challenged. In the near future, endovenous ablation procedures are likely to edge out HL/S and emerge as the new gold standard. The passion for high technology among clinicians and patients coupled with frenzied campaigning by the industry have led to an unacceptable and wanton practice of endovenous

Table 8.3 Comparison of HL/S, EVLA/RFA/USFS

Technique		HL/S	Laser	RFA	USFS
Indication		Large veins, localized dilatation, grade II reflux, <1 cm from skin surface	All classes, smaller more tortuous veins, 1 cm below the skin after tumescence	Larger straighter truncal tributary	All classes but with mild-grade I/II reflux
Mechanism of action		Surgical disconnection	Heating of tip of bare fiber to 100°	Resistive heating	Chemical damage to venous endothelium
Complications	*Pain*	Present	Pain present due to vein perforation	Less than laser	Nil
	Matting	Nil	Nil	Nil	Present
	Skin changes	Scar	Burns, bruising	Burns, bruising	pigmentation
	Neurological	Postoperative neuralgia possible in total stripping	Nerve injury possible if BK treated	Nerve injury possible if BK treated	Stroke-like symptoms possible
	DVT/SVT	2–10 %	<1 %	1 %	<1 %
	Visual disturbance	Nil	Nil	Nil	Possible
	Neovascularization	Common	Rare	Rare	Negative
	Recurrence	10–35 % long term	Midterm 1–3 %	Midterm 3–10 %	High
Advantages		Anatomical correction	Minimally invasive, cosmetic, treatment of C1, and perforators possible	Minimally invasive, less pain compared to laser, more cost-effective, new fibers for treatment of perforators available	Inexpensive, day case, all classes can be treated, useful in recurrent VV
Disadvantages		Not cost-effective	Not cost-effective if treatment is IP	Higher recurrence rate and less cosmetic as compared to laser	High rate of recurrence, multiple sessions required

procedures currently, diluting its genuine advantage. It is recommended that these procedures be adopted only in appropriate setting for clear clinical indications.

Summary

Endovenous procedures for the control of saphenous incompetence have the advantages of simplicity and effectiveness. The minimally invasive nature of these procedures along with early recovery and return to work has made them a popular alternative to open surgery. Endovenous thermal ablations can be performed either by using laser or radiofrequency waves. The choice would depend on the size of veins and the extent of tortuosity. Early, midterm, and 3-year outcomes are comparable to or even better tan HL/S. Duplex scan studies after thermal ablation have confirmed occlusion of the GSV. The criticism of endovenous procedures was that it cannot control the terminal tributaries. The posttreatment duplex scans have revealed that the majority of the terminal tributaries are competent. Moreover, neovascularization is an extremely rare event in thermal ablation unlike HL/S. In the foreseeable future, thermal ablation techniques would totally side track HL/S and is likely to emerge as the new gold standard. The flip side of it is a tendency to overtreat based on duplex scan reports. Hence, the caution by Meissner, do not treat the duplex scan but treat the patient [35].

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Sclerotherapy

9

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Contents

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Introduction

Sclerotherapy targeted endovenous chemical ablation of veins by injection of liquid or foamed sclerosing agents. Intradermal, subcutaneous, and/or transfascial veins can be treated by this method. The technique could also be used for superficial and deep venous malformations. The sclerosant induces chemical damage to the endothelium and inner media [1, 2]. The long-term effect of sclerotherapy is to transform the treated vein into a fibrous cord, a process known as sclerosis [3–5]. Thrombosis of the vein may occlude it temporarily but is likely to get recanalized in the course of time.

This chapter will focus on the following issues:

- History of sclerotherapy
- Chemistry and mechanism of action of various sclerosing agents
- Types of sclerotherapy
- Technique of injection
- Results of treatment
- Complications of sclerotherapy
- Sclerotherapy and microcirculation

History of Sclerotherapy

The earliest report of the use of sclerotherapy in phlebology appeared in medical literature in the later years of nineteenth century following the invention of syringe by Rhynd [6, 7]. Earlier "sclerosing" agents were thrombogenic rather than

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sclerosing. Hypertonic saline and sodium morrhuate, the ideal agents, came into picture in the early twentieth century [8]. Microsclerotherapy was introduced by Biegeleisen in 1930 [9]. The earliest report of using foam sclerosant in the literature was by Stuard McAusland. He used froth generated by the technique of shaking the vial, in treating telangiectasia [10]. Egmont James Orbach described air-block technique and displacement of blood in 1944 [11]. Robert Rowden Foote, Karl Sigg, Heinz Mayer, and Hans Bruke made further contributions [12, 13]. In 1963, Peter Lunkenheimer reported the first use of polidocanol foam. In 1986, Michael Grigg described a new foam production procedure with double syringes and a connecting tube. This can be considered as precursor of Tessari's technique which is universally practiced at present. In 2000, Lorenzo Tessari published his technique using double syringes and a three-way tap, the so-called "Tourbillion" technique [14]. Tessari subsequently made a more detailed description standardizing the pumping technique to make foam [15, 16]. At present, this technique is widely accepted and followed.

Sclerosing Agents

An ideal sclerosing agent should be nonallergic, strong enough to sclerose even the largest vessel. It should have no systemic toxicity and should not produce local injury even if extravasations occur. It should not produce staining or scarring and should be painless on injection. Most importantly, it should be inexpensive. Endothelial damage by sclerosants can occur due to change in surface tension of plasma membrane, alteration of intravascular pH, and osmolarity. Sclerosants produce fibrosis, thrombosis, or both but excessive thrombosis is not desirable since it can lead to recanalization. For effective sclerotherapy, endothelial damage should lead on to vessel wall necrosis [1, 2, 17].

Classification of Sclerosants

Sclerosants may be of three categories – detergents, hypertonic sclerosants, and cellular toxins.

Detergents

Detergent molecules form a lipid bilayer that disrupts the cell membrane and steals essential proteins from the cell membrane surface. This causes a delayed cell death [18]. Several sclerosants come under this group. *Sodium morrhuate* is a mixture of saturated and unsaturated fatty acids extracted from cod-liver oil. It was introduced in 1920 and is available even today. It is unstable in solution and produces extensive necrosis if extravasated. *Ethanolamine oleate* is a synthetic preparation of oleic acid and ethanolamine. The high viscosity of this agent makes injection difficult. High concentration is needed for effective sclerosis. It can cause red cell hemolysis, hemoglobinuria, and renal failure at higher dozes. *Sodium tetradecyl sulfate* (*STD*), *0.25–3 %*, was reapproved by FDA in 2004. It is proven to be a reliable, safe, and effective sclerosant. It can cause hyperpigmentation and matting. Incidence of anaphylaxis is 0.1–0.3 %. *Polidocanol* is hydroxy-polyethoxy-dodecane. This was originally developed as a non-ester, non-amide local anesthetic. Because intravascular and intradermal instillation of this agent produced sclerosis of small-diameter blood vessels, polidocanol was withdrawn as an anesthetic agent. It was proposed as a sclerosing agent in 1967 and is now the most popular agent used worldwide followed by STD. The drug has been approved by USFDA in 2010 for the treatment of telangiectasias and reticular veins. It is painless but can cause necrosis if injected intradermally. Hyperpigmentation, telangiectatic matting, and anaphylaxis are occasionally observed following use of this agent.

Hypertonic Sclerosants

These agents produce dehydration of endothelial cells through osmosis leading onto electrostatic changes on endothelial cells [19]. *Hypertonic saline* as a 23.4 % solution is the most common preparation. It rapidly disrupts vascular endothelial continuity. It is associated with significant pain and cramping. Extravasation causes necrosis. It can cause red cell lysis and marked hemosiderin pigmentation. *Hypertonic saline and dextrose mixture* is a combination of 25 % dextrose and 10 % sodium chloride. Effects are

Table 9.1 Vessel size and sclerosant strength

0.1–0.5 mm vessel		0.6–0.9 mm vessel		1.0–4.0 mm vessels		>4 mm vessels	
Hypertonic saline	11.7 %	Saline	11.7–23.4 %	Saline	23.4 %	STD	1–3 %
STD	0.1–0.2 %	STD	0.2–0.3 %	STD	0.3–0.5 %	Polidocanol	2–5 %
Polidocanol	0.2–0.5 %	Polidocanol	0.2–0.75 %	Polidocanol	1.0–2.0 %		
Glycerin	50–72 %						

similar to hypertonic saline. Both solutions are too weak for large veins. Epidermal necrosis can occur with extravasation.

Cellular Toxins

Chromated glycerine and polyiodinated iodine come under this group. They exert direct or indirect chemical toxicity to the endothelial cells resulting in their damage. There is deposition of fibrin on the endothelial wall along with platelet adhesion [20]. *Polyiodinated iodine* is a mixture of elemental iodine and sodium iodide. It acts by producing localized ionic disruption of cell surface proteins. Anaphylaxis, renal toxicity, and extravasation necrosis can occur with iodinated solutions. *Chromated glycerine* is 72 % solution. It is more viscous and is a weak sclerosant which can be used in small vessels. It causes less hyperpigmentation and telangiectatic matting compared to other agents. It rarely causes extravasation necrosis. Hematuria has been reported occasionally following its use.

Concentration of Sclerosing Agents

It will be ideal to deliver the minimum volume and concentration of sclerosant that will cause irreversible damage to the endothelium of the injected vessel only. Too weak sclerosants are ineffective and a too strong sclerosants produce tissue damage. Sclerosants can be very strong, strong, moderate, or weak in strength, and the choice will depend on the size of the vessel [21]. Based on the vessel size, the ideal concentration and strength of various sclerosants are presented in Table 9.1.

The recommended dose of STD by the manufacturer is 2 ml of 1 % or 3 % solution (20 or 60 mg) per injection site with a maximum of 10 ml per treatment session. Polidocanol is recommended at a dose of 0.1–0.3 ml per injection site to a maximum of 10 ml per treatment session.

Indications and Contraindications

Optimal indications for sclerotherapy include telangiectasias, reticular veins, isolated varicosities, below-knee varicosities, and recurrent varicosities. *Less than optimal indications* include symptomatic reflux, aged, or infirm patients who are not surgical candidates. *Debatable indications are* SFJ reflux, SPJ reflux, large varicosities, and large perforators which are refluxing [21, 22].

C*ontraindications* for sclerotherapy include allergy to sclerosant, bedridden patients, postthrombotic syndrome, acute thrombophlebitis, uncontrolled malignancy, and local or severe systemic infections [21, 22].

Sclerotherapy has been extensively used to treat axial refluxes and large incompetent perforators. More evidence is needed before this can be recommended for widespread practice. With the available evidence, it may be ideal to treat axial refluxes and large veins by surgery or by endovenous thermal ablation. This can be followed by sclerotherapy for smaller veins and telangiectasias [23].

Types of Sclerotherapy

Microsclerotherapy and macrosclerotherapy were the techniques in common use when liquid sclerosant alone was available. Foam sclerotherapy was introduced with the invention of foam sclerosant. Ultrasound-guided foam sclerotherapy (USGFS) and catheter-directed foam

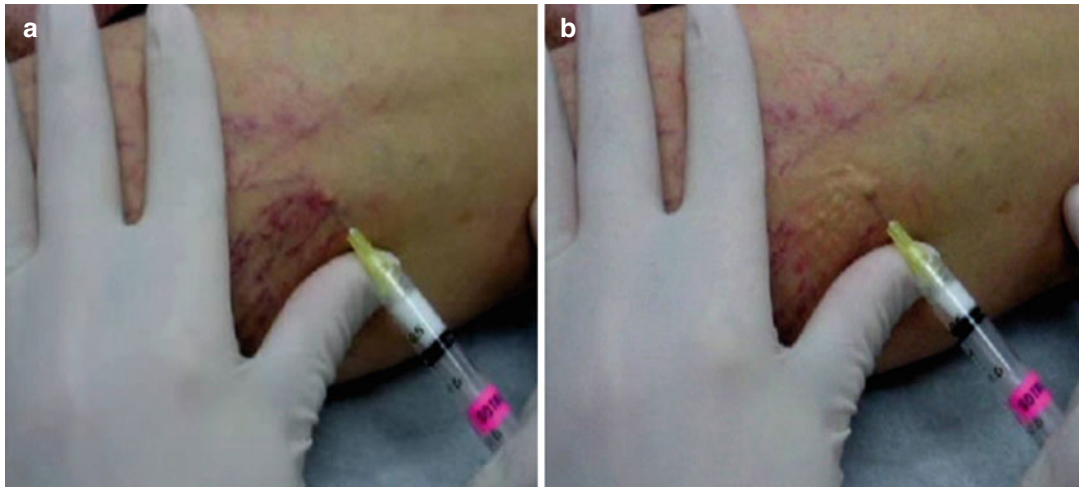

Fig. 9.1 Microsclerotherapy. (**a**) Cannulation. (**b**) Postinjection with blanching

sclerotherapy are further modifications. They are more effective and produce fewer complications [24].

Microsclerotherapy

This term refers to the treatment of telangiectatic blemishes and reticular veins using liquid sclerosant [25]. Weak sclerosing solutions are generally used for the procedure. Pretreatment duplex scan can reveal an incompetent saphenous and perforating system refluxing into these vessels [26]. The source of venous hypertension which has led to the development of these lesions must be controlled before therapy. The feeding reticular veins connecting to the telangiectasias should be injected first. If such a feeding vein cannot be identified, telangiectasias can be injected directly, beginning at the point at which the branches converge. Although liquid sclerotherapy is ideal for C1 class [27–29], foam sclerotherapy is an additional option [30–32].

The technique of injection varies among different practitioners. The patient is in horizontal position and the skin is cleaned with alcohol to remove the excess keratin and allow better visualization of the target vessel. Thirty G needles, bent to 10–20°, fitted with 1 ml syringes are employed for injection. Skin adjacent to the vein is stretched and the needle is introduced into the vein tangentially. Gentle pressure on the plunger ejects sclerosant into the vein. Magnification and good light can improve the performance. Injections should be performed very slowly taking 10–15 s. The amount of sclerosant per injection site should be limited to 0.1–0.2 ml (Fig. 9.1).

Persistent blanching of skin to a waxy white color indicates extravasation. If such an event occurs, the area should be flushed thoroughly with normal saline to dilute the extravasated sclerosant and relieve vasospasm. Veins larger than 0.5 mm and protruding above the skin surface should have sustained compression for 72 h at least following injection. Small veins that do not protrude above the skin surface need not be compressed. Class II compression therapy is provided after completion of injection. Protuberant telangiectasias and large reticular veins need compression for at least 72 h. Patients who need multiple sessions are called at 2–4 weeks interval. In case of reticular varicosities, volume of injection can be 0.5 ml per site. Multiple punctures give best results [21, 33]. We have used 0.25 % sodium tetradecyl sulfate and 0.5 % polidocanol for microsclerotherapy.

Macrosclerotherapy

Macrosclerotherapy is the method of treatment of larger veins (tributaries and truncal veins) using liquid sclerosing agents. The sclerosants used for

this purpose are 1–1.5 % sodium tetradecyl sulfate or 1–2 % polidocanol. Multiple site injections are followed by compression for at least 2 weeks. This technique has largely been replaced by foam sclerotherapy.

Foam Sclerotherapy

Foam sclerotherapy (FS) is a method of endovenous chemical ablation using foamed sclerosants. There are several advantages for this technique.

- FS fills up the large veins into which it is injected by expanding the volume of the sclerosant injected. The sclerosing agent which is at the surface of the bubbles establishes good contact with the endothelium. Once the gas gets absorbed, the vein walls collapse. The chemical action on the endothelium would be initiated by this time.
- Ultrasound-guided foam sclerotherapy (USFS) has an additional advantage that the sclerosant can be tracked in the vein lumen, since air is a good contrast medium. Ultrasound permits selective guided venous puncture avoiding injury to adjacent arteries. It also permits a postinjection evaluation of the extent of distribution of the sclerosants and its reaction on the vein wall [34–37].
- USFS is an office-based procedure not requiring hospitalization.
- It is cost-effective compared to other modalities like HL/S or endovenous thermal ablation.
- In the event of recurrence, the procedure can be repeated easily.

Foam Generation

Detergent-type sclerosants such as polidocanol or sodium tetradecyl sulfate can be transformed into fine-bubbled foam by special techniques. It is produced by turbulent mixture of liquid and gas in two syringes connected via a three-way stopcock, Tessari method. In the original Tessari method, the ratio of sclerosant to gas was 1:4 [16]. The Tessari double-syringe-system (DSS) technique involves the turbulent mixing of sclerosant with gas in a ratio of 1:4 in two syringes linked via a two-way connector. The use of atmospheric air in foam production does not give rise to any adverse effects [38].

In our experience, we could obtain stable and fine-bubbled foam by a modified Tessari technique. The required materials are two 10-ml syringes with a Luer-Lock connection (omnifix syringe and inject syringe), one three-way adaptor, and a 0.2-mm filter for sterilization of air. 8 ml of air is drawn into the inject syringe via the sterile filter. Air filter is discarded and 2 ml of 3 % polidocanol is also drawn into the syringe. The two syringes are connected through the three-way adaptor. The air sclerosant mixture is passed between the two syringes to generate foam. The initial five passages are done by offering mild resistance to the piston of the recipient syringe. Further 15 passages are performed without any resistance (Fig. 9.2). This will generate a foamed sclerosant of 10 ml. The DSS technique offers a fixed sclerosant-air ratio of 1:4, a half-life of approximately 150 s, and an initial bubble size of 70 μm [39].

Technique of Injection

In our practice, all patients with significant axial reflux had a preliminary high ligation under local anesthesia. Multiple site cannulation of the dilated and tortuous veins with 22G cannula or butterfly needle (4–6 sites) is preformed under US guidance (Fig. 9.3).

Each site is injected with 2–3 ml of foam with limb elevated to 45° angle and monitored by US imaging (Fig. 9.4).

In cases with nonsignificant reflux or no reflux at SF junction, high ligation is avoided, and USFS alone is done. In such cases, one of the requirements is to prevent the spillage of FS into the femoral vein. One technique is to track the foam with ultrasound, and once it reaches the SF junction, compression is applied at the site with the duplex probe followed by compression bandage. On completion, the distribution of the sclerosant and the reaction of the vein including spasm are checked. Injection is followed by immediate compression using gauze pad and elastic bandage and maintained for 2 weeks. Histological studies suggest that at least 12 days of fibroblastic healing

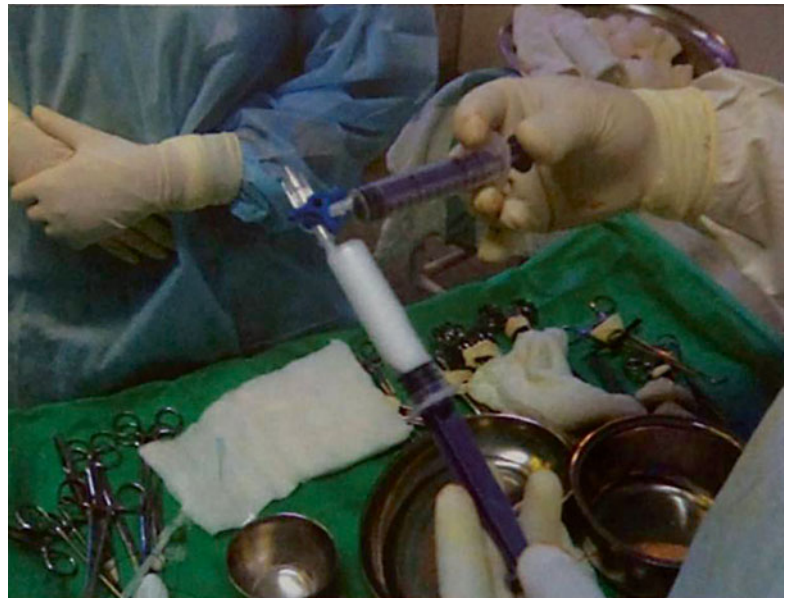

Fig. 9.2 Generation of foam sclerosant

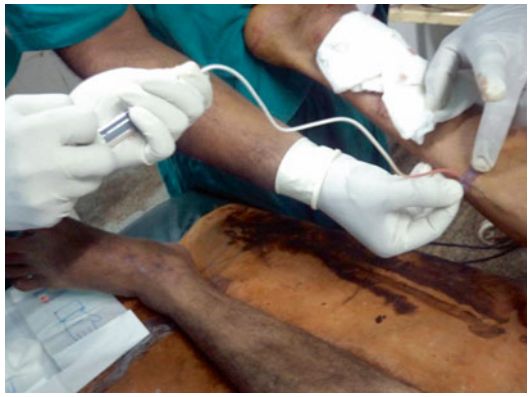

Fig. 9.3 Cannulation of the vein

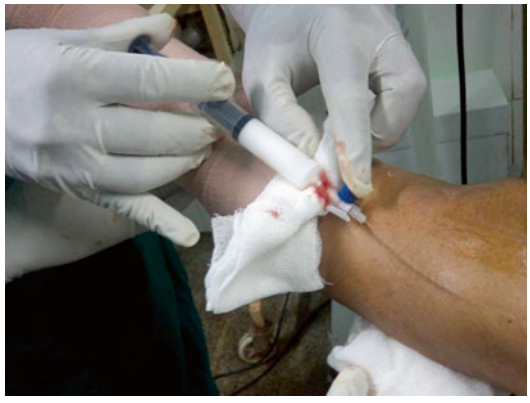

Fig. 9.4 Injecting foam sclerosant

is required for obliteration of moderate-sized veins [17]. Fegan had suggested 6 weeks of compression following liquid sclerotherapy. The length of compression treatment period varies between different authorities. In our practice, 2 weeks of compression treatment is given following foam sclerotherapy. After two weeks, the patient is advised to wear class II compression stockings for the next 4 weeks.

Nearly all workers in this field advise that the patient should walk for at least 30 min after the procedure. This will permit any allergic reaction to be manifested and treated. The comfort of the elastic compression can also be evaluated. Ambulation promotes deep venous circulation to flush out any sclerosant that has spilled over [21].

All our patients were assessed with duplex ultrasound scan at 2 weeks, 3 months, 6 months, and 1 year.

Outcome

During a 2-year period, we treated 40 patients with C5–C6 clinical class with combined high ligation and distal USFS. Ninety percent of the limbs showed obliteration of the injected veins at the end of the 6 months. There was an upgrada-

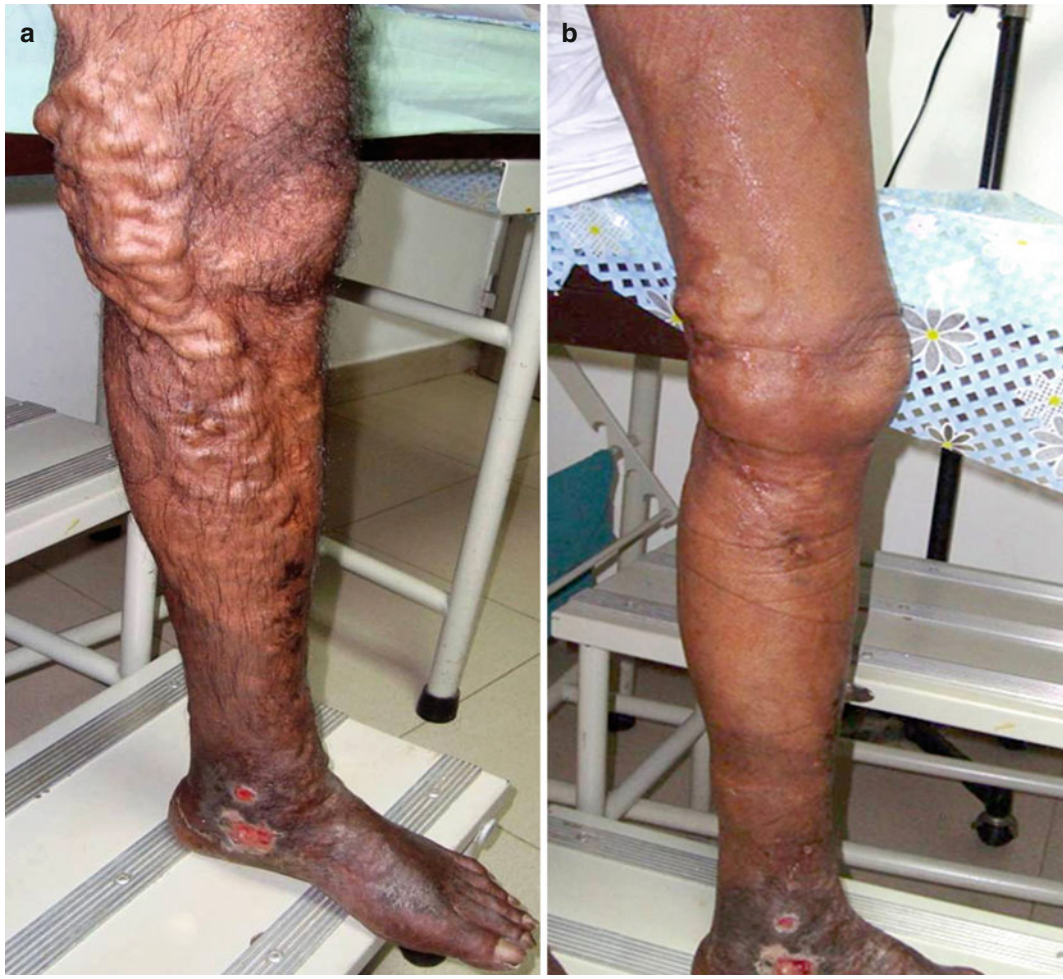

Fig. 9.5 Foam sclerotherapy outcome (**a**) a leg with varicose veins before foam sclerotherapy, (**b**) the same leg after foam sclerotherapy

tion of CEAP class in all our patients. The ulcers healed in all the C6 class patients. Two patients had superficial thrombophlebitis and two patients had calf vein thrombosis. All patients settled with treatment. No major/minor neurological events were noted in our patients (Fig. 9.5).

Saphenectomy combined with ultrasound-guided foam sclerotherapy is reported to give results equivalent to classical surgery in terms of obliteration of veins, ulcer healing, and improvement of CEAP class. The time taken for USFS was significantly lower (45 min vs 85 min) [40, 41]. The role of surgery and thermal ablation in the treatment of incompetent saphenous system is well established. Many groups have used sclerotherapy in isolation for this purpose and have reported comparable results [28, 42–46]. One of the requirements is to prevent the spillage of FS into the femoral vein. One technique is to track the foam with ultrasound, and once it reaches the SF junction, compression is applied at the site with the duplex probe followed by compression bandage (Fig. 9.6).

Another method is using Sigg's technique with an inflatable balloon called Safeguard® for echo-guided compression of saphenofemoral junction [47]. For optimum control, it will be more logical to inject the FS close to the source of reflux, a perforating vein/saphenous junctions. Carbon dioxide or CO_2/O_2 mixture has been used to make foam instead of air. No extra advantages

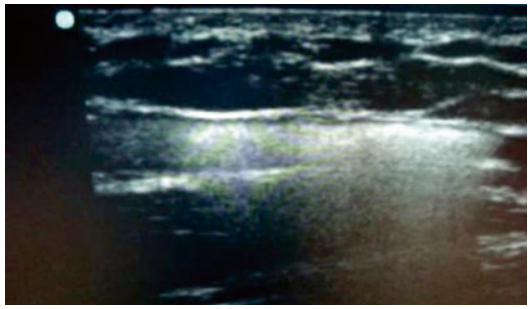

Fig. 9.6 Tracking of foam sclerosant with ultrasound

are reported with these methods. Total volume of sclerosant required for treatment was more with CO_2 foam group [48].

A recent modification of USFS is a catheter-directed foam sclerotherapy. An angiography catheter is introduced into the GSV at or below knee under US guidance and advanced up to the saphenofemoral junction. Saphenofemoral junction is occluded and then the catheter is slowly withdrawn while injecting foam through the catheter. The technique allows more precise delivery of the required quantity of foam into each segment of the vein to be obliterated [49]. It resembles endovenous ablation using RFA or laser. Foam sclerotherapy using triple-lumen double-balloon catheters are reported, but no extra benefits were observed. In 70 % of cases, occlusion was complete at 1 year, partial in 14 %, and in 16 %, there was recanalization [50].

Bilateral varicose veins can be treated with foam sclerotherapy at a single sitting without affecting the vein occlusion rate or increasing the complications. Volume of foam sclerosant required would be obviously higher in bilateral groups compared to unilateral (17.5 ml vs 10 ml) [51].

Results of foam sclerotherapy have been compared with the results of standard surgery as well as with laser and radiofrequency ablation techniques. Comparative results with liquid sclerotherapy are also available. Foam sclerotherapy is found to be more effective than liquid sclerotherapy. Both sodium tetradecyl sulfate and polidocanol are equally effective when used as foam [52]. Ultrasound-guided foam sclerotherapy was found to be associated with less pain and analgesia requirement, time off work, and quicker return to driving compared with conventional surgery [43]. At the end of 2 years, recurrent reflux irrespective of venous symptoms was more in USFS group compared to classical surgery (35 % vs 21 %) [43]. But symptomatic recurrence was found to be comparable. The reduction in cost of treatment was significant with USFS [53].

The technical failure rate at the end of one year was highest after USFS in comparison to surgery and endovenous thermal ablation (USFS 16.3 %, conventional surgery 4.8 %, laser 5.6 %, and RFA 4.8 %). The pain scores were significantly low with RFA and USFS and highest with laser and conventional surgery [43]. In recurrent varicose veins, USFS was found to be superior to surgery. A single session of USFS can eradicate reflux in above-knee and below-knee great saphenous vein in over 93 % of patients with symptomatic recurrent great saphenous vein varicosities [54].

Foam sclerotherapy is generally safe in the treatment of short saphenous varicosities also. Medial gastrocnemius vein thrombosis is reported in 0.6 % patients following USFS of SSV. Two anatomical features that can aggravate risk of DVT are relevant in this context. Direct entry of the SSV into popliteal vein and the presence of medial gastrocnemius vein perforators [55]. An early duplex scan may be ideal in such patients.

Complications of Sclerotherapy

Sclerotherapy is an efficient method of treatment with a low incidence of complications, if performed in a systematic manner [56]. Some of the commonly encountered complications are discussed below.

Anaphylaxis

Incidence of anaphylaxis is extremely rare. The severity of the reaction may range from mild pruritis and urticaria to shock and death [57]. The most common agent producing anaphylaxis is sodium morrhuate, followed by sodium tetradecyl sulfate. It is least common with polidocanol [21].

Thrombophlebitis

Reported incidence of thrombophlebitis varies from 0 to 45.8 % (mean 4.7 %) [58–60]. However, the definition of phlebitis after sclerotherapy in the literature is controversial. An inflammatory reaction at the injected part of the vein should not be taken as phlebitis. Superficial thrombophlebitis can develop after sclerotherapy, but its real frequency seems to be low [22]. Incidence of thrombophlebitis can be minimized with compression therapy after sclerosant injection.

Deep Vein Thrombosis

Severe thromboembolic events (i.e., proximal DVT/pulmonary embolism) occur only rarely after sclerotherapy. The overall incidence of thromboembolic events is less than 1 % [60–62]. Most of the DVTs were distal and asymptomatic [63, 64]. Large volume FS increases the risk of DVT [65–67]. Patients with previous history of DVT or thrombophilia warrant additional prophylactic measures [65, 68]. Deep vein thrombosis can be obviated by post sclerotherapy exercises that flush the deep veins.

Cutaneous Necrosis

Skin ulceration and cutaneous necrosis can result from extravasation of the sclerosant or from injection into a terminal arteriole [69]. This can happen during injection of reticular veins or telangiectasias [70, 71]. This has been described as embolia cutis medicamentosa or Nicolau phenomenon [72, 73]. Complication of extravasation can be minimized by using dilute solutions, especially in telangiectasias and also by slow injection of small quantities to each site.

Hyperpigmentation

Hyperpigmentation can occur following treatment of reticular veins and telangiectasias. Reported frequency is 0.3–30% in the short term [69, 74]. It is most common following sodium tetradecyl sulfate and hypertonic saline and least with polidocanol and chromated glycerin. Pigmentation is due to hemosiderin derived from the extravasated RBCs. This may be minimized by the use of weak solutions and minimum pressure during injection. Any coagulum formed should be removed by minithrombectomy [75]. Post sclerotherapy hyperpigmentation largely disappears over a prolonged period [76].

Telangiectatic Matting

Telangiectatic matting or neoangiogenesis is the appearance of red telangiectasias at the site of sclerotherapy. It can also occur after surgical or thermal ablation of varicose veins [69]. All the measures to prevent pigmentation can be practiced here also. Residual reflux if any should be eliminated [59]. Pulsed-dye laser therapy for the treatment of neoangiogenesis has been found to be effective [21].

Inadvertent Arterial Injection and Gangrene

Inadvertent arterial injection and resultant gangrene have been reported following both liquid and foam sclerotherapy. Extensive tissue necrosis can occur following such an episode [77, 78]. If severe pain occurs during an injection, it should be stopped immediately. If intra-arterial injection is suspected, local catheter-directed thrombolysis should be performed, if possible. This may be followed by systemic anticoagulation. Early administration of systemic steroids may reduce the inflammation [59]. The possibility of this complication should be less with ultrasound-guided puncture of veins. Injection around ankle for the medial calf perforating veins is a high-risk situation for inadvertent intra-arterial injection. Amputations were required in 50 % of reported cases [79].

Nerve Injury

Compared to other treatment modalities like surgery/thermal ablation, incidence of nerve injury is very rare after sclerotherapy [80].

Visual Disturbances, Headache, and Migraine

Transient migraine-like symptoms can rarely occur after any type of sclerotherapy. It is more common with FS than with liquid sclerotherapy [63, 64, 81]. It has been suggested that a right-to-left shunt, which is present in 30 % of the population, might be a factor allowing foam bubbles to cross over to arterial circulation.

Visual disturbances following sclerotherapy resemble migraine with aura than transient ischemic attacks [82]. They are subjective and transient. Visual disturbances may also be associated with paresthesia and dysphasia. Visual or neurological symptoms are not clearly attributed to the bubbles. A recent study has suggested possible relation with increased endothelin-1 level from vessels injected with sclerosants [83, 84]. Multiple injections with small volume at each site may reduce the passage of sclerosant into deep veins [85].

Stroke and Transient Ischemic Attacks

Early onset neurological disturbances following sclerotherapy have been attributed to air bubbles in the cerebral vessels. This entity does not seem to be related to thromboembolic pathology [64, 66, 86–88]. Such cases always had a complete or near-complete recovery [89, 90]. On the other hand, late onset neurological events are related to paradoxical clot venous embolism and are associated with poor prognosis [91]. Delayed strokes have also been reported following other treatment options for varicose veins [92]. To minimize neurological complications, the following precautions may be observed. (1) Avoid injecting large volume foam or liquid sclerosant. (2) Patients should avoid Valsalva maneuver during and soon after the injection. (3) Ambulation is delayed in patients who had neurological symptoms in the previous sessions [22].

Sclerotherapy and Microcirculation

One of the advantages claimed for sclerotherapy over surgery and endovenous procedures is its ability to close the small microvenous channels. It has been reported that failure of valves in the small superficial veins is an important cause for the development of skin changes in patients with varicose veins. Till recently, it was believed that valves do not exist in veins <2 mm in size. But now, this has been disproved. In fact, such microvalves have been identified up to the sixth-generation tributaries of GSV [93]. Incompetence of microvalves can occur even in the presence of a competent GSV. Obviously combined micro- and macrovalve incompetency would produce more severe symptoms. Venous ulcers and lipodermatosclerosis are connected to an incompetent perforator through a leash of vessels below them. Thus, the pathological ambulatory venous hypertension is transmitted to these lesions [94]. These small vessels are inaccessible for open surgery and endovenous thermal procedures. HL/S or thermal ablation can have an indirect effect on these microvessels. It is suggested that foam sclerotherapy has a direct access to this microcirculation and can obliterate the small cluster of veins underneath venous ulcers and lipodermatosclerosis [94].

Summary

Sclerotherapy, as it stands today, is one of the cornerstones of treatment of varicose veins. Liquid sclerotherapy is the method of choice for ablation of telangiectasias and reticular veins. Foam sclerotherapy is an alternate treatment method in this situation with comparable occlusion rates and side effects. FS of saphenous trunk and its branches is more effective than liquid

sclerotherapy. Midterm failure rates of FS are slightly more than conventional surgery or thermal ablation techniques. But symptomatic recurrences seem to be comparable between these groups. Advantage of FS is that it can be repeated easily on an outpatient basis in case of recurrence. Treatment cost is also low compared to other modalities. FS should be the treatment of choice in recurrent varicose veins, below-knee varicosities, isolated varicosities, bleeding varicose veins, and varicose veins in aged patients with high risk for anesthesia. Moreover, there is growing evidence to prove that foam sclerotherapy has a direct access to the microcirculation. Overall, it appears that USFS has the potential to be a cost-effective approach to a common health care problem.

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Recurrent Varicose Veins

10

Pradeep Jacob

Contents

Introduction

Recurrence of varicose veins after surgery is a common problem. Many surgeons have a pessimistic view on the outcome of surgery for varicose veins and consider recurrence inevitable. The problem is confounded by the inability to clearly define recurrence. Variations in the definition of recurrent varicose veins result from the multiple modalities of interventions employed for the initial treatment of chronic venous disorders (CVD). To streamline these issues, an international consensus meeting was held in Paris in 1998 to provide guidelines for the definition and management of recurrent varicose veins after surgery (REVAS).

This chapter addresses the following issues.

- Definition of recurrent varicose veins
- The prevalence of the problem
- Classification of recurrence and identification of factors responsible for recurrence
- Patterns of recurrence after nonsurgical interventions
- Evaluation and management of recurrent varicose veins

Definition

At the international consensus meeting in Paris in 1998, recurrent varicose veins after surgery (REVAS) were defined as "the presence of varicose veins in a lower limb

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previously operated for varices with or without adjuvant therapies" [1].

This is a broad-based clinical definition and includes true recurrences, residual veins, and veins developing from progression of the disease.

van Rij has defined clinical recurrence as appearance of new varices not observed before surgery or reappearance of varices which had been eliminated at surgery or progression of signs of venous insufficiency including ulceration as observed by the clinician or reported by the patient [2]. Browse had emphasized the distinction between residual veins and recurrent varicose veins. The REVAS definition is comprehensive and includes all these entities.

Irrespective of the cause, for a patient, presence of any varices after surgery is considered a failure of treatment [1].

Incidence

The reported rate of recurrence after surgery for varicose veins varies widely. van Rij and team reported a recurrence rate of 51 % for varicose veins 3–5 years after surgery [2]. Ten to thirty-five percent of patients have clinically significant recurrence, 5–10 years after surgery for varicose veins; incidence of minor duplex detected recurrences was much higher (70 %) [3]. Ten to twenty percent of patients seeking treatment in a hospital for varicose veins have had some form of previous interventions [3].

Despite technically correct surgery, confirmed by postoperative duplex scan studies, a recurrence of reflux at the saphenofemoral junction (SFJ) was noted in 13 % of patients; at the saphenopopliteal junction (SPJ), it was 30 %. The combined reflux rate was 36 %. The mean time for recurrence was 6.3 years and the mean time for symptoms to manifest was 8.5 years [4].

Recent prospective studies have shown recurrence rates ranging from 28 to 51.7 %. All these patients had preoperative duplex scanning followed by high ligation, stripping, and stab avulsion [2, 5].

Following radiofrequency ablation (RFA), a recurrence of 22.7 % was observed at the end of 5 years [6].

Pathophysiology

Perrin has extensively reported on this problem. He has listed four possible mechanisms for REVAS [1].

- Tactical error
- Technical error
- Neovascularization
- Progression of disease

Tactical Errors

These are due to failure to identify reflux at SFJ, SPJ, and/or perforators. It could also result from deliberate failure to treat identified or unidentified superficial incompetent veins. The routine use of preoperative duplex scans has significantly reduced these errors.

Technical Errors

These errors result from incorrectly executed interventions. Failure to correct reflux at SFJ, SPJ, and perforating veins or any other sites preoperatively identified is a common error. Technical errors could be recognized by a check postoperative duplex scan.

Correction of SFJ/SPJ incompetence can revert some of the incompetent perforators. Similarly, following endovenous procedures, an incompetent SFJ/SPJ can be rendered competent. Hence, tactical and technical errors need not always lead on to recurrence.

Neovascularization

Neovascularization is defined as the presence of multiple new small tortuous veins in anatomic proximity to a previous venous intervention [7]. This develops in the form of small new venous channels in the granulation tissue around SFJ and SPJ. They subsequently enlarge and connect deep veins to superficial veins. This is an important factor responsible for REVAS following conventional surgery with high ligation [8, 9]. Neovascularization is infrequent

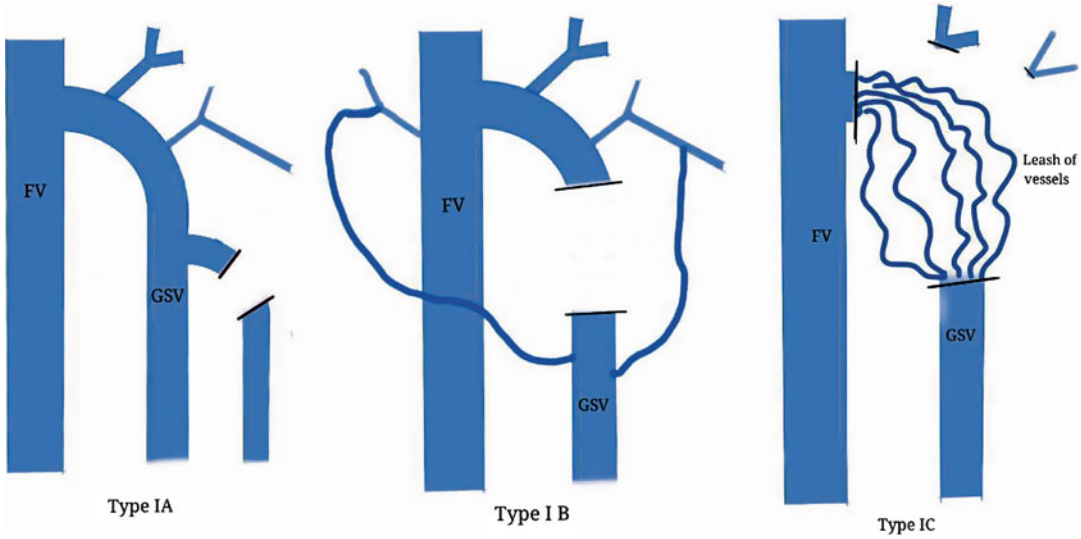

Fig. 10.1 Groin anatomy in recurrent varicose vein. Type I. SFJ patent. *Type I A* main stem (GSV intact). *Type I B* tributary (missed tributaries in the groin). *Type I C* neovascularization. *FV* femoral vein, *GSV* great saphenous vein

following RFA [10]. Neovascularization is confirmed by histological examination of the venous tissue blocks excised during surgery. The histological features include tortuosity of veins, small size, mural asymmetry, and lack of intramural nerves on immunohistochemical stains using S100 [11].

Progression of the Disease

CVD is a progressive disease. Hence, previously unaffected segments may become pathological in the course of time.

Recurrent Varicose Veins: Classification

There are many methods of classifying recurrent varicose veins. Most of them are based on the anatomical findings during reexploration along with clinical and duplex scan findings. Most of the studies have focused on the SFJ.

Fischer et al., based on the sonological findings, offered the following classification of recurrence at SFJ:

- A – No recurrence at SFJ
- B 1 – Junctional; strand/leash of vessels from former site of ligation
- B 2 – Single-lumen junctional recurrence from former site of ligation
- C – Circumjunctional recurrence from subfascial veins other than CFV in the region of ligation [12]

Stonebridge and team offered a classification based on varicographic findings [13].

- Type 1 Recurrent – residual connection between the superficial and deep system at or immediately around the SFJ. This was further subdivided into three (Fig 10.1).
  A. Main stem
  B. Tributary
  C. Neovascularization
- Type 2 Recurrent – saphenofemoral venous complex obliterated. This has two subdivisions (Fig. 10.2).
  A. Cross groin
  B. Mid thigh

The presence of GSV was noted and the length of thigh vein graded on a 0–3 scale.
0 = no GSV
1 = GSV present in lower thigh

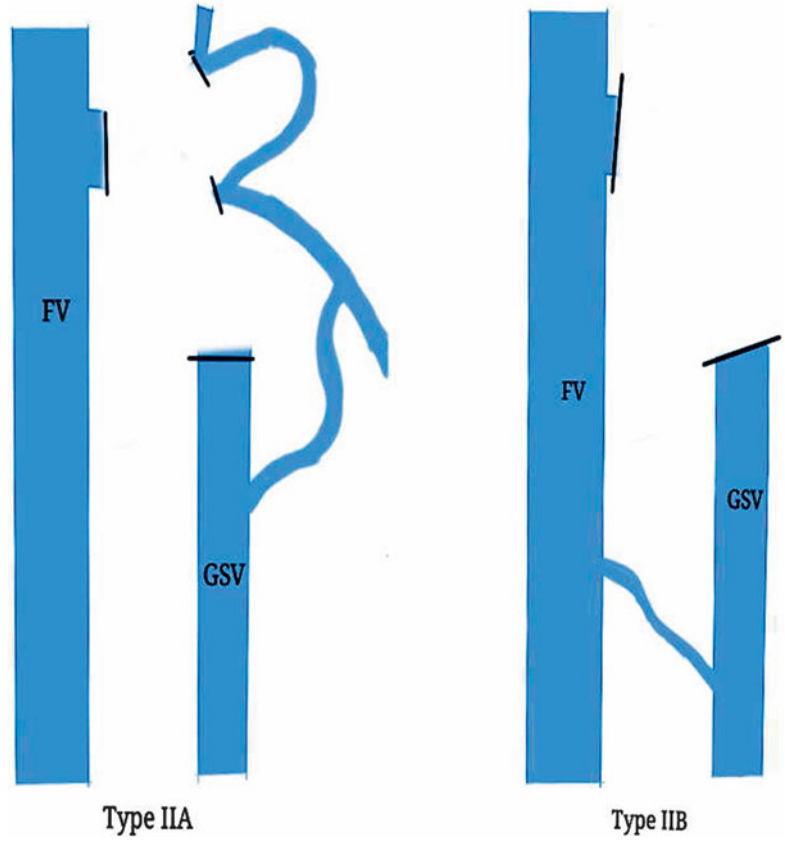

Fig. 10.2 Groin anatomy in recurrent varicose veins – type II. SFJ obliterated. *Type II A* cross groin. *Type II B* mid thigh. *FV* femoral vein, *GSV* great saphenous vein

2 = present in upper thigh but not to the groin
3 = present to the groin

The current most widely accepted system of classification for recurrent varicose veins is the REVAS classification. This would be discussed in detail.

REVAS Classification

The REVAS classification includes six items:

- Topographic sites of REVAS – *T*
- Source of reflux – *S*
- Degree of reflux – *R*
- Nature of sources – *N*
- Contribution from persistent incompetent saphenous trunk – *P*
- Possible contributory factors – *F*

1. *Topographic sites (T)*

Groin (g)	1
Thigh (t)	2
Popliteal fossa (p)	3
Lower leg including ankle and foot (l)	4
Others (o)	5

2. *Sources of reflux (S)*

No identified source	0
Pelvic and/or abdomen	1
SFJ	2
Thigh perforators	3
SPJ	4
Popliteal perforator	5
Gastrocnemius vein	6
Lower leg perforators	7

3. *Degree of reflux (R)*

Probable clinical significance	R+
Unlikely clinical significance	R–
Uncertain clinical significance	R?

4. *Nature of sources (N)*
N ss – same site of previous surgery

Technical failure	1
Tactical failure	2
Neovascularization	3
Uncertain/unknown	4
Mixed	5

N ds – different site

Persistent	1
New	2
Uncertain/unknown	3

5. *Contribution from a persistent incompetent saphenous trunk (P)*

GSV – AK (above knee)	1
GSV – BK (below knee)	2
SSV	3
Neither/others	4

6. *Possible contributory factors (F)*
General factors (Fg)

Family history	1
Obesity	2
Pregnancy	3
OCP	4
Lifestyle factors (prolonged standing, lack of exercise, chair sitting)	5

Specific factors (Fs)

1. Primary deep vein reflux	1
2. Post-thrombotic syndrome	2
3. Iliac vein compression	3
4. Angiodysplasia	4
5. Lymphatic	5
6. Calf pump dysfunction	6

In practice, this system is applied with the aid of the REVAS sheet which contains a checklist for all the parameters. The REVAS classification is much more comprehensive and was found to be useful for routine clinical practice as well as research studies. The intraobserver concordance of the system was found to be satisfactory, but the interobserver concordance was not uniform [1].

Clinical Presentation and Evaluation

In the REVAS survey, 76.7 % of patients were symptomatic with unsightly recurrent varicose veins, pain, night cramps itching, restless legs, etc. [14]. Detailed evaluation of the patients is very important in planning proper treatment strategy. This should include the following aspects:

- Family and personal history – pregnancy, hormone therapy, h/o superficial/deep vein thrombosis, etc.
- Details of previous treatment – date and type of surgery and postoperative complications.
- Nonsurgical treatment if any – sclerotherapy, phlebotonic agents, compression stockings,etc.
- General examination focusing on any systemic illness, obesity (BMI), and abdominal examination.
- Local examination. The recurrent varices may not follow an anatomic pattern. The CEAP classification should be focused. It is important to document the scars of previous surgery. Any saphenous/sural neuralgia to be noted. Ankle joint mobility and calf muscle efficiency are to be assessed.
- The pedal pulses should be evaluated and ankle brachial pressure index to be noted.
- The symptom severity can be assessed by clinical disability scores.

Investigations in REVAS

Duplex Scan

Currently, this is the gold standard in the evaluation of a patient with REVAS. The advantages claimed are:

- It can precisely define the topographic details.
- It can localize source of reflux from deep to superficial veins.
- The degree and intensity of reflux can be assessed.
- The nature of source as to whether it is the site of original surgery or a different site can be monitored.
- It can also evaluate the perforators and the deep veins.

Varicography

For precise anatomical delineation of the pattern of recurrence, several workers recommend this technique. This is especially useful for the short saphenous system [13].

Other Investigations

These include air plethysmography; ambulatory venous pressure studies; venography, both ascending and descending; and three-dimensional imaging. However, these modalities are not routinely employed. In women with pelvic congestion syndrome, transvaginal ultrasonography to rule out ovarian reflux is very useful.

Treatment

General Measures

Compression Therapy. By below-knee graded compression stocking of the class II type can offer considerable symptomatic relief in compliers. It is important to rule out lower limb ischemia before prescribing compression stockings.

If the patient has an ulcer, it should be cared for as per the prescribed standards. Ambulatory compression therapy is instituted to promote ulcer healing.

Pharmacotherapy: *Phlebotonic Drugs.* The most widely used drug is micronized purified flavonoid fraction (MPFF). Edema and aching pain may be relieved by these agents.

Guided Exercise Program. The objective is to improve the efficiency of gastrocnemius and soleus and keep the ankle joint supple.

Periodic Evaluation and Counseling. Progression of the disease is assessed by frequent clinical examination supported by duplex scan if needed. Patient should be counseled on lifestyle modifications especially control of weight and care of the limb.

Therapeutic Options

Sclerotherapy

Ultrasound-guided foam sclerotherapy is a simple and inexpensive method. The advantages are that it is less invasive and multiple attempts can be tried. The technique is particularly useful when the recurrence does not involve the SFJ or SPJ.

Open Surgery/Endovenous Procedures

Perrin has pointed out three scenarios based on the hemodynamic evaluation of REVAS, when such interventions would be required [1].

- Presence of significant deep to superficial reflux. This could be due to recurrent reflux at SF/SP junction or due to incompetent perforators.
- Presence of axial refluxing varices.
- Presence of reflux in deep veins.

The procedures described below can be undertaken in isolation or in combination and tailored to individual patient needs.

Recurrent Deep to Superficial Reflux

Reexploration of Saphenofemoral or Saphenopopliteal Junction

Reexploration is a difficult undertaking. The problems are distorted anatomy with dense fibrous tissue, presence of friable tortuous venous

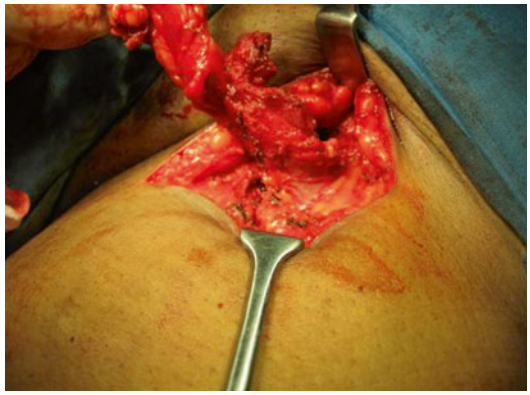

Fig. 10.3 Groin reexploration. Note the dense scar tissue and distorted anatomy

channels, and enlarged groin lymph nodes and lymphatics (Fig 10.3).

To avoid entering the scar tissue, it has been suggested to approach the femoral vein first [15] or to approach the saphenofemoral junction through a higher incision if the previous incision was low [16]. Dodd and Cockett advocated approaching the medial side of the femoral vein and this was adopted by Greaney and Makin [17, 18]. The incompetent saphenofemoral stump is then flush ligated. The guidelines of the American Venous Forum recommends double ligation of the SFJ with nonabsorbable suture but suggest against the use of a patch to cover the saphenous stump [4].

Using a silicone or polytetrafluoroethylene interposition patch showed less recurrence and neovascularization [19], but RCTs have not confirmed the effectiveness of this procedure in preventing neovascularization.

Reexploration of the SP junction is technically a much more demanding undertaking. The abnormal venous anatomy and the limited space make the exploration very difficult. Bleeding from a large number of tributaries can confound the problem. Initial dissection and control of the popliteal vein with meticulous control of all the tributaries and refashioning and control of the previous stump in a slow methodical approach are the keys to success.

Incompetent Perforators

Hemodynamically significant perforators with presence of skin changes would need disruption. The preferred option is subfascial endoscopic perforator surgery (SEPS).

Presence of Axial Refluxing Channels

This can happen when stripping had been avoided or improperly performed. This will result in persistent refluxing channels. The therapeutic options include:

- Stab avulsion and phlebectomy
- Stripping
- Endovenous laser ablation (EVLA) or RFA

Reflux in Deep Veins

Presence of reflux in deep veins especially the popliteal vein is considered to be an important cause of REVAS. In a small subset of such patients, valvuloplasty or axillary segment transfer could be considered.

Follow-Up and Results

Redo surgeries for REVAS are technically very demanding procedures. Complications described include bleeding and hematomas, lymphatic leaks, infections, and recurrence.

Van Groenendael et al. in a nonrandomized prospective study compared the outcome of conventional surgery (149 limbs) and EVLA (67 limbs) for recurrent great saphenous varicose veins. Wound infections and paresthesia were more common with surgery. EVLA group had more perioperative pain and feeling of tightness. At 25 weeks follow-up, the recurrence rate of surgery was 29 % and for EVLA 19 % [20]. The same group reported similar outcome for recurrent short saphenous varicose veins too.

Creton and Uhl reported 93 % closure of saphenous stump with no recurrence by combining US-guided foam sclerotherapy and surgery for recurrent great saphenous varicose veins [21].

Based on the results of these reports, it can be concluded that for the treatment of recurrent varicose veins, endovenous interventions are superior compared to open surgery. The former procedures are less likely to induce wound complications and neovascularization.

Summary

Recurrent varicose veins after surgery are a distressing problem for both the patient and surgeon. The precise definition of REVAS is difficult. The clinical definition proposed at the summit in Paris in 1998 is widely accepted. This includes all true recurrences, residual veins, and veins developing from progression of the disease.

The incidence of REVAS is variable. The factors involved in the pathogenesis of REVAS include tactical errors, technical errors, neovascularization, and progression of the disease. Neovascularization seems to be the main culprit.

Many systems of classification based on varicography, duplex scan, and operative findings are available. But the most comprehensive method is REVAS classification.

Duplex ultrasound scan is the most useful method to evaluate these patients.

Conservative measures along with interventions such as foam sclerotherapy, endovenous ablations, and surgical procedures are the therapeutic options available. The choice would depend on the hemodynamic defect identified in individual patients.

Redo surgery in REVAS is a formidable challenge. Complications such as bleeding, infection, hematoma, lymphatic leak, and recurrence are common. Many surgeons prefer endovenous chemical or thermal ablations over surgery, since these procedures produce less complications and are less likely to induce neovascularization.

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Part III

Chronic Venous Insufficiency and Leg Ulcer: C3–C6 Clinical Class

Chronic Venous Insufficiency and Venous Ulcers: Pathophysiology

11

Subramoniam Vaidyanathan

Contents

Introduction

Progression of a clinical Class 2 venous disease to higher classes is an unpredictable but unfortunate event in the natural history of chronic venous disorders (CVD). It is not an essential event in all patients with CVD. Only a subset of patients go through this process. The triggering factors responsible for this transformation are not well understood. It is a slow degenerative process taking months and years. But when it does happen, the venous reflux which initially commenced in the superficial system extends to involve the deep veins and the perforators. Other symptoms such as edema (C3), venous eczema/lipodermatosclerosis (C4), and ulcers (C5–6) also become prominent. The term, primary chronic venous insufficiency (CVI) or simply CVI, is used to denote this condition. It includes the clinical classes from C3 to C6. Venous hypertension with microcirculatory impairment is the root cause for the clinical manifestations. The intensity of the morbidity associated with CVI was comparable with those seen in congestive cardiac failure and chronic lung disease [1].

There is another category of patients with almost identical clinical manifestations, secondary chronic venous insufficiency, resulting from post-thrombotic damage to deep veins. This is a late sequel of acute deep vein thrombosis (DVT). It is an acquired inflammatory pathology resulting in reflux, obstruction, or a combination of both in the deep veins. Involvement of the superficial

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veins is a late event [2, 3]. It is commonly known as the *post-thrombotic syndrome* and is discussed in detail in Chap. 14. This chapter would focus on the pathophysiology of CVI. The following aspects would be reviewed:

- *Risk factors for ulceration in CVI*
- *The stages and location of the lesions*
- *Structural changes in the veins and other tissues*
- *Molecular events*

Risk Factors for Ulceration in CVI

Venous ulcer is the end stage in the evolution of chronic venous insufficiency. It is reported that venous ulcers affect around 1 % of the population during their lifetime [4]. Considering the prolonged and expensive treatment of venous ulcer, it will be more prudent to prevent the ulcers in the first setting itself. Identification of the risk factors for ulceration in a patient with varicose veins is essential for undertaking any such preventive strategies. Several population-based epidemiological studies focusing on the risk factors for varicose veins are available. Some studies have focused on the risk factors for ulceration in patients with established varicose veins [4, 5]. The etiology of venous ulcer is certainly multifactorial. Some of these may be related to the venous disease per se. A number of disease-unrelated factors are also identified for the causation of ulcers. A brief review of these conditions is presented.

Venous Disease-Related Risk Factors for Ulceration

- *Presence of skin changes* such as lipodermatosclerosis, corona phlebectatica, and dermatitis in a patient with varicose veins aggravate the risk of ulceration [4]. These findings indicate an advanced clinical class of CEAP classification. The extent and severity of the varices were also reported to be significant. Forty-nine percent of patients with ulcer had grade III varicose veins (extensive/severely symptomatic varicose veins – Basle classification), whereas only 33 % of the non-ulcerated limbs had grade III varices [4].
- *Reflux in deep veins* was found to be associated with higher incidence of ulceration. Of special interest is the status of the popliteal valve. Reflux in the popliteal vein is associated with a high incidence of ulceration [4]. In our experience, combined superficial, deep, and perforator incompetence (multisystem disease) is an important factor rather than involvement of an isolated segment. More than 50 % of our patients had reflux involving all the three systems.
- *Failure of the microvenous valves* in the small superficial veins along with degenerative changes in the small vessel network is being identified as a key to the skin changes including ulceration. It has been demonstrated that valvular incompetence can extend even up to the sixth-generation tributaries. Degeneration and valve failure are required at both the larger proximal vessels and the small superficial veins for the development of skin changes including ulceration. This issue is discussed later on in this chapter.
- *DVT in patients with varicose veins* increases the risk for ulceration by 25.7 times [5]. In the study reported by Robertson et al., 28 % of patients with ulceration had a positive history of DVT or pulmonary embolism. The figure for the group without ulceration was 8 % [4]. Varicose veins patients have a slightly increased risk of developing DVT (5.6 %) compared to general population (0.9 %) [6]. Deep vein reflux is a common finding in patients with C3 to C6 classes. Primary valvular incompetence (PVI) is one of the pathologies for such reflux. In this subset of patients, distal DVT are not uncommon below the refluxive valve [7]. Many of these episodes of DVT can be silent and asymptomatic, and these patients can present with late symptom of leg ulceration.

Disease-Unrelated Factors

- *Age and gender*. Generally, venous ulcers are observed at fairly advanced age. The mean

age for ulceration reported in one of the studies was 59 years [5]. For the non-ulcerated group, the mean age was lower by 10 years. In the same study, 60 % of patients with ulcers were men [5]. In contrast, for varicose veins, there is a female dominance. The Edinburgh vein study has also reported a higher incidence of CVI among men [8]. In our series, the mean age of the patients with ulceration was 57.10 years. We have also observed a higher male incidence among our CVI patients; 54.2 % of our patients with CVI were men.

- *Increased BMI*. Obesity (BMI 30 or more) is a significant risk factor for ulceration [4, 5]. But there are conflicting reports on this issue.
- *Cigarette smoking* was associated with a greater risk of ulceration. Those who smoked between 10 and 19 cigarettes per day were 1.8 times more likely to develop an ulcer [4, 5].
- *Prolonged standing* is a significant factor in the pathogenesis of CVD in general. But there is no evidence to show that this increases risk of ulceration [4]. More importantly many patients were found to be sedentary with low levels of physical exercise. Physical activity stimulates the calf muscle pump and reduces the venous hypertension [4].
- *Deficiency of calf muscle pump* function in CVI has been extensively reported. Whether calf muscle pump impairment is the cause or effect of CVI is a debatable issue. This is discussed in detail later in this chapter.
- *Restricted mobility of ankle joint* can contribute to and aggravate calf muscle pump dysfunction. Patients with ulcers demonstrated reduced dorsiflexion of the ankle joint, compared to normal controls [4]. Here again the cause-effect relationship is difficult to establish.
- *Comorbidities*. The incidence of heart diseases, diabetes, and hypertension was higher in the ulcerated group compared to the non-ulcerated group [5]. This could be related to the more advanced age of this group of patients.
- *Associated leg injury*. In one of the published reports, history of major trauma to the leg such as fractures was not uncommon in the group of patients with varicose veins and ulceration [5]. This in turn can be a risk factor for clinical or subclinical DVT. It is pointed out that major trauma to the leg in patients with varicose veins increases the risk of ulceration by 4.7 times compared to those without any major injury [5].
- *Genetic predisposition to venous leg ulcers* is an area of relatively recent interest. In a study conducted in Italian population, Zamboni and group have reported that in patients with CVD, the presence of hemochromatosis C282Y gene mutation consistently increases the risk of developing venous leg ulceration. In post-thrombotic disease, this association was not observed. The authors have recommended testing this mutation to screen high-risk patients of CVD and select them for early interventions to prevent ulceration [9]. Yet another mutation studied extensively was the coagulation factor XIII. But no correlation was observed between mutations of coagulation factor XIII and leg ulceration. In fact, the presence of factor XIII Leu 34 and Leu 564 was associated with smaller ulcer surface area and may indicate a favorable prognosis [10].

Stages and Location of Lesions in CVI

The structural and functional changes in the lower limb venous system alter the normal venous hemodynamics and result in venous hypertension. This is the root cause of CVI [11, 12]. Traditionally, the term venous stasis syndrome was used to describe the changes in the skin and soft tissues of lower leg. This was under the mistaken belief that venous stasis is the primary pathology in these patients. But now, it is well-recognized that venous hypertension is the key factor; CVI is the preferred term rather than venous stasis syndrome. Several stages are identified in the evolution of skin lesions in CVI: [2, 12].

- Corona phlebectatica. This is also known as ankle flare or malleolar flare and is considered to be an early sign of advanced venous disease. It presents as a fan-shaped pattern of numerous intradermal veins on the medial or lateral aspect of ankle and extends toward the

foot. This results from dilatation of the intradermal venules due to the increased venous pressure. The apex of the flare is in relation to an incompetent perforator. The venous hypertension is transmitted through this vessel. It fans out toward the sole of the foot.

- Eczema and pigmentation present as an erythematous dermatitis progressing to blistering, weeping, or scaling eruption of the skin of the leg. This can be associated with brownish dark pigmentation of the skin. The venules are thin walled and cannot withstand the high pressure. They rupture and the blood extravasates into the tissues. The resultant hemosiderin pigments are responsible for the itching and discoloration.
- Venous lipodermatosclerosis (LDS). This is a sign of severe disease and is characterized by localized chronic inflammation and fibrosis of skin and subcutaneous tissue of the lower leg. It can produce fibrosis and contracture of the tendoachilles. The lesion can present as an acute or chronic form; the latter is more common. Pathologically it is a form of sclerosing panniculitis. This lesion is also in relation to an incompetent perforator, and through that it is connected to the main venous systems of the lower limbs. LDS is located over the site of maximum venous hypertension.
- Stage of ulceration. This is a full-thickness defect of the skin commonly located around the ankle region. The ulcer fails to heal spontaneously and is sustained by the CVD. The ulcer is also in relation to the medial calf perforating veins (Fig. 11.1).

These lesions of CVI are typically located in the skin and subcutaneous tissue around the ankle joint, an area known as ulcer-bearing area or gaiter area [12]. This area extends from the lower border of the soleus muscle to the ankle. The impact of the ambulatory venous hypertension is experienced maximally at this site. Several anatomical features make this area vulnerable [12].

- This region is located farthest from the heart and has therefore a high venous pressure even in normal persons. In subjects with CVD, the pressure is further elevated due to the venous pathology.

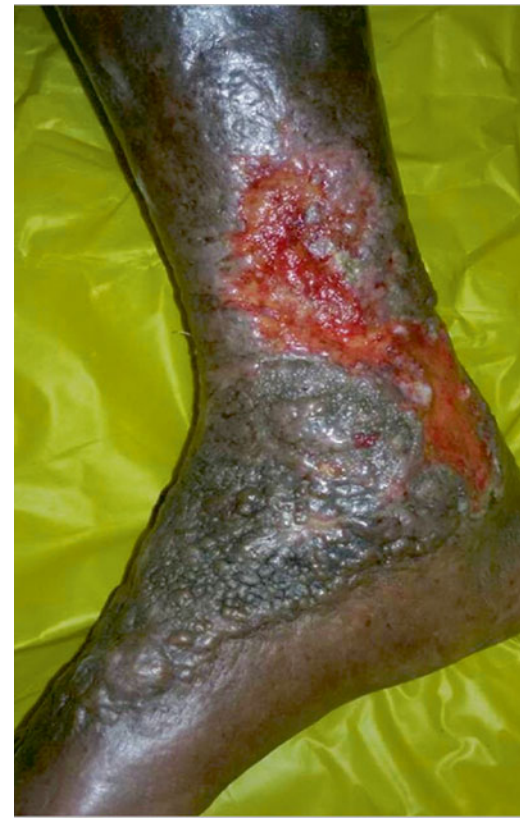

Fig. 11.1 Venous ulcer with lipodermatosclerosis. Fixed ankle joint

- The area has a relatively poor arterial supply.
- The action of the foot muscle pump can produce an extra load in this area. The venous flow in the foot is from deep to superficial veins when the foot muscle pump acts [13–15]. In a patient with defective calf muscle pump, this extra load around the ankle may create a strain.

Structural and Functional Changes in CVI

Failure of the calf muscle pump and impaired venous return from lower extremity generate venous hypertension. It is now accepted that venous ulcer cannot exist in the presence of a normally functioning calf muscle pump. Calf muscle pump function can be adversely affected

in the presence of structural or functional changes in several systems and locations. These locations are enumerated below:

- Reflux in the venous systems
- Nonthrombotic iliac vein lesion
- Changes in the calf muscles
- Changes in the deep fascia
- Ankle joint dysfunctions
- Changes in the lymphatic system

Reflux in the Venous System

Venous reflux is the most consistent structural change observed in patients with CVI. Reflux commences in the superficial veins, and as the clinical class progresses, it extends to the perforator and the deep systems.

Reflux in the superficial venous system is the initial event in primary CVI. Venous ulcers are considered to be rare in patients with isolated superficial vein reflux, but 15.2–20 % of patients had isolated superficial vein incompetence only [16, 17]. Ulceration is commonly observed when reflux exists in both superficial and deep systems. Robertson et al. reported that in 43 % of patients with ulceration, there was combined superficial and deep vein reflux [4]. As already mentioned, CVI primarily and predominantly affects the superficial system [3].

Incompetent medial calf perforators are considered to be an important factor in the genesis of venous ulcer. They can produce a high pressure leak of blood from the deep to superficial vein during the contraction of the calf muscles producing ambulatory venous hypertension [18–20]. An incompetent calf perforator is considered significant, only when the calf muscle pump is defective or when there is pathology in the deep veins [21]. Objective findings of such pathological perforators include outward flow duration more than 500 ms and size equal to or more than 3.5 mm [22]. Incompetent perforators in a C2 class of patient revert to normal when the superficial reflux is eliminated.

Reflux in the deep veins, along with superficial and communicating vein incompetence, is a common finding in patients with venous ulcers (C6 class) [23–25]. Deep vein reflux is seen in less than 10 % in C2 class in comparison to 70 % in C6 class [3]. Two causes are suggested for reflux in the deep veins, the valve theory and the wall theory [26].

The valve theory suggests that reflux results from a thrombotic or nonthrombotic pathology. The most widely identified etiology for the damage and destruction of valves in the deep veins is post-thrombotic pathology. The nonthrombotic cause for deep vein valve failure was first identified and described by Robert Kistner. He coined the term primary vein valve incompetence (PVI) for this condition. In this condition, the valve cusps are stretched and elongated, floating freely in the vein lumen. The two cusps fail to meet and close in the midline, thus permitting reflux [23]. These changes are predominantly located in the proximal segments. Many etiological factors are suggested for this: wear and tear, phlebitis, connective tissue defects, etc. [26]. PVI can develop in the deep veins in discontinuous segments. The failure of deep vein valves may not happen in a sequential ascending or descending fashion [26].

The wall theory: The basic problem here is circumferential dilatation of the vein wall at the level of valve apparatus. The valve cusps are normally formed, but because of the increase in luminal circumference, they fail to meet across and close the vein lumen. Several factors are suggested for this defect. They include phlebitis and defect in the connective tissue framework [26].

Irrespective of the cause, reflux in deep veins impairs the lower limb venous return. In normal individuals, the calf muscle pump along with the competent valves ensures a streamlined, unidirectional cephalad flow in the deep veins. When there is reflux in the deep veins, this is converted into a bidirectional, turbulent, up and down movement – the "yo-yo" effect (Fig. 3.5). The net effect is volume overload leading on to hypertension in the deep venous system. The perforator and superficial systems become incompetent secondary to this overload – the safety valve effect. The crucial factor in genesis of leg ulcer is the status of the popliteal vein valve. When this is competent, ulceration is rare even with extensive disease. On the other hand, incompetence of this valve results

in ulceration. Hence, the popliteal valve is referred to as the gatekeeper [4]. Lim and colleagues have tried to define the precise clinical and hemodynamic significance of deep vein reflux (DVR) while controlling reflux in the superficial system. The study included 3,222 limbs in 2,349 patients using duplex ultrasound, CEAP classification, and venous filling index (VFI). According to them, DVR to the level of the knee and calf is associated with more severe disease irrespective of reflux in superficial veins [25].

Isolated involvement of a single system is extremely rare in clinical practice. According to Raju, multisystem multilevel reflux is more pathological than a single-system single-level reflux [24]. Our experience has been the same; 58 % of our patients had combined reflux in the superficial, perforator, and deep systems.

Reflux in the microvenous valves is now in the center stage. Till recently, it was believed that valves do not exist in veins <2 mm in diameter. This is now disproved. Reflux in the smaller venous tributaries is now recognized as an important factor in the pathogenesis of skin lesions in CVI. Microvenous valves can exist up to the sixth-generation tributaries with the third generation forming the boundary in pathological states. Failure of microvalves is shown to be a key factor for skin changes. Such changes can be present even in the absence of reflux within the GSV or its branches. Macro- and microvessel involvement when combined aggravates the severity of the lesions [27]. Sometimes even with extensive varices, some patients do not develop skin problems. This could be explained by the presence of competent microvalves especially in the third-generation boundary venules. These vessels are inaccessible for surgical intervention. There is robust evidence to show that foam sclerotherapy can obliterate them.

Nonthrombotic Iliac Vein Lesion

Nonthrombotic iliac vein lesion (NIVL) results from extraluminal compression of the left common iliac vein. The vein is compressed at its commencement by the right common iliac artery. This is a permissive lesion which requires another pathology such as trauma, cellulitis, edema, etc., to become clinically manifested. This condition is also known as May-Thurner syndrome and is being increasingly identified in a large number of CVD patients. The pathology can be totally corrected by endovenous stenting [28]. This is the only condition of primary CVI where obstruction of the deep vein is identifiable.

Calf Muscle Changes in CVI

Structural changes in the calf muscles are identified in a number of patients with CVI. The clinical relevance of such findings is not properly understood. Significant functional impairment of the calf muscles was reported by Yang and his colleagues in 1999 [29]. Diminished calf muscle pump function is reported as a risk factor for ulceration in patients with varicose veins [4]. Biopsy and electron microscopic study of gastrocnemius muscle in patients with CVI has demonstrated several structural changes [30]. The changes correlated with ambulatory venous pressure (AVP) findings [30]. A recent study has reported increased calf muscle deoxygenation in patients with CVI [31]. It has been proposed that, rather than the calf muscle impairment resulting from CVI, the poor calf muscle itself may be responsible for pump failure in some patients with leg ulceration [4]. It has been reported that calf muscle pump function and dynamic calf muscle strength improved in a group of CVI patients after 6 months of structured exercise [32]. Such structured exercise program has been suggested as an adjuvant to mainstream treatment in patients with CVI [32].

Changes in the Deep Fascia of the Leg

The deep fascia of the leg has a major role in the calf muscle pump mechanism. Patients who have undergone emergency fasciotomy for traumatic conditions are reported to have impaired calf

muscle pump function leading onto CVI [33]. Similar changes have been reported in a group of patients who have undergone elective fasciotomy for chronic exertional compartment syndrome [34].

Ankle Joint Dysfunction

Limitation of ankle joint movement is a risk factor for the development of ulcers in patients with varicose veins [4]. Two findings noted in patients with nonhealing venous ulcers are restricted movements at ankle joint and calf muscle wasting [35]. The relevance of ankle joint mobility on venous ulcer healing and calf muscle pump function has been emphasized by several workers [36–38] (Fig. 11.1).

Changes in the Lymphatic System

Absorption of interstitial fluid and lymph is markedly disrupted adjacent to venous ulcer bed. Lymphatics were found to be absent in the ulcer bed and were present only sporadically in the intermediate zone [39].

The exact significance of these structural and functional alterations in the different locations is not fully understood. Whether they are the cause or the effect of CVI is also a debatable issue. It is well understood that these changes affect the calf muscle pump adversely and aggravate the venous hypertension setting in a vicious cycle. Correcting these changes would break the vicious cycle and improve the calf muscle function.

Molecular Events in Chronic Venous Insufficiency

The external manifestations of CVI are only the proverbial tip of the iceberg. At the cellular and molecular levels, a complex cascade of events is identified. Lim and Davies [26] and Perrin and Ramelet [40] have reviewed these complex changes, and the following is a summary based on their report.

Venous inflammation is a key factor in producing vein wall and valve damage, leading onto venous hypertension. The venous hypertension in turn causes further damage, setting in motion a self-propagating process. The changes involve the wall and the valves of the macro veins (the superficial and to some extent the deep veins). The changes in the macrovessels affect the microcirculation and finally the target tissue of CVI, the skin over the gaiter area. Thus, one can identify the molecular events at three levels: macrovessels, microcirculation, and dermal tissues.

The changes in the macrocirculation affect the vein wall and the valves. They commence from the venous endothelium. Areas of intimal hypertrophy with increased collagen content alternate with hypotrophic segments, with few smooth muscle cells (SMC) [26, 41]. The extracellular matrix (ECM) proteins are broken down, mostly by the action of the enzyme matrix metalloproteinases (MMPs). Venous hypertension is a stimulus for the upregulation of MMPs. The activity of MMPs is inhibited by several tissue inhibitors of MMPs (TIMPs).

MMP-TIMP imbalance is reported in patients with CVD [42]. The smooth muscle cells become dedifferentiated from a contractile to secretory phenotype and lose their ability to contract [43]. Apoptosis becomes dysregulated. These events result in dilatation and relaxation of the veins along with loss of venous tone. Repeated postural stress from prolonged standing leads to pooling of blood and more distortion of valves, resulting in leakage of blood. The endothelium exposed to flow reversal initiates endothelial and leukocyte activation. This activates the inflammatory response further.

The trigger for all these is an inflammatory pathology. Repeated inflammatory response brings in recurring damage to vein wall and the valves. Several inflammatory mediators are identified in this setting. They include vascular cell adhesion molecule I, intercellular adhesion molecule I, transforming growth factor beta, fibroblast growth factor beta, and vascular endothelial

growth factor. The inflammatory cascade is a self-reinforcing process and damages the valves and affects the remodeling of vein wall.

In *the microcirculation*, venous hypertension increases the hydrostatic pressure leading onto interstitial edema. Leukocyte adhesion to capillary endothelium is promoted by venous hypertension, initiating intense inflammatory response. The inflammation leads onto widening of the gaps between the endothelial cells. The capillary permeability increases facilitating escape of macromolecules and RBCs into the interstitial space. An alternative theory is that there is an active transportation of RBCs and macromolecules through transendothelial channels [43]. Two other contributory factors are lymphatic damage and dysfunction of local nerve endings. Changes in the large veins would in turn produce alterations in the microcirculation and development of microangiopathy [44, 45]. Vincent and his colleagues have reported that failure of microvalves in the third- to sixth-generation tributaries would produce dermal backflow and skin changes, even in the absence of proximal reflux. Presence of reflux in the large veins further aggravates the skin changes [27].

Changes in the skin and dermal tissues over the gaiter area are obvious and visible. The target organ in CVI is the skin and subcutaneous tissues of the gaiter area. Several theories are offered to explain the skin and subcutaneous tissue damages. The stasis theory, the arteriovenous fistula theory, and the fibrin cuff theory have all been negated [43, 46]. The white cell trapping theory was proposed by Coleridge Smith and colleagues [46, 47]. This theory suggests that circulating neutrophils are trapped in the venous microcirculation as a consequence to venous hypertension and dependency of the limbs. The sluggish circulation and hypoxia in turn activate the neutrophils. The activated neutrophils produce tissue damage. Leukocyte activation is a major factor in the pathophysiology of CVI. But neutrophils could not be demonstrated in the capillaries. Hence, the credibility of the Coleridge Smith hypothesis has been challenged.

Pappas and colleagues have extensively reported on the venous microcirculation and endothelial cell characteristics [43, 48]. The dermal endothelial cells in patients with CVI were found to be normal on electron microscopic studies. There were no gaps between the cells. Gaps between the endothelial cells were considered to be the reason for escape of fluid and macromolecules leading onto tissue edema. These workers postulated that there is a transendothelial transportation of macromolecules. The macromolecules and red cells stimulate release of inflammatory mediators. Following this, leucocytes migrate to the interstitial space. Biopsy of gaiter areas in classes 4 and 5 patients revealed dominance of mast cells and macrophages. Lymphocytes, plasma cells, and neutrophils were not present in the perivascular space. Fibroblasts were observed in large numbers. The mast cell enzyme chymase is a potent activator of matrix metalloproteinases 1 and 3. The most characteristic finding observed in the dermal microcirculation in patients with CVI was the perivascular cuff and the accompanying collagen deposition. Originally, the perivascular cuff was thought to be due to fibrinogen extravasation and was erroneously referred to as "fibrin cuff." It is now realized that this cuff is formed by a ring of ECM proteins. These ECM protein cuffs can lead onto altered tissue remodeling and fibrosis. They also stimulate capillary angiogenesis. Pappas and team have suggested that endothelial cells of the dermal microcirculation are involved in the ECM cuff formation. These events are diagrammatically represented in Fig. 11.2a–c.

The cuff does not act as a diffusion barrier to oxygen and nutrients. Immunohistochemical studies have shown that the cuff "traps" TGF-β1 and α2-macroglobulins in its interstices. These trapped molecules are not available for the healing and regeneration of the dermal tissue resulting in altered tissue remodeling and fibrosis. This is known as the "trap hypothesis" [49].

Senescence of fibroblasts as a cause for ulceration was postulated by Hasan and colleagues based on the biopsy study of venous ulcers [50]. Failure to reepithelialize is the main reason for delayed healing of venous ulcers. These workers identified that dermal fibroblasts from venous ulcers are unresponsive to the action of transforming growth factor-β1. This could result from senescence of the cells. This defective response may cause faulty deposits of extracellular matrix which

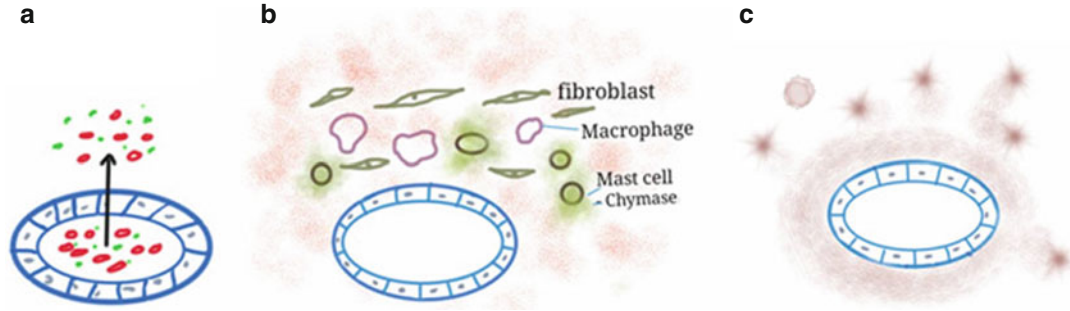

Fig. 11.2 Diagrammatic representation of molecular events. (**a**) Transendothelial migration of RBC and macromolecules. Endothelial cell gap normal. (**b**) Inflammation with presence of mast cell, macrophages, and fibroblasts. Mast cell chymase – activator of MMPS I and III. (**c**) ECM breakdown and formation of ECM cuff

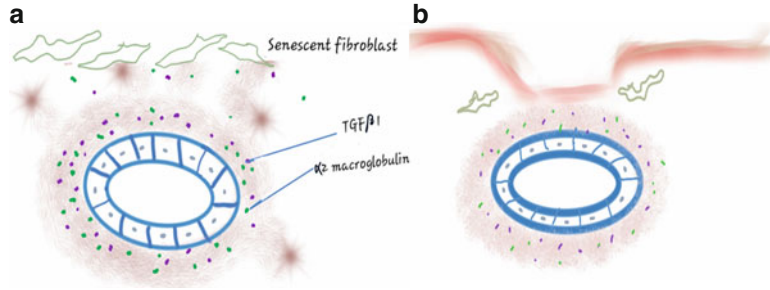

Fig. 11.3 Diagrammatic representation of molecular events. (**a**) Trapped TGF-β and α2-macroglobulin. Senescent fibroblasts. (**b**) Final outcome – chronic nonhealing ulcer

is needed for reepithelialization and wound healing. It was observed that basic fibroblast growth factor, epidermal growth factor, and interleukin-Iβ restored the growth potential of the senescent cells. This observation might imply a therapeutic potential for these factors in CVI [51] (Fig. 11.3a, b).

In conclusion, the microcirculatory events in CVI are a complex interplay of several factors. Venous hypertension is the trigger for these events. Alteration in ECM metabolism from overexpression of MMPs is a key factor along with diminished dermal fibroblast proliferation. Proper understanding of these cellular events can make way for the development of novel strategies for the prevention and treatment of venous ulcer.

Summary

Progression of a C2 clinical class of CVD to CVI is an unexplained and unpredictable event. A patient with varicose veins and leg ulcer is a common problem in clinical practice. The recurrent cycles of healing and breakdown of the ulcer impose considerable fiscal burden and social isolation for the patient. The basic hemodynamic defect in CVI is ambulatory venous hypertension.

Typical lesions of CVI are located over an area around the ankle, known as the gaiter area or ulcer-bearing area. There are specific anatomical reasons making this area vulnerable for such lesions.

Structural changes in the superficial and perforating veins in CVI are well known and easily correctable. Reflux in the deep veins due to valve failure is a finding constantly observed in a large number of patients along with reflux in superficial and perforator veins. Other areas demonstrating functional changes are the calf muscles, deep fascia of the leg, the ankle joint, and the lymphatic system.

A complex cascade of molecular events resulting from phlebitis has been identified. This is initiated by venous hypertension. The molecular events involve the large veins and the capillaries. The final target organ for these is the dermal tissue. A significant defect identified is an imbalance between MMPs and TIMPs.

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Chronic Venous Insufficiency: Clinical Features and Investigations

12

Subramoniam Vaidyanathan

Contents

Introduction

The clinical diagnosis of chronic venous insufficiency (C3 to C6 clinical classes) is relatively simple with the telltale evidence of varicose veins and the dermal changes in the gaiter area. The external manifestations are very often similar in both primary and secondary CVI. Identification of the underlying hemodynamic abnormalities is necessary in making this distinction. History and clinical examination cannot always indicate the nature and severity of the underlying pathology. Detailed diagnostic investigations are needed to sort out these issues. This is an essential requirement since the treatment options are different in the two sets of patients.

This chapter would consider the following aspects:

- Clinical assessment of CVI. Standout symptoms and signs of CVI from a C2 class would be highlighted.
- Rational use of different modalities of investigations in CVI.
- Classification of the disease and assessment of severity.
- The major differences between primary and secondary CVI.

Clinical Assessment of CVI

Clinical examination is the most neglected step in the total care of a patient with CVI. Most often the patient presents with reports of several tests

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performed on different occasions. It is not an uncommon practice among clinicians to make a treatment decision without any clinical evaluation of the patient, based on these reports alone. This is unfortunate. It is well known that the sensitivity of clinical tests for diagnosis of varicose veins is very poor. Bradbury and Ruckley have stressed the importance of clinical evaluation of patients with CVI, notwithstanding the easy availability of duplex and other investigations. According to them clinical assessment is important for the following reasons [1]:

- To guide the choice of investigations
- To interpret the results of the tests more objectively
- To provide direction when investigations reach a dead end
- To avoid over investigating relatively minor problems

Patients with chronic venous insufficiency are much older compared to C2 class of patients, with a long history of CVD [1, 2]. While varicose veins in general are more common in women, several reports have identified a higher incidence of CVI among the male population [2, 3]. In fact we have also noted a higher male incidence for CVI in our series (57 %). *The history* should focus on risk factors for ulceration, any history of previous interventions for varicose veins including surgery. A positive history of DVT can go a long way in supporting the diagnosis of post-thrombotic syndrome. *The common symptoms* include aching, heaviness, leg tiredness, cramps, itching, sensations of burning, swelling, and the restless leg syndrome [4]. Venous claudication is a symptom experienced by some patients with post-thrombotic syndrome. Excruciating pain should alert the clinician about the possibility of arterial insufficiency. Because of the advanced age of these patients, other comorbidities are common. It is very common for the patients to attribute all the symptoms in the leg to the varicose veins which is the most obvious and visible pathology. This can sometimes compel the unwary surgeon to perform an unwanted venous surgery in a patient with musculoskeletal pain or with unrecognized ischemia.

Venous evaluation is carried out in the erect and supine positions. The patient should be examined in the standing position with both lower limbs and the lower abdomen fully exposed. Adequate light is an important requirement. For optimum filling of all the veins, the patient should remain in the upright posture for at least 2 min before the examination is commenced. Inspection of the lower abdomen for presence of any prominent collateral veins is an important step in ruling out venous outflow obstruction. Distribution of varices (GSV/SSV) and their location (AK/BK) and whether unilateral or bilateral are noted. The pattern can be distorted in recurrent varicose veins following previous surgery, endovenous procedures, or sclerotherapy. A bizarre pattern of distribution of varices with or without prominent suprainguinal collaterals is a finding supporting a post-thrombotic lesion. Pattern of varices, truncal, tributary, reticular, and telangiectasia is noted. The dermal changes around the ankle such as edema, corona phlebectatica, and lipodermatosclerosis are the features that separate a CVI patient from C2 class. Of course the most obvious feature is the presence of venous ulcer. The cough impulse test and the Trendelenburg tests can give us information regarding location of deep to superficial reflux. The modified Perthes' test is not very sensitive to assess the deep veins. The clinical evaluation is concluded by confirming the findings with a handheld Doppler.

An important step in clinical evaluation is to palpate the pedal pulses and document the ankle brachial index (ABI) in all patients with CVI. This is especially relevant in elderly patients to rule out coexisting ischemia. Pelvic examination has provided useful information, especially in patients with post-thrombotic syndrome. In the large majority of patients, clinical examination can help to differentiate between primary and secondary CVI.

The Specific Signs of CVI

Eklof and team have highlighted the following specific signs suggesting CVI [5].

Edema of the foot and *ankle* is typically pitting, and extends toward the leg. It is worse toward the evening when the patient experiences tightness of the stocking or footwear. Unilateral edema is most likely to be venous in origin.

Corona phlebectatica is also known as inframalleolar flare or ankle flare and is commonly considered to be an early sign of advanced venous disease. This presents as a fan-shaped pattern of small intradermal veins on medial or lateral aspect of foot in relation to an incompetent calf perforator and results from increased venous pressure [1, 5].

Eczema is an erythematous dermatitis which may progress to blistering, weeping, or scaling eruption of skin of leg. This is located over varicose veins but may be located anywhere in the leg. Usually seen in uncontrolled CVD, it can also be the result of sensitization to topical application of creams and ointments.

Skin pigmentation is a brownish darkening of skin from extravasated blood. This is commonly located over ankle region but can extend to leg or foot.

Lipodermatosclerosis (*LDS*). This is considered to be a sign of severe CVD. This is a localized chronic inflammation and fibrosis of skin and subcutaneous tissues of lower leg. It may be associated with scarring and contracture of the tendo Achilles. This may be preceded by diffuse, painful, inflammatory edema of the skin known as hypodermatitis. LDS should be differentiated from other causes of local inflammatory conditions such as lymphangitis. Signs of acute inflammation such as fever, warmth, and acute tenderness are absent in LDS. This lesion is also related to venous hypertension and is located over incompetent calf perforators [1] (Fig. 11.1).

Atrophie Blanche (*White Atrophy*). This is again a sign of severe CVD and is characterized by localized, circular, whitish, and atrophic areas of skin surrounded by dilated capillaries and sometimes hyperpigmentation. Such lesions are not the result of ulceration and develop independent of ulceration. They should be distinguished from scars of healed ulcers.

Venous Ulcer. The current definition of venous ulcer is as follows [6]: A full-thickness defect of the skin, located in the lower leg, typically with pigmentation and/or skin changes, presence or history of venous disease, documented history of DVT, or documented axial venous reflux or deep vein obstruction and absence of another condition that could be the essential cause of the ulcer. The duration is more than 30 days. When combined with other pathologies, the ulcers are categorized as, "mixed origin." The contribution of the venous pathology in such mixed ulcers should be clearly defined [6]. It is important to rule out other causes of leg ulcers such as ischemia, vasculitis, connective tissue disorders, and trauma.

Late Deformities and Changes in CVI

Ankle Joint Dysfunction. A finding observed in a large number of patients is limitation of dorsal and plantar flexion of ankle joint. This results from extensive fibrosis around the ankle and in turn impairs calf muscle pump function. The relevance of ankle joint dysfunction in the pathogenesis of CVI was discussed in Chap. 10. Therapeutic exercise program designed to improve the movement of the ankle joint is now accepted as an adjuvant to mainstream treatment in patients with CVI [7]. *Equinus deformity of* foot can result from fibrosis and contracture of Achilles tendon (Fig. 12.1).

The champagne glass appearance (narrow ankle and expanded calf segment) is another deformity from fibrosis around the ankle and LDS changes.

Malignant change in venous ulcer (*Marjolin's ulcer*) is an uncommon but dangerous event. The commonest type of malignancy is squamous cell carcinoma; basal cell carcinomas are also reported. The transformation to a malignant pathology is a slow process taking on an average 20–40 years. The lesion can destroy the underlying bone. Diagnosis is confirmed by a biopsy; MRI is the recommended imaging technique. Excision with a surrounding margin of 3–4 cm followed by skin grafting of the defect is the recommended treatment. Nodal involvement is not common because of fibrosis; but if the lesion extends to

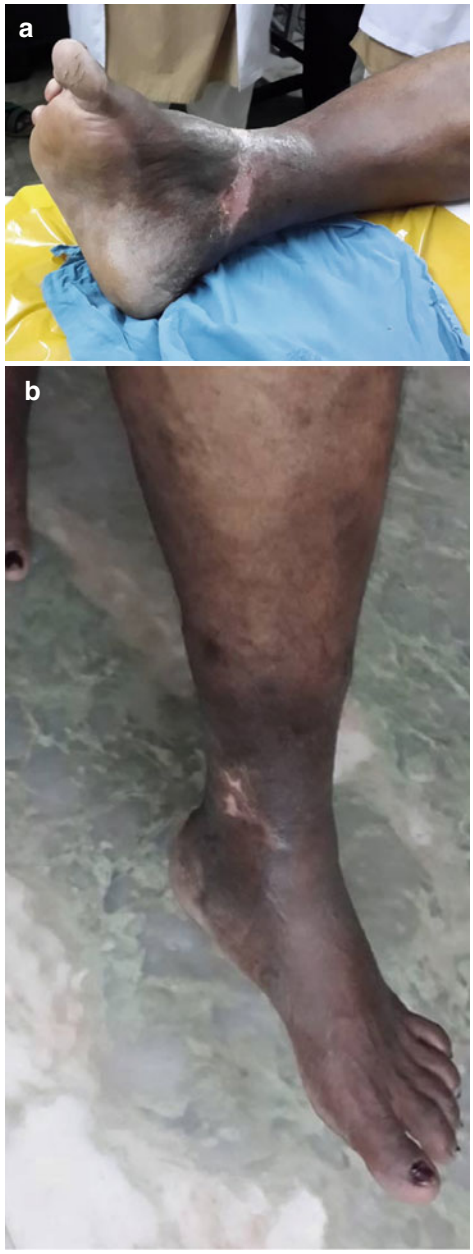

Fig. 12.1 (**a**) Late changes in the foot – equinus deformity. (**b**) Late changes in the foot – champagne glass appearance

involve the normal tissue beyond the margin of the ulcer, regional lymph nodes can be affected. If lymph nodes are involved, lymphadenectomy is recommended. Inoperable lesions are treated by combination of radiation and chemotherapy with 5 FU, cisplatin, and methotrexate [8] (Fig. 12.2).

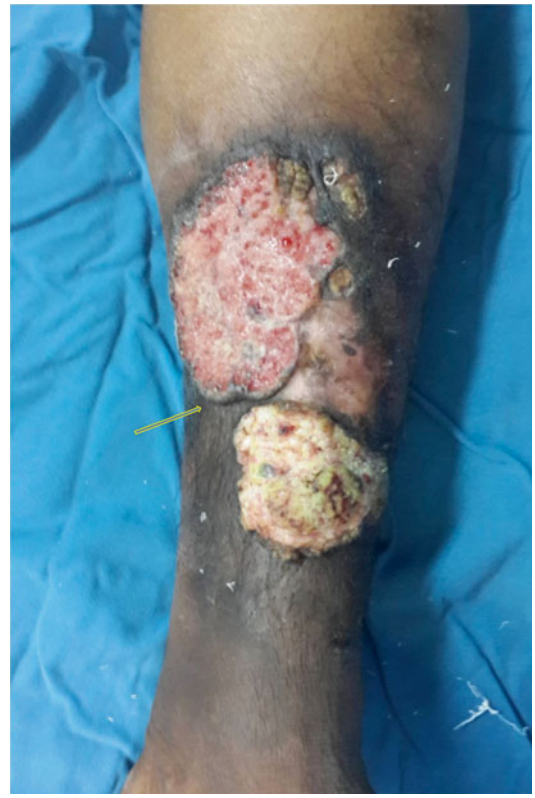

Fig. 12.2 Squamous cell carcinoma in a long-standing venous ulcer (Marjolin's ulcer). The *arrow* points to the everted edge

Chronic Venus Insufficiency: Investigations

The end stage of CVI is the venous ulcer. The defect in a patient with venous ulcer may vary from simple reflux in the saphenous system to extensive structural changes in the deep venous system. The pathology in the deep venous system is strikingly different in the primary and secondary category of CVI. Again a patient with leg ulcer can have comorbidities that can affect wound healing.

The goals of investigations are to clarify the following issues: to identify any systemic illness or factors that can interfere with wound healing, to differentiate primary from secondary CVI, and to identify the specific pathology in primary CVI.

Laboratory Studies

This would include routine hemogram and blood biochemistry. Anemia and diabetes are important systemic factors interfering with wound healing. Leg ulcers can result from multiple causes. These include ischemic ulcers, vasculitic ulcers, rheumatoid ulcers, and numerous other causes. Tests to rule out dyslipidemia, vasculitis, rheumatoid, and autoimmune diseases would be needed in relevant cases. Thrombophilia studies are relevant in patients with post-thrombotic ulcers.

Diagnostic Venous Investigations

An array of tests both invasive and noninvasive are available for the diagnosis of CVD. Some of them are useful in assessment of the morphological changes and others for the hemodynamic alterations. The choice of the investigations should be need based. Based on the severity of the problem and the management strategies planned, three levels of investigation are suggested [5]. Level one investigations include clinical examination and evaluation by HHD. Level 2 investigations include duplex scan along with plethysmographic studies. Level 3 studies include invasive tests such as ascending and descending venography, CT/MR venograms and venous pressure studies, intravascular ultrasound, etc. This approach is useful in optimizing the use of these tests. Patients who are to be managed by conservative methods need only level 1 studies; when superficial vein ablation and perforator surgery alone are decided, level 2 would be sufficient. Patients requiring complex procedures such as valve reconstructions or venous bypass or endovenous stenting would need level 3 tests. Good number of patients with CVI would need level 3 studies. To obtain maximum diagnostic accuracy, it is important that these tests are performed and interpreted by clinicians or technicians who are well versed with venous problems [4].

Duplex Scan Evaluation in CVI

Currently this is considered the gold standard for the evaluation of patients with CVI. Duplex scan combines ultrasound imaging along with a Doppler evaluation. Color coding of the images makes interpretation of reverse flow very rapid and easy. The pulse wave Doppler of a 4–7-MHz linear array transducer is ideal for examination of most of the veins. Reflux and obstruction involving superficial perforator and deep venous systems can be easily identified objectively and precisely localized [9].

Reflux is the predominant finding in patients with primary CVI. Apart from reflux, the morphological distortions of walls of the deep veins and the presence of collaterals would help to differentiate CVI from post-thrombotic pathology (Fig. 12.3). Reflux is confirmed by the use of provocation maneuvers, manual compression, and release or rapid inflation/deflation of cuff. Several workers have standardized the duration of pathological reflux in different venous segments. The current recommendations are as follows: for saphenous, tibial, deep femoral, and perforator reflux, the cutoff is 500 ms; for common femoral, femoral, and popliteal veins 1 s [9–11]. According to Abai and Labropoulos, for the perforators the cutoff time is 350 ms [9]. Nicolaides has summed up the duplex scan findings in CVI patients [4]:

- Multisegment reflux is more common in ulcerated limbs compared to non-ulcerated limbs (75 versus 22 %).
- In two-thirds of patients with CVI, reflux was observed in two or more systems.
- CVI is common when entire length of GSV is affected or when reflux is present in both GSV and SSV.

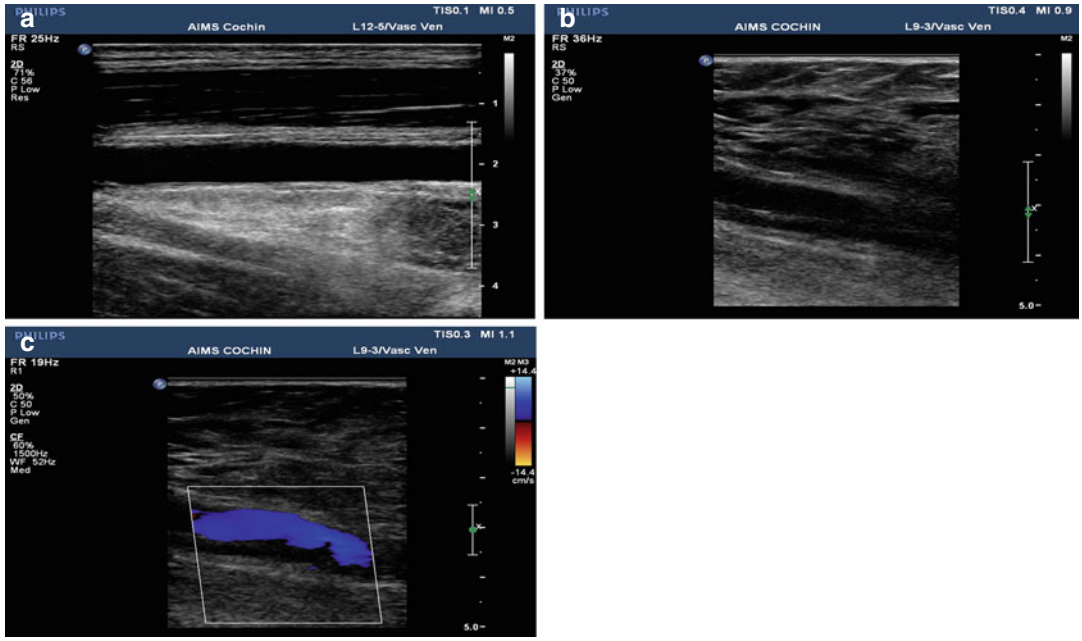

Fig. 12.3 Duplex scan findings in deep veins in primary CVI and post-thrombotic pathology. (**a**) Normal femoral vein showing smooth outline and flow. (**b**) Post-thrombotic vein showing wall irregularity and luminal membranes and filling defects. (**c**) Color coding demonstrating the irregular lumen

- Reflux in the above-knee segments rarely cause ulcer in the absence of obstruction.

Two observations regarding reflux in deep veins in patients with CVI deserve attention. According to Lim and colleagues, deep vein reflux (DVR) to the level of knee and calf is associated with more severe disease irrespective of reflux in superficial veins [12]. The crucial factor in genesis of leg ulcer is the status of the popliteal vein valve. When this is competent, ulceration is rare, even with extensive disease. On the other hand, incompetence of this valve results in ulceration [13].

Duplex scan is helpful to some extent in differentiating between primary and secondary CVI. The morphological features of the deep venous system can be strikingly different in these two conditions. In primary CVI the deep veins are smooth, not scarred, and the lumen is totally free of any irregularities. In contrast, in post-thrombotic syndrome (secondary CVI) the deep vein walls can be irregular, scarred with multiple filling defect (Fig. 12.3). However, in some patients with PTS, the deep veins can still remain unscathed.

In our study of duplex scan in CVI patients, more than 50 % had reflux involving the superficial, deep, and perforator systems. In the deep veins the commonest location of reflux was in the femoral vein (85.41 %) followed by the popliteal vein (41.7 %). In the clinical class C1 to C3, the incidence of deep vein reflux was 27.1 %; in the C4 class it was 31.3 % and in the C5–6 class 41.7 %. All patients had reflux in the superficial venous system.

Plethysmographic Studies

Plethysmographic studies are generally complementary to duplex scans [11]. Photoplethysmography (*PPG*) was used to detect reflux. It is useful in assessing the effect of different modalities of treatment. The technique is not useful in localizing lesions. A more advanced technique, quantitative digital PPG is used to assess calf muscle pump function and venous outflow obstruction [4]. *Air plethysmography* (*APG*) is based on the measurement of changes in the

limb volume by displacement of air in the cuff. It is useful to assess reflux, obstruction, and also evaluation of muscle pump function [4]. This is recommended in the evaluation of patients with advanced CVD, if duplex scan is inconclusive [11]. *Ambulatory strain gauge plethysmography* measures calf volume changes with exercise by using a strain gauge [4]. It is used to assess muscle pump function in terms of reflux and expelled volume [4].

Venography

Contrast venography provides information on the morphology of the venous system. *Ascending venography* was the gold standard investigation but is now mostly replaced by duplex scan. In a patient with CVI, ascending venogram is useful to rule out post-thrombotic pathology [4]. Some surgeons recommend this prior to valve reconstruction in deep veins.

Descending venography was introduced by Kistner to assess the extent of reflux in the venous system. It is performed by cannulating the femoral vein and introducing a contrast media with the patient in the standing position and performing Valsalva maneuver [14]. Depending on the extent of descent in the deep veins, five grades of reflux are identified: grade – 0 no reflux, grade -1 reflux in femoral vein to mid thigh, grade -2 reflux to lower thigh, grade -3 reflux to below knee, and grade 4 reflux to ankle level [4, 14]. Duplex scan has now almost totally replaced descending venogram. But some surgeons routinely perform this before valve reconstruction in deep veins. Another indication suggested is before redo surgery for recurrent varicose veins when duplex scan is not conclusive [4].

CT Angiogram: Useful to evaluate the anatomy of the entire venous system including the pelvic veins and the iliac segment and IVC. It is employed as an imaging modality prior to any intervention, including venous stenting.

MR Venogram: This has the same applications as CT but is preferred in the setting of venous malformations.

Venous Pressure Studies

Ambulatory Venous Pressure Study (*AVP*): AVP studies are primarily aimed at measuring the ability of the calf muscle pump in reducing the pressure in the veins of the leg during muscle contraction. The resting pressure, post exercise pressure, and recovery time are monitored with and without the use of tourniquet [15]. It gives useful information regarding the functional status of the lower limb venous system. It is the best method of assessing venous hypertension [4]. It is reported to be the venous equivalent of the ankle arterial pressure [16]. In our experience, the occlusion effect (the fall in the post exercise pressure after application of above-knee tourniquet) is a sensitive predictor of treatment outcome [15]. Patients with CVI and a prominent occlusion effect are likely to have superficial reflux as the dominant pathology. If the occlusion effect is negligible, multisystem involvement is to be considered. Patients, in whom the post exercise pressure remains high even after treatment, are likely to develop ulcer recurrence.

Foot-Arm Pressure Differential with Reactive Hyperemia: It was considered to be very sensitive in differentiating obstruction from reflux, but currently it is abandoned because a normal study may not rule out obstruction [17]. In practice this test is useful in selecting patients for venous bypass procedure. A bypass is not recommended unless a high arm-foot pressure differential is present [4].

Elevation of Resting Foot Pressure with Valsalva Maneuver: Raju has recommended this as a test to measure reflux in the venous system. But it is not very sensitive [17].

Intravascular Ultrasound (IVUS)

This is gaining acceptance especially to guide interventions. This has a catheter-based ultrasound probe. This is superior to venography in the assessment of iliac segment obstructions. Many apparently normal looking venograms demonstrated significant stenosis on reassessment with IVUS. The technique is especially useful in the diagnosis of nonthrombotic iliac vein

lesion (NIVL – May-Thurner syndrome).Very often an ascending venogram fails to pick up this pathology. Raju and Neglen have reported a high prevalence of this pathology in patients with CVD. Endovenous stenting offers total cure for this subset of patients [18].

Other Investigations

Assessment of arterial circulation is an essential step. Lower limb ischemia can coexist in patients with CVI. Revascularization of the limb should receive priority over treatment of the venous pathology in this setting. Graded compression stockings can be dangerous in the presence of ischemia. An AB index of 0.8 or less should alert the clinician about ischemia.

Biopsy of the ulcer edge is recommended if there is any induration of the edge.

X-ray of the ankle and lower leg has revealed periosteal reaction and irregularity of tibia and fibula in a large number of our patients with long-standing ulcers.

The basic goal of all these investigations is to have a working knowledge regarding the etiopathogenesis of CVI in each patient. This information is necessary in planning a rational treatment strategy.

Classification of the CVI and Assessment of Severity

At the end of clinical and lab evaluation, the next step is to properly classify the disease in each individual patient. The CEAP classification is now universally accepted. For routine clinical practice, the basic CEAP system would be sufficient. The full or advanced CEAP classification is used for research purposes [5]. The clinical stage of the CEAP classification is useful in judging the severity of the CVD for routine purposes. For more objective evaluation, the systems usually considered are: Venous Clinical Severity Score (VCSS), Venous Segmental Disease Score (VSDS), and Venous Disability Score (VDS). Severity assessment and outcome measures are needed for research and publication purposes. Several questionnaires are available to make QoL assessment based on patient-reported outcomes.

Primary and Secondary CVI: A Comparison

There are more similarities than differences between the two groups. In fact many clinicians believe that this distinction is unnecessary. The clinical symptoms and manifestations are almost the same in both groups. Compression therapy is very effective in both groups and is the primary modality of treatment. However, a distinction between the two conditions becomes essential in planning proper definitive treatment. Post-thrombotic disease may need interventions to relieve deep vein obstructions such as endovenous stenting of the iliac segment or bypass surgeries. Prolonged anticoagulation treatment may be needed in some patients with increased risk factors for thrombosis.

Clinical symptoms and signs are useful in a limited way to make the distinction. History of DVT with severe manifestations of CVI is more common in the post-thrombotic group. A bizarre pattern of distribution of varices with suprainguinal collaterals is diagnostic of venous outflow obstruction. The most striking difference is that in the primary type, major involvement is of the superficial veins, whereas in the secondary type (post-thrombotic type), the dominant lesion is in deep veins [19]. Duplex scan in the post-thrombotic group demonstrates scarred, partially occluded, and irregular deep veins with or without reflux [9] (Fig. 12.3).

However, it may not be possible to demonstrate such changes always. In the primary type, reflux is the dominant finding and the intima of the vein is healthy [9]. An ascending venogram

Table 12.1 Differences between primary and secondary CVI

Parameters	Primary venous insufficiency	Secondary venous insufficiency
Basic pathology	Degeneration of wall and valves	Acquired inflammatory
Etiology	Reflux pathology	Obstruction + reflux
Location	Superficial vein involvement	Deep vein involvement
Course	Class progression from C2	Follows DVT
Progression	Slow	Rapid
Intimal involvement	Unaffected	Damaged
Prognosis	Relatively better outcome	Outcome not very good

Adapted from Kistner and Eklof [19]

can also demonstrate the structural changes of post-thrombotic pathology.

Kistner and Eklof have stressed the basic pathophysiological differences between the two conditions. These are summarized in Table 12.1

Summary

Clinical evaluation of a patient with C3 to C6 class follows the same steps as for a patient in C2 class. The diagnostic features of CVI are the presence of the signs of venous hypertension. These include edema, corona phlebectatica, venous lipodermatosclerosis, atrophie blanche, and venous ulcers. Coexisting systemic diseases should be excluded in all patients. It is important to consider other causes of leg ulcers. Particularly relevant is to rule out coexisting ischemia.

Rational choice of investigations from among several tests is important in arriving at a correct diagnosis. Certain investigations provide information on morphology while others provide hemodynamic information. Duplex scan remains the gold standard. It is important that these tests are performed and interpreted by personnel conversant with venous problems. On completion of evaluation, the disease should be properly classified by the CEAP classification. Many methods are available for assessing the severity of the disease.

There is a close similarity between primary and secondary types of CVI. The most important difference is that the former affects the superficial veins predominantly, while the latter involves the deep veins.

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Principles of Treatment of Chronic Venous Insufficiency

13

Subramoniam Vaidyanathan

Contents

Introduction

Chronic venous insufficiency (CVI) is a disabling disease. The clinical manifestations of CVI result from venous hypertension. The primary goal of any treatment for CVI should be to lower and normalize the elevated venous pressure. While healing of ulcers can be achieved relatively easily by observing certain basic principles, the challenge is to prevent recurrence. Till recently, the mainstay of treatment was surgical control of incompetent superficial veins along with the stripping operation. The introduction of newer diagnostic techniques and availability of several treatment options offer multiple choices for the clinician. In this setting of rapid change, clinical practice guidelines would greatly help the clinician in selecting the most appropriate therapy.

This chapter would focus on the general principles in the management of primary CVI. The post-thrombotic syndrome would be highlighted in the next chapter. The areas covered in this chapter are:

- *Conservative measures for control of CVI*
- *Definitive treatment for CVI*
- *Strategies for prevention of venous ulcers*

Conservative Treatment

The conservative measures are primarily aimed at restoring the altered physiological functions of the venous system. These measures include

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elevation of the limb along with supportive measures, care of the ulcer precursor stages, care of the frank ulcer, compression therapy, pharmacotherapy, and structured exercise program.

Elevation of Limb and Other Supportive Measures

It is customary to speak of *four* "*E's*" *in* the management of CVD: elevation, elastic compression, evaluation, and education. *Elevation of the limb* for venous diseases was practiced from ancient times to overcome the effects of gravity. As long as the feet are at or just above the level of the heart (toes above nose position), the venous pressure in the tissues around the ankle falls to nearly zero [1]. In this position, all lesions that are directly related to venous hypertension such as ulcers, eczema, and swelling resolve with no other treatment. Even very large ulcers commence to heal. The effect is so consistent that it can be used as a test to decide whether an ulcer of doubtful etiology is primarily venous in origin [1]. Although limb elevation is a very effective method of reducing venous pressure, it is not always a very practical strategy. It is cumbersome for the patient and is not very cost-effective in terms of lost work hours.

Elastic compression therapy is the primary treatment for venous ulcer. Basically this is an ambulatory form of treatment. Many methods are available for providing compression therapy (CT). The four-layer elastic bandaging (4LB) or the short stretch bandaging (SSB) is the most widely practiced technique. The introduction of graded compression stocking with varying degrees of pressures at the ankle region is a major advance in CT. Intermittent pneumatic compression system (IPC) has a limited role in a subset of patients. *Evaluation* of venous disease is not a one-time event since CVI is not a static problem. It may progress or improve, and the CEAP classification can alter, requiring fine-tuning of therapy. This can be achieved only by frequent reevaluation, clinical as well as duplex scan. *Education* of the patient on lifestyle adjustments is an important aspect in the total care. The strategies would include control of weight, care of the limb, and optimum exercise to keep the calf muscles and ankle joint supple.

Ulcer Precursor Stages

This is an important consideration in the treatment of patients with CVI. The two important lesions before frank ulceration are venous eczema and lipodermatosclerosis (LDS).

Venous Eczema (C4a)

This is an erythematous dermatitis which may progress to blistering, weeping, or scaling eruption of the skin of the leg. It is most often located over varicose veins but can present anywhere in the leg [2]. The condition results from increased venous pressure and may be related to an increase in the expression of ICAM-1 and VCAM-1 on the vascular endothelium in the affected skin. The patients are usually elderly or middle-aged women. The changes are modified by secondary contact dermatitis, infection, and rubbing. Allergic dermatitis and dermatitis medicamentosa are common [3].

The treatment should focus on the primary venous pathology responsible for the venous hypertension. This includes compression therapy and surgical treatment of the underlying venous disease. The local care includes saline soaks for a weeping lesion along with systemic antibiotics if there is infection. Mild topical steroids may be used to relieve irritation. Use of potent steroids should be limited to short periods [3]. Topical antibiotics and antiseptics can cause sensitization of skin. Topical tacrolimus (macrolide lactones – calcineurin inhibitor) has been reported to be effective [3]. Itching is controlled by antihistamine tablets.

Venous Lipodermatosclerosis (C4b)

This is a form of sclerosing panniculitis resulting from chronic venous hypertension. It was believed to result from obstruction to dermal oxygen transport by pericapillary fibrin cuff. It is now realized that the changes result from complex interactions in and around the endothelial cells. The exact

mechanism is not known, but several cytokines, growth factors as well as matrix metalloproteinases are involved. Histologically there is a combination of fat necrosis and lobular panniculitis. There is fibrous thickening of the fascia along with fibrous septae in the subcutaneous tissue. The lesions are typically seen in obese middle-aged women as well-circumscribed indurated plaques over the medial aspect of the leg. It can present in an acute or chronic form. In the acute type which is less common, the plaques are erythematous, painful, and tender. In the more common chronic type, the lesion is skin colored with hemosiderin staining. The intense fibrosis can produce narrowing of the leg [3]. The lesion overlies an incompetent perforator [4]. It can mimic cellulitis in both acute and chronic stages. Unlike an infection, local heat is absent, and there are no features of infection such as pyrexia, leucocytosis, or regional lymphadenopathy [4]. LDS is considered to be very resistant to treatment. Control of the underlying venous disease along with control of obesity and compression stockings is reported to be beneficial. Foam sclerotherapy has an access to the microcirculation and is reported to have a direct effect in obliterating the perforating veins in relation to LDS [5]. Stanozolol, an anabolic steroid, is considered to be effective in both acute and chronic forms [6]. But this drug is banned in many countries. Defibrotide (a profibrinolytic and antithrombotic agent) in a dose of 800 mg/day for 3 months along with compression stockings is shown to reduce the extent of LDS and promote healing of ulcers in post-thrombotic limbs [7]. Topical capsaicin, 0.075 % cream, for 3 weeks is reported to be effective in the acute stage. This deletes substance P and thus reduces nociceptive pain and neurogenic inflammation [8].

Care of Established Ulcer (C6 Clinical Class)

Care of a limb with an established ulcer is a long drawn out process involving several sequential steps. The basic goals are to relieve pain, control the exudates, and promote healing of ulcer. Several sequential steps such as cleaning, debriding, and dressing are all relevant in the care of ulcer. Several types of dressings are used for covering the ulcer. No special advantage was observed for the occlusive type of dressings. Topical antibiotics are not recommended since they can induce reaction of the surrounding skin. G-CSF applied topically is reported to improve ulcer healing according to some workers [9]. It is proper that ulcer care and compression therapy are carried out by a fully dedicated and specially trained team.

Compression Therapy (CT) for Venous Ulcers

Compression therapy is defined as the direct application of external pressure to the limb with the idea of improving the signs and symptoms of CVI. This is considered to be the primary modality of treatment for venous ulcer. It is an ambulatory form of therapy and has replaced the time-honored method of treating venous ulcers by absolute bed rest and limb elevation. CT is practiced in combination with other interventions, and not in isolation. Such a combined approach would improve the outcome and minimize ulcer recurrence [10]. CT can be applied by several methods. Four-layer compression bandage (4LB) is the most widely practiced method. Alternatives include short stretch bandaging (SSB) and compression hosiery. Time taken for ulcer healing with CT is approximately 3 months [11]. CT was found to be effective as an adjuvant therapy to interventions to prevent recurrence [12]. Details of ulcer care and compression therapy are presented in Chap. 15.

Pharmacotherapy of CVI

Several drugs are used for the control of symptoms of CVI. They broadly fall into three classes, venoactive drug (VAD – phlebotonic drugs), hemorheological agents, and antiplatelet agents [9, 13]. The general finding is that pharmacotherapy is effective for relief of symptoms such as edema, pain, cramps, and restless legs. There is

insufficient data in supporting the widespread use of these agents [11]. The most promising agent is micronized purified flavonoid fraction (MPFF – Daflon). The drug has been in clinical use for quite some time. Trials have confirmed the efficacy of this drug in improving symptoms of CVI and promoting ulcer healing [9].

Structured Exercise Therapy in CVI

Therapeutic activation of the calf muscle pump, using a structured exercise program, is now emerging as a management option in patients with CVI. Functional and structural changes in the calf muscles along with diminished mobility of the ankle joint are important factors contributing to the severity of CVI. Two major defects of calf muscle pump function observed in chronic venous ulcer patients include restricted range of ankle mobility and calf muscle wasting [14]. It is reported that the normal range of movement at the ankle is 58°, and in patients with venous ulcers, this is reduced to 28° or less [14]. Padberg and his colleagues have reported on a series of 31 patients of C4, C5, and C6 classes who were offered a supervised regime of exercise along with class II stockings. The authors concluded that physical conditioning to enhance calf muscle strength and ankle mobility improved calf muscle pump function. According to them, direct physical conditioning of the calf musculature may prove beneficial for venous ulcer patients with or without alternative management [15].

Definitive Treatment for CVI

General Considerations

Definitive treatment of a patient with chronic venous insufficiency is a major challenge. The goals of therapy are to promote the healing of ulcer and prevent its recurrence. It is also important to maintain the patient professionally and socially active with minimum lifestyle restrictions. The fundamental issues relating to therapy should be clearly understood by both the patient and the clinician. The therapy can be long and drawn out with periods of remission alternating with symptomatic phases. Surgery or other interventions do not represent the end point of treatment; it is only one stage in the total care of the patient. In fact multiple interventions may be needed to keep the disease under control. Constant surveillance is necessary to track the progress of the disease and fine-tune the treatment. Compression therapy (CT) is the mainstay of treatment. This may be required even after interventions, as long as the risk for ulceration persists. Noncompliance to CT is widely prevalent and is an important cause of recurrence.

Treatment Options and Sequence

Several types of interventions are employed for the treatment of CVI. Surgical interventions include open techniques and endovenous procedures. The nonsurgical interventions include sclerotherapy or interventional radiological procedures such as endovenous stenting. The choice of the procedures and the sequence of their performance depend on the hemodynamic defect identified in individual patients. The basic dictum is that therapy should be tailored to individual patient needs. There is no “one size that fits all” here.

It is important to differentiate primary CVI from post-thrombotic pathology. Clinical features combined with morphological and hemodynamic studies would help to settle this issue. In primary CVI, venous reflux is the dominant finding. Multisystem multilevel involvement is common in classes C3 to C6. The treatment options would depend on the site and location of the reflux. Reflux in the superficial system is the primary and dominant feature [16]. Reflux in the deep and perforator system increases as the clinical class progresses. Deep vein reflux is seen in less than 10 % of patients in the C1–C2 classes. In the C6 class, the incidence of deep vein reflux is 70 % [17]. Reflux in superficial and perforator veins can be eliminated by ligation/ablation of incompetent channels. Reflux in the deep veins

is corrected by reconstructing or replacing incompetent valves in them.

Occasionally, in a small subset of patients, extraluminal compression of the left common iliac vein by the right common iliac artery may become symptomatic (May-Thurner syndrome). Apart from this, obstruction of deep veins is not a common finding in primary CVI, unlike in patients with the post-thrombotic syndrome. In such cases of extraluminal compression, patency can be restored by endovenous stenting or by surgical bypass. The former is the preferred option.

Kistner had suggested total correction of all the three systems as a primary procedure in a single sitting in patients with venous ulcers (C6). This is not widely practiced at present. In many patients, ulcers remain healed for long periods of time even with the less extensive procedure of elimination of saphenous reflux with or without perforator interruption [18]. Valve reconstruction in the deep veins in primary CVI is now performed as a staged procedure in patients with recurrent ulcers after correction of the superficial and perforator incompetence [18]. For May-Thurner syndrome, endovenous stenting with or without elimination of reflux in superficial and deep veins is the primary treatment option [19, 20]. An open ulcer is not a contraindication for intervention [21]. But majority of the clinicians prefer a limb with healed ulcers prior to interventions.

A brief review of the different interventions is presented here. Details are discussed in appropriate sections in the various chapters.

Eliminating Reflux in Superficial Veins

This is an essential step in the treatment, since reflux in superficial veins is the dominant finding in CVI. The guidelines of the American Venous Forum (AVF) recommend correction of superficial reflux along with compression therapy (CT) in patients with venous ulcer (level I A) [12]. Studies have shown that when open surgery for eliminating superficial reflux was combined with CT, recurrence rate of ulcer was significantly low compared to patients who received CT alone [22–24]. Endovenous thermal ablation is now emerging as the preferred treatment option for correction of superficial reflux. In a study of 25 patients presenting with C6 lesions, endovenous thermal ablation by either laser or radiofrequency (RFA) waves improved ulcer healing and minimized recurrence [25]. At present endovenous thermal ablation is preferred to open surgery and chemical ablation for eliminating superficial vein reflux [12] (Level IB).

Elimination of Incompetent Perforators

Treatment of perforating vein incompetence in patients with CVI is a debatable issue. Incompetent perforators in a C2 class patient revert to normal following correction of saphenous reflux [26]. In C6 class, the incompetent perforators are associated with deep vein dysfunction and become pathological. The objective duplex scan findings of such hemodynamically significant perforators include outward flow duration more than 500 ms and size equal to or more than 3.5 mm [12]. Correction of reflux in superficial veins will not normalize them, and hence disconnection of such perforating veins is recommended [9]. The open subfascial ligation is mostly replaced by subfascial endoscopic perforator surgery (SEPS). Good outcome in terms of ulcer healing and low recurrence is reported following SEPS combined with superficial vein surgery.

Correction of Deep Vein Reflux

Several surgical techniques are available for the repair of the incompetent valves in the deep venous system. These include internal valvuloplasty, external valvuloplasty, segment transfer, and axillary vein transfer. There are several methods for creating artificial valves, both autologous and nonautologous. Reconstruction of the valves in the deep veins is usually considered when all the other options for ulcer healing are exhausted. It is not a stand-alone surgical treatment in CVI and is considered as a staged procedure in patients

in whom the ulcer has recurred after saphenous and perforator surgery.

Restoring Deep Vein Patency

Percutaneous endovenous stenting of the iliac vein is the primary treatment in patients with symptomatic May-Thurner syndrome. The outcome after stenting is reported to be excellent even without correcting the coexisting superficial and deep reflux [19, 20].

Treatment Policies: Our Data

Between 1990 and 1995, we had treated 150 patients with primary CVI of classes C4 to C6. Fourteen patients had total correction of all the three systems as a primary procedure (three internal valvuloplasties, ten external valvuloplasties, and one axillary segment transfer to femoral vein along with superficial and perforator surgery). At the end of 2 years, four patients had ulcer recurrence in this subset (28.5 %). One hundred and thirty-six patients had HL/S with perforator surgery by the open technique; in 118 patients, perforator surgery was combined with HL/S, and in 18 it was a staged procedure. Thirty patients in this group of 118 patients developed ulcer recurrence at the end of 2 years (29 %). Valve reconstruction was performed as a staged procedure in the group of patients with ulcer recurrence ($n=30$). Our total number of deep vein valve reconstruction for the entire group was only 44/150 (29 %). Recurrence rate after valve reconstruction at the end of 2 years was very high, 60 %.

Our treatment policy with C6 class of patients has changed substantially after 2000 following the introduction of endovenous procedures and SEPS. Now our policy is to eliminate reflux in the superficial and perforator systems first, either as a combined or staged procedure. The choice between HL/S or endovenous thermal ablation is based on the duplex findings and the preference of the patient. HL/S is preferred in veins with grade iii reflux and localized blow outs such as saphena varix. We have attempted ultrasound-guided foam sclerotherapy (USFS) in a small group of 40 patients with C5 and C6 lesions combined with flush tie under local anesthesia. The midterm results are encouraging. The open technique of subfascial ligation is totally abandoned in favor of SEPS. Patients presenting with recurrence after superficial and perforator surgery are evaluated for any recurrent superficial incompetent channels. USFS or endovenous thermal ablations are useful minimally invasive methods to control such sites of recurrence. Ensuring ankle joint mobility is an important step along with optimum CT. Deep vein valve reconstruction (triple external valvuloplasty) is considered only if all these measures have failed. Since we do not routinely rule out May-Thurner syndrome among our patients with the C6 class, we cannot comment on the prevalence of this problem in our population (Fig. 13.1).

Treatment Outcome: Current Literature

In contrast to a C2 lesion where all interventions have shown to produce considerable improvement in the VCSS and QoL, the outcome in patients with C4, C5, and C6 classes is more disappointing. The literature on this subject is voluminous. A brief cross-sectional analysis is provided below.

- The ulcer recurrence rate in patients undergoing saphenous surgery with postoperative compression therapy (CT) was 12 % at the end of 1 year. When CT alone was employed, the rate was 28 % [12].
- Only few reports on endovenous thermal ablations, in patients with C6 class, are available. In a study of 25 patients with C6 lesion, recurrence of ulcer was observed in only one patient after 6–12 months follow-up, after RF or laser ablation [25].
- The North American SEPS registry reports an ulcer recurrence rate of 28 % at the end of 2 years. The rate was 35 % in the SEPS alone group and 25 % in the group who had SEPS along with superficial vein ablation [27, 28].
- The recurrence of ulcers after deep vein valve reconstruction depends on the technique of

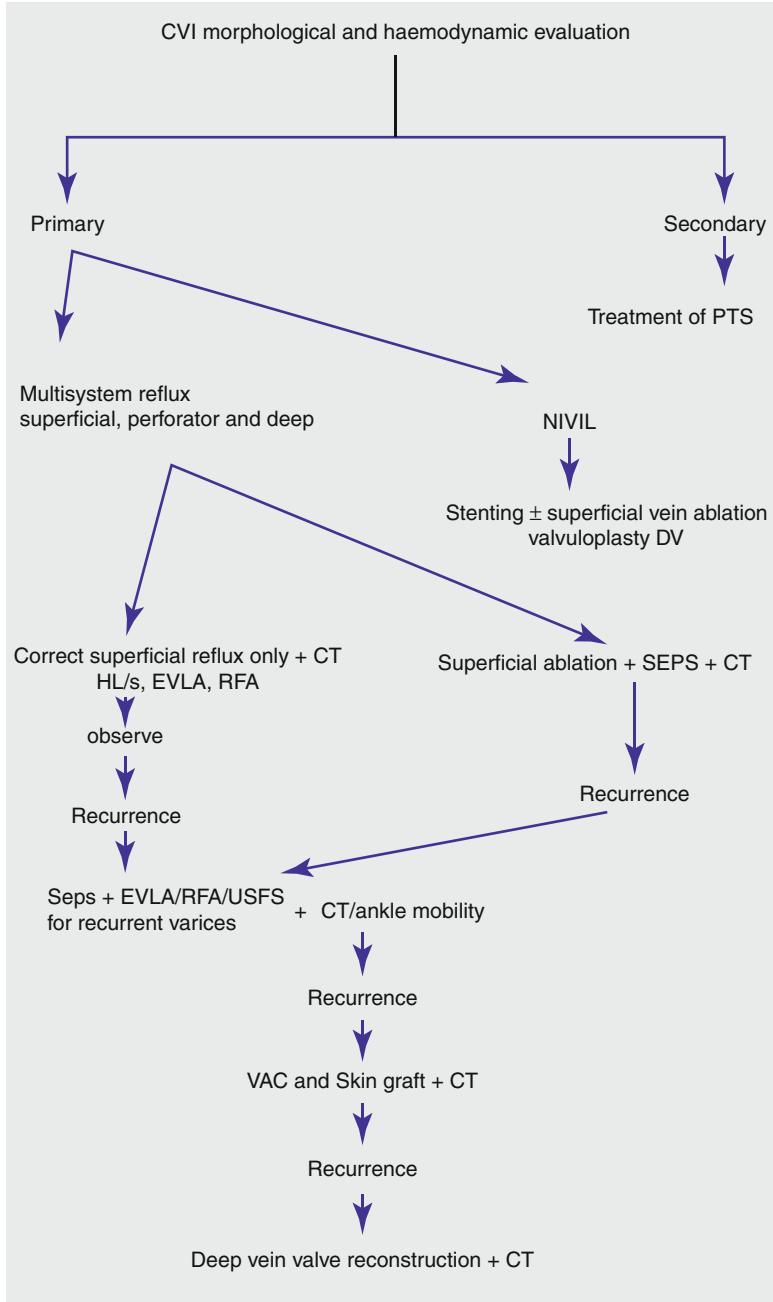

Fig. 13.1 Flow chart for the management of primary CVI

repair, site of repair, and whether single or multiple sites were repaired. It is difficult to provide a standard figure, but the recurrence rate varies from 12 to 50 % at the end of 5 years.

- The cumulative patency rate of 100 % was reported following iliac vein stenting for May-Thurner syndrome after 72 months [20].

Post-interventional Care

There is sufficient data to show that continued use of CT minimizes ulcer recurrence after interventions in a C3 to C6 class patient [12]. This is in contrast to a C2 class, where CT is provided for only 1 week postoperative. For patients with

combined superficial and deep axial reflux, elimination of superficial reflux with continued use of CT is suggested to minimize ulcer recurrence [29].

Occasionally local secondary procedures may be needed in some patients. The procedures used include ablation of recurrent veins, SEPS, skin grafting, and vacuum-assisted closure (VAC), etc. USFS is an extremely useful strategy in the management of recurrence as a day-case procedure. A neglected area is attention to correction of morbid obesity. This strategy can sometimes work wonders [30].

Strategies for Prevention of Venous Ulcers

Treatment of an established venous ulcer is a prolonged and expensive affair. The focus should be on prevention of venous ulcers rather than on the lengthy and costly treatment of established ulcers. The Pacific Vascular Symposium 2009 was convened with the goal to reduce the incidence of venous ulcers by 50 % globally in 10 years [31]. One of the important considerations was to formulate the guidelines for a "standardized chronic venous scan" to bring in uniformity in the assessment of CVD [29]. Three approaches were suggested for reducing the incidence of venous ulcers – identify risk factors for progression of class, prevent/minimize recurrence of established venous ulcer, and focus on certain nonmedical initiatives.

Risk Factors for Class Progression and Preventive Measures

This is a difficult but important consideration. The incidence of progression to CVI from C3 to C6 was 2 % per year [19]. Risk factors identified for such class progression include residual axial deep vein reflux especially popliteal reflux, residual/recurrent superficial vein reflux, and persistent venous hypertension [19, 32]. Feeling of swelling in the limb, corona phlebectatica, mechanical dysfunction of the calf muscle pump, and diminished ankle joint movement are also important. It has been identified that presence of hemochromatosis C282Y gene mutation in patients with primary CVD increases the risk of development of ulceration [33].

Early interventions in high-risk group to prevent ulceration would be a logical step. CT, pharmacotherapy, and endovenous/open surgical procedures have all been tried with this end in view. Studies have not confirmed the effectiveness of any of these measures [19]. Open/endovenous interventions to correct superficial reflux are practiced extensively in C2 and C3 clinical classes. It is reported that 100 patients with varicose veins need to be operated to prevent one ulcer; the number comes down to 10 when limbs with C4 class alone are considered [19].

Prevent/Minimize Recurrence of Established Venous Ulcer

Compression, correction, and surveillance are the three strategies to prevent recurrence of venous ulcers [29]. *Compression* is the primary treatment of venous ulcer of any etiology. Continuation of CT is recommended as long as the risk for recurrence exists [29]. *Correction of reflux and obstruction* is significant in preventing recurrence since these procedures eliminate the basic cause for venous hypertension. *Surveillance* is by constant evaluation to assess the progression of the disease and adopting prompt treatment strategies to prevent tissue damage [29].

Nonmedical Initiatives to Decrease Venous Ulcer Prevalence

These measures are aimed at improving the awareness of the problem by patients and health care personnel [34]. Funding for research in venous ulcer treatment and prevention and establishing a strong central organization to streamline the various activities are effective supportive measures.

Summary

The treatment of a patient with CVI and leg ulceration would need the coordination and cooperation of several disciplines. It is important that the clinician is aware of the proper guidelines in the total care of these patients.

Treatment of a patient with established venous ulcer is a long affair. Ulcer care and CT are the mainstays of management. MPFF has shown promising results in symptomatic improvement and ulcer healing. An emerging strategy is guided exercise program for optimizing calf muscle pump function and improving ankle joint mobility.

Several interventions, surgical and nonsurgical, are available. Proper selection of the optimum procedure and meticulous execution of the same would go a long way in improving the final outcome. The most rational approach would be to prevent venous ulceration in high-risk patients.

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The Post-thrombotic Syndrome: Pathophysiology, Clinical Features, and Management

14

Subramoniam Vaidyanathan

Contents

Introduction

Post-thrombotic syndrome (PTS) is a late sequelae of acute deep vein thrombosis (DVT). It is also known as secondary chronic venous insufficiency (CVI). Considered as an opprobrium of surgery, an aura of therapeutic nihilism surrounds this condition. Patients and physicians believe that no effective therapy exists for this disease. However, significant progress has been achieved in the management of this condition during the last two decades.

This chapter would highlight the following aspects of PTS:

- The definition and incidence of PTS
- Natural history of DVT
- Pathophysiology of PTS

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- Risk factors for the development of PTS
- Clinical features and scoring systems
- Investigations and management

Definition and Incidence

Post-thrombotic syndrome (PTS) is a late complication of acute DVT. It is a sequelae of DVT that occurs despite optimal anticoagulation. Symptoms include pain, heaviness, swelling, and cramping of the leg, aggravated by standing and exercising. Advanced cases present with venous ulceration [1]. A prospective study of patients with the first episode of symptomatic DVT revealed an incidence of 22.8 % after 2 years of the index event, 28 % at 5 years, and 29.1 % at 8 years [2]. It is reported to occur in 25–46 % of patients after anticoagulation alone for acute DVT [1].

Natural History of Deep Vein Thrombosis

Three interrelated events are identified in the natural history of DVT. They are venous thrombogenesis, thrombus organization and recanalization, and recurrent venous thrombosis. The interrelationship of these events is the key factor that determines the genesis of post-thrombotic syndrome.

Venous Thrombogenesis

Rudolf Virchow had pioneered the study of venous thrombosis. He had proposed three factors, Virchow's triad, primarily responsible for genesis of thrombosis: abnormalities of blood flow, abnormalities of blood, and vessel wall injury [3]. At present, biomechanical injury to the vein wall, induced by a pro-inflammatory reaction rendering the endothelium prothrombotic, is considered to be the triggering factor [4]. It is believed that many episodes of acute DVT result from an imbalanced activation of the coagulation system [4]. There is robust evidence to indicate that the cell adhesion molecule P-selectin has a major role in the pathogenesis of venous thrombosis [5]. Once the thrombus is fully formed, an intense inflammatory reaction involving the thrombus and vein wall follows. The natural history of the thrombus and the extent of damage to the vein wall and valves are determined by their response to this inflammatory process [4, 5].

Thrombus Organization and Recanalization

Thrombus organisation and recanalisation are complex events. The process resembles wound healing. The vein wall and in vivo thrombus, both are biologically active and play major roles in the process. An acute to chronic inflammatory response in the vein wall and the thrombus follows [4, 5]. There is an early elastinolysis of the vein wall followed by late fibrosis. This makes the vein wall very stiff and noncompliant. This is further facilitated by increased MMP-2 and 9 activities [4]. Such changes in the vein wall and the valves induced by recanalization are the basis of PTS. The generalized vein wall damage may be more important for the production of PTS than isolated valve destruction [5]. Serial duplex ultrasonographic studies have shown that the faster and more completely a DVT lyses, the less the incidence of PTS [5]. The process of recanalization begins at the point of attachment of thrombus to vein wall. In thrombus adherent to valve cusp, the intense inflammatory changes would involve both the valve and the vein wall [4, 6].

Recurrent Venous Thrombosis

Recanalization of the thrombus is not the only end point of venous thrombosis. As long as the risk for clotting exists (in some patients, the hypercoagulable phase can be prolonged), recurrent thrombosis can develop side by side with recanalization. This event undoubtedly can damage the veins more intensely. Recurrent ipsilateral venous thrombosis is the single most important risk factor in the genesis of PTS. Anticoagulation treatment as per the standard protocol is very effective in preventing recurrent thrombosis. Several factors are identified for the development of recurrent thrombosis. Residual thrombus in the affected vein on ultrasound

scan at the completion of anticoagulant treatment is a major risk factor [4]. The risk of recurrence is maximum during the first 6–12 months after the index event [5]. It is more in patients with spontaneous or idiopathic event or those with unmodifiable risk factors compared to those with transient risk factors [7]. D-dimer levels of more than 500 ng/ml estimated 1 month after completion of anticoagulants are also major risk factor [8].

The following basics tenets regarding DVT are relevant in clinical practice and in the genesis of PTS [1]:

- Obstructive DVT is more injurious than DVT with perithrombus blood flow. The direct contact of thrombus to vein wall aggravates the inflammatory reaction. It is not clear whether the same rule is applicable to valves.
- The longer the thrombus remains in contact with the vein wall, the greater the damage.
- Simple mechanical distension of the vein wall without thrombus cannot initiate the inflammatory changes.
- Leukocyte activity along with several mediators is responsible for the wall and valve changes.
- Thrombus induces changes in the vascular smooth muscle cells from a contractile to a synthetic state. This promotes collagen and other matrix accumulation leading onto increased vein wall fibrosis.

Post-thrombotic Syndrome: Pathophysiology

The late changes in the deep veins following an episode of DVT include valvular damage and reflux, combination of reflux and obstruction, and obstruction alone. The current understanding is that in the majority of patients with PTS, there is a combination of obstruction and reflux [9]. These changes in turn lead onto venous hypertension and clinical manifestations.

Valvular Damage and Reflux

This can be located at two sites: reflux at segments involved by DVT and reflux at uninvolved segments. *Reflux in the involved segment* of deep veins is the commonest finding. Markel and colleagues have noted maximum reflux in segments previously affected by thrombosis [10]. Valvular destruction and reflux are not an inevitable event following clinical DVT. When thrombi are not adherent to valves, they are spared during recanalization [11]. *Reflux in uninvolved segments* is observed frequently. Caps and colleagues have shown that 29.3 % of patients developed valve reflux in segments uninvolved by thrombus in the ipsilateral limb [12]. In many instances, this reflux was transient. The exact mechanism for this is not understood. It may be related to persistent proximal obstruction [4]. Failure to detect thrombus initially may be another reason [12]. The incidence of reflux and its severity are certainly more in the involved segment compared to the uninvolved segments.

Combined Obstruction and Reflux

The most severe forms of PTS result from combination of residual obstruction and reflux, rather than from either anomaly in isolation [9, 13]. Limbs with PTS had more than three times the odds of having combined obstruction and reflux [14].

Obstruction of Deep Veins

The contribution of obstruction of the deep veins in the genesis of post-thrombotic morbidity is often underplayed. The recently introduced technology of intravascular ultrasound (IVUS) has identified a large cohort of CVI patients with significant outflow obstruction that were overlooked on phlebography. The possibility of long-segment wall damage after DVT has imparted further relevance to obstructive pathologies [13]. Apart from frank luminal obstruction, perivenous and vein wall fibrosis and neovascularization are common findings [15]. The fibrosis is more often extensive and macroscopic. In a subset of patients, fibrosis can be microscopic, and the veins may look normal on gross inspection [15].

The extent and severity of obstruction depend on the location of the DVT. Only 20 % of Iliocaval

thrombosis completely recanalize and form a normal and patent lumen [16]. Hence, this segment is the commonest site for the development of post-thrombotic obstructive pathology. In the femoropopliteal segment, approximately 50 % recanalize [17]. Muscular calf vein thrombi involving the gastrocnemius and soleus venous sinuses are considered more benign than axial calf vein thrombosis affecting the paired tibial and peroneal veins [4].

Extensive collateralizations may be observed when there is obstruction. The collaterals could be axial, transpelvic, or ascending lumbar collaterals. An unusual pathology in the iliac segment is the development of a stiff and diffusely narrow segment with no collaterals. This results from intense inflammation of the wall. When the inflammation subsides, a fibrotic cylinder is formed, resisting expansion of the vein and development of collaterals. The term *Rokitansky stenosis* is used for this condition. In such cases, significant outflow obstruction can exist even in the absence of collaterals [18].

In the femoropopliteal segment, following obstruction of femoral vein, the profunda femoris vein undergoes significant dilatation. This happens in a subset of patients, and this change is described as *axial transformation of the profunda femoris vein*. The profunda may be mistaken for femoral vein. Patients with axial transformation of the profunda can develop extensive skin changes [19].

Risk Factors for Post-thrombotic Syndrome

An understanding of the different factors that make a patient vulnerable for the development of PTS is relevant in the overall management strategy. They can be broadly classified into nonspecific and specific factors.

Nonspecific Factors

Age and gender. Several workers have reported advancing age and male gender as a risk factor for development of PTS [20–22]. *Body mass index* (*BMI*). There are several reports of association of higher BMI and PTS [1, 20, 22–25]. *Blood group and incidence of PTS*. Incidence of PTS is reported to be higher in "A"-positive blood type [26].

Specific Factors: Relating to Thrombosis

Location of thrombus. Reports regarding the difference in the frequency of PTS in proximal and distal DVT are conflicting and confusing. The consensus is that the incidence of PTS is greater following proximal DVT [1, 27, 28].

Duration and intensity of anticoagulation. Standard anticoagulation treatment is very effective in preventing recurrent thromboembolism. Incidence of PTS was low when anticoagulant treatment for the index episode was adequate in intensity and duration [1, 21, 24].

Recurrent thrombosis. According to the currently available evidence, this is the most powerful predictor of PTS [1, 20, 27]. The risk of PTS is reported to be six times greater among patients with rethrombosis [1]. Residual thrombus on follow-up ultrasound scan after completion of anticoagulation treatment is a marker of increased recurrence [7].

Nature of initial DVT. There is no evidence to support a higher incidence of PTS in patients with unprovoked DVT compared to those with associated risk factors [20]. Patients who have significant symptoms 1 month after DVT are at greater risk for PTS [1].

Thrombophilia and PTS. There is no evidence to indicate that the risk of PTS is greater in patients with thrombophilia [1, 20, 29]. Factor V Leiden is not a risk factor [29].

D-*dimer level* has been used to monitor thrombus activity and identify patients at greater risk of PTS [1, 27, 29]. Values higher than 500 ng/ml at 1 month after withdrawal of oral anticoagulation is reported to be an independent risk factor for recurrent DVT and greater possibility of developing PTS [8].

Henke and his group have recommended a "DVT-PTS risk prediction score" based on the features of acute DVT. The parameters considered are *symptom severity*, *etiology*, *anatomy*, *and pathology* (*SEAP*) [30].

Clinical Features

The clinical presentation of patients with PTS is similar to those with primary CVI. The similarities often outweigh the distinctions. Many believe that the distinction is not very essential, since compression therapy is the primary modality of treatment for both conditions [31]. But the basic pathology of the two conditions is totally different, and the differentiation of the two conditions is relevant in selecting rational treatment programs. Clinical features that lead one to suspect PTS are as follows:

- *Past history of DVT* may not be available in a large number of patients. Thirty percentage of DVT may be silent [9]. *Thrombophilia* should be excluded in young patients, recurrent thrombosis, thrombosis at unusual sites, and those with positive family history of DVT.
- *Symptoms include* heaviness, pain, swelling, itching, cramps, paresthesia, and bursting pain. Typically, symptoms are worse on standing and walking and are relieved with rest and recumbency [20]. Edema, itching, and ulceration are distressing symptoms. Generally, the intensity of all symptoms is much more severe than primary CVI.
- *Venous claudication* is a symptom considered typical of PTS patients with persistent obstruction to iliocaval segment. Characteristically, the patient experiences severe pain and a feeling of tightness over thigh on vigorous exercise [32]. In contrast to claudication from arterial disease, venous claudication needs 15–20 min of rest with limb elevation for relief [32]. In addition to pain, the patient can also develop cyanosis, further swelling, and dilatation of superficial veins of thigh [32]. The pathology rests in the collaterals, which bypass the obstruction. In patients with chronic iliofemoral venous occlusion, the collateral vessels offer a high resistance to venous outflow from the lower limbs [32]. This is prominent at rest but becomes significantly elevated following exercise when there is an increased arterial inflow. This will result in a substantial increase in femoral venous pressure which takes a long time to normalize [32]. This is the pathogenesis of venous claudication. In a series of 39 patients with chronic iliofemoral venous obstruction, 43 % developed venous claudication on follow-up for 5 years. In 15.4 %, the pain was severe enough to force cessation of walking [33].
- *Clinical signs include* marked swelling and edema and a bizarre distribution of varicose veins, not conforming to any anatomical pattern. Very often superficial varices may not be very prominent, and the SF and SP junctions will be competent. Distended supra-inguinal and anterior abdominal wall collaterals are a telltale sign of venous outflow obstruction (Fig. 14.1).

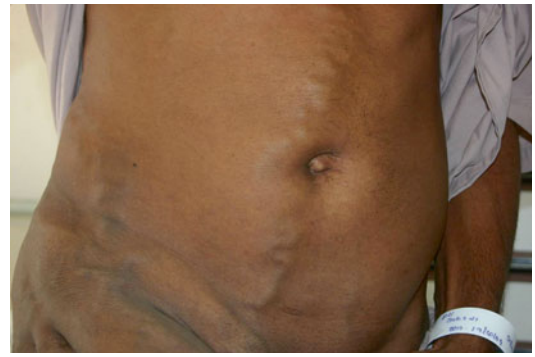

Fig. 14.1 Venous outflow obstruction showing prominent distended veins in the anterior abdominal wall and supra-inguinal collaterals

Specific features of CVI such as corona phlebectatica, eczema, lipodermatosclerosis, and atrophie blanche have already been described in an earlier chapter. Venous ulcers are the final event. They can be multiple, large, recurrent, and difficult to heal (Fig. 14.2).

Late deformities such as fixed ankle joint, equinus deformity, and champagne glass appearance are all suggestive of a chronic smoldering pathology.

Differential Diagnosis

Usually the diagnosis of PTS is quite evident from history and clinical examination. Several clinical situations may mimic PTS.

- *PTS vs. primary CVI*. The primary treatment in both is to provide external CT. A matter of

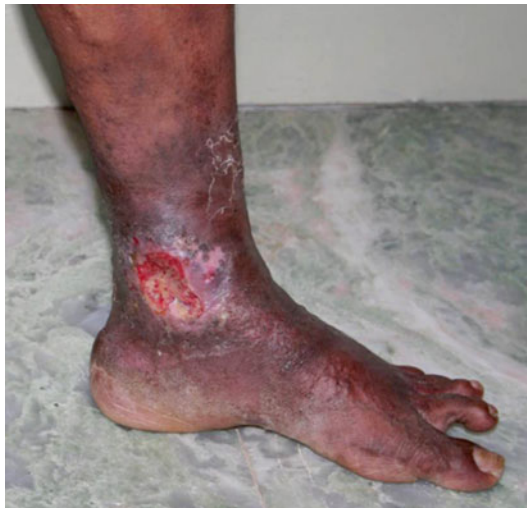

Fig. 14.2 Post-thrombotic ulcers

concern is the need for long-term anticoagulation in patients with hypercoagulable state. The distinction is relevant in considering patients for endovenous stenting.

- *Combined arterial and venous insufficiency*. This is not uncommon in elderly persons, hence the need for arterial evaluation in all patients beyond 40 years, presenting with PTS. Arterial pathology should receive the priority of treatment in such settings [9].
- *Conditions that mimic PTS would include* [9] ruptured Baker cyst, rheumatoid arthritis, AV malformations of calf muscle, and drug reactions with pain and skin changes.
- *Other causes of leg ulcer* are to be ruled out.

Scoring Systems

Two specific diagnostic tools were developed for confirming PTS and for identifying the severity of the condition: the Villalta standardized scale and Ginsberg measure.

The Villalta Scale

This was conceived by Prandoni and introduced in 1994 to clarify the severity of PTS. It is a disease-specific assessment in the evolution of PTS [34]. It is composed of *five symptoms* (pain, cramps, heaviness, pruritus, and paresthesia) and *five signs* (pretibial edema, induration of the skin, hyperpigmentation, new venous ectasia, redness and pain during calf compression) in a graded scoring system. Each has a 4-point scale starting from 0 (absent) to 3 (severe) [35]. A score less than five is not diagnostic of PTS. Two consecutive scores of five to fourteen indicate mild to moderate PTS. A score of fifteen or more in two checkups or presence of ulcer on one occasion indicates severe PTS [35]. Villalta score system is simple and easy. It is standardized and validated. It can track the progress of the disease, and it can be applied in clinical settings and in research areas [1].

The Ginsberg Measure

This is based on the persistence of symptoms or development of new symptoms 6 months after the index DVT. In comparison to the Villalta scale, the Ginsberg measure identifies more severe cases of PTS [35]. The criteria recommended for the Ginsberg measure are as follows [20, 35–37]:

- Persistent swelling and leg pain for 1 month after DVT
- Pain and swelling developing 6 months after DVT
- Above symptoms aggravated by standing and walking
- Relieved by rest and elevation

In a comparative study of the two systems, agreement was found to be poor [37]. The proportion of patients diagnosed to have PTS was almost fivefold higher by the Villalta scale than by the Ginsberg measure. It has been concluded that the Ginsberg measure identifies more severe forms of the diseases [37].

The Venous Clinical Severity Score (VCSS)

This was introduced by the American Venous Forum for assessment of CVD. This has also

been used for the severity assessment of PTS [35]. This was validated along with duplex and hemodynamic parameters. VCSS was also compared with the Villalta scale. It has been concluded that VCSS could be useful for the screening of PTS [34, 35].

The CEAP System

This is useful in defining any CVD including PTS. It is a static measure, and does not address QoL issues or functional status [1].

In a single-center prospective study of 40 legs in 34 patients with PTS, Lattimer et al. observed that the Villalta scale had a good correlation with VCSS and CEAP classification. But when venous filling index (VFI) was used as a hemodynamic benchmark, the Villalta scale was superior to the other parameters [38].

Investigations

The objective of investigations is to localize the disease and assess the severity. Both anatomical and hemodynamic studies are relevant in this situation. As already mentioned, reflux and obstruction can coexist in PTS.

Duplex Scan

This is the baseline investigation in most centers. The obstructive changes observed in duplex scan are very characteristic. The deep veins are echogenic, are contracted, and have thick irregular walls. There could be multiple channels, intraluminal webs, and wall thickening. Presence of dilated collaterals indicates obstruction; but their absence does not exclude it [39]. A vein seen one centimeter away from the artery is usually a collateral [39]. Reduced or absent phasicity on duplex scan is an indirect evidence of obstruction. Duplex scan cannot quantify obstruction [9].

Duplex scan is very useful for assessment of reflux. The recommended cutoff value for reflux is 500 ms [39]. Valve closure time and peak reflux velocity have been tried as a measure of quantifying reflux using duplex scan; but they are found to have poor correlation with the severity of reflux [9].

The limitation of duplex scan is that it cannot be used in isolation. It cannot grade reflux properly. It is not sensitive in evaluating the iliac segment [9].

Hemodynamic Studies

Obstructive pathologies can be diagnosed by hemodynamic tests. But they are not very accurate. The tests include plethysmographic outflow determination and hand-foot pressure differential. These tests are not very sensitive. Femoral venous pressure measurements are more objective. Findings suggestive of obstruction are prestenotic pressure rise in supine position more than 2–4 mm of Hg on provocation, slow return to base level (more than 30 s), and a pressure differential more than 2–5 mm of Hg compared to contralateral limb [18].

Reflux can be diagnosed by hemodynamic tests. Several techniques are available. They include *air plethysmography* (*APG*), *strain gauge plethysmography* (*SGP*), *and photoplethysmography* (*PPG*). The refill time is a reflection of reflux, and the use of tourniquet can localize the reflux to different segments. Plethysmography is complementary to duplex scanning.

Venogram

- *Ascending venogram*. This is useful to provide a road map for infrainguinal lesions. An important finding in femoral vein block is axial transformation of the profunda femoris vein. The profunda functions as an important collateral pathway in femoral vein occlusion. On account of contrast dilution, visualization of IVC and Iliac segments would be poor with ascending venogram [9].
- *Transfemoral venogram*. This is preferred for assessment of iliac and pelvic venous lesions. However, the sensitiveness of venogram in

confirming iliac vein occlusion is only 60 % [9]. Absence of collaterals need not rule out an obstructive pathology as in the case of Rokitansky vein.

Intra Vascular Ultrasound (IVUS)

This is considered to be the most sensitive tool for the diagnosis of vein pathologies [9]. It can pick up both intra- and extraluminal pathologies. The procedure is strongly recommended prior to iliac vein stenting.

Ambulatory Venous Pressure (AVP)

This gives an overall assessment of the functional status of the lower limb venous system. The parameters monitored are the drop in the post exercise venous pressure and the recovery time. However, the technique is cumbersome and time consuming and is mostly used as a research tool [40].

Management

Treatment of a patient with a fully established PTS is a difficult and prolonged process. Several impressive newer strategies are available for this condition. Despite these measures, the outcome of therapy may not always be bright. The priority should be in preventing the development of PTS.

Prevention of Post-thrombotic Syndrome

A brief review of the various measures useful to prevent the development of PTS is presented below.

Prevention of DVT in Clinical Practice

The strategies for this would involve risk stratification and appropriate prophylactic measures, pharmacological or mechanical.

Optimum Treatment of Established DVT by Adequate Anticoagulation

Optimum anticoagulation therapy in established DVT can minimize risk of PTS [21]. It has been postulated that size of the thrombi becomes small with adequate anticoagulant therapy. Such mini-sized thrombi cannot induce valve damage or obstruction [36]. In high-risk patients with DVT, long-term anticoagulation can minimize recurrent DVT and reduce the incidence of PTS.

The two markers to identify patients who need long-term anticoagulation would be the presence of residual thrombus in duplex scan 1 month after completion of treatment and high level of D-dimer (500 ng/ml) 1 month after anticoagulant treatment [1].

Active Thrombus Removal

Direct contact of the thrombus to vein wall is known to aggravate the "biomechanical injury" [1]. Also, the longer the thrombus remains in contact with the vein wall, the greater the damage [1]. Naturally it is reasonable to assume that early thrombus removal would reduce the risk of PTS. This could be achieved by catheter-directed thrombolysis, surgical thrombectomy, and combined pharmacomechanical therapy [35]. These procedures have not percolated down to routine widespread clinical practice. When therapeutic strategies of early thrombus removal is successful, PTS will be avoided or minimal [1]. However, there are no randomized trials to confirm this finding.

Early Ambulation and Use of Compression Therapy for Acute DVT

Early ambulation along with leg compression with below the knee stockings (ankle pressure 30–40 mm of Hg) in patients with acute proximal venous thrombosis is reported to reduce the incidence of PTS by 50 % at the end of 2 years. There was no increase in the incidence of PE [1]. The beneficial effect of early ambulation and compression was confirmed by a study reported by Partsch and colleagues [41].

Treatment of Established Post-thrombotic Syndrome

The basic principles of treatment are the same as primary CVI as outlined in the earlier chapter. The ulcers of PTS are more resistant and prone for recurrence. It is important to rule out coexisting arterial insufficiency in all these patients.

Care of the Skin and Ulcer

The treatment strategies are the same as mentioned in the earlier chapter.

Compression Therapy

CT is still the traditional and primary method of treatment for all venous ulcers including PTS. In the presence of an active ulcer, a supervised program of ambulatory compression therapy using bandages, in dedicated clinics, can produce good outcome. The details and techniques are presented in Chap. 16. CT using *compression hosiery* is an alternative. The use of below the knee elastic stockings with ankle pressures of 30–40 mm of Hg would minimize the severity of PTS [1]. *Intermittent pneumatic compression* (*IPC*) is reported to be useful in the treatment of venous ulcers refractory to previous ambulatory compression alone [42]. A new therapeutic approach in severe CVI with reflux is to use an *external valve closure compression pump*. This pump can generate intermittent pressure peaks synchronized with calf pump. The device can be specific for the degree of reflux and size of the leg [43]. CT should be continued as long as the risk of ulceration persists.

Pharmacotherapy

Several agents are available for improving symptoms and promoting ulcer healing in patients with CVI. But none of them are specific for the treatment of PTS. Two agents which are promising are *micronized purified flavonoid fraction* (*MPFF*) *and pentoxifylline* [1, 44]. *Statins* are known to protect the endothelium from cardiac events [1]. A randomized trial has proven that rosuvastatin in a dose of 20 mg a day significantly reduces the incidence of DVT [45]. It is not known whether statins will reduce the incidence of PTS [1].

Definitive Treatment

Correction of anatomical defects by open surgery or endovenous interventions has been attempted in treating patients with PTS. Barring stenting all other interventions employed in the treatment of PTS are of secondary importance only [46].

The indications for surgical/endovenous interventions in PTS are as follows:

- Chronic iliac vein occlusion – an indication for endovenous stenting [46]
- Failure of conservative therapy [47]
- Recurrence of PTS symptoms [47]
- Young patients with significant stasis symptoms and signs [47]

Endovenous Stenting for Chronic Iliac Vein Occlusion

In properly selected patient, this technique in isolation provides optimum outcome even without correction of the associated reflux in deep veins [9]. Valve reconstruction in deep veins can be undertaken in recalcitrant cases and those in whom stents have failed [9]. Concurrent ablation of incompetent saphenous system and iliac vein stenting are reported to have better outcome in a set of patients [48]. Patients with long-segment stenting and those with poor inflow are at high risk of stent failure [1]. The primary, assisted primary, and secondary cumulative patency rates for iliac vein stenting for thrombotic lesions were 57, 80, and 86 %, respectively [49]. One of the technical issues is the development of frequent

in-stent re-stenosis and the need for frequent re-interventions. This is because the currently available stents are not specifically designed for the venous system. Development of dedicated stents for the venous system including modular systems for the iliocaval confluence would further improve outcome [43].

Venous Bypass Surgeries

These procedures are considered in patients with stent failures, unsuccessful stenting, and long-segment occlusions where stenting may not be feasible [47]. They are technically more demanding and would need long-term anticoagulation. Patency rate can be improved by establishing an arteriovenous fistula [47]. The procedures include *cross-over* (*Palma*) *bypass*, the in-line femoroiliocaval bypass with stented graft, the *Husni bypass for femoropopliteal occlusions*, and *the perforator bypass for infragenicular obstruction*. The results of these open procedures are not very encouraging.

Endophlebectomy

Partial obstruction of post-thrombotic veins is caused by endovenous scar tissue that creates synechiae and septae. *Endophlebectomy* involves removal of endoluminal synechiae and masses, with preservation of as much of the intimal surface of the vein as possible. Hence, technically it is different from arterial endarterectomy. In a report on 23 venous segments (from iliac to tibial segments) in 13 patients, a primary patency of 77 % at the end of 8 months has been documented after endophlebectomy [50].

Correction of Deep Vein Reflux

Patients with the most severe forms of PTS have a combination of reflux and obstruction in the deep veins [9, 13, 14]. Stenting of the iliac segment is preferred over valve reconstruction in such situations [1]. Raju considers valve repair in the PTS patients as a "last ditch salvage effort" [15]. Transcommissural repair is suggested if there is no gross damage to the valve apparatus [9]. Axillary vein segment transfer would be the procedure of choice in many cases [17]. The post-thrombotic vein can be disobliterated by endophlebectomy, if necessary to make a suitable anastomosis [15, 50]. Several methods are available for the creation of artificial autologous valves in PTS. The most promising results are reported for the *Italian valve of Maleti*. These are bicuspid/monocuspid sheaths dissected out from the intima and media of the thickened post-thrombotic vein wall. They can be fashioned as valves and can function effectively [51].

Generally the outcome of valve repair in the PTS group is much less impressive compared to the primary CVI group of patients.

Elimination of Superficial Reflux

Ablation of the superficial veins to eliminate reflux in them in patients with PTS and chronically obstructed deep veins was condemned in view of the potential collateral function of these vessels. However, it has been postulated that an incompetent saphenous system would aggravate the burden, and extirpation of these would improve the hemodynamics in them [52]. A single-stage iliac segment stenting with ablation of the incompetent saphenous system provides significant clinical and hemodynamic improvement [48]. Superficial reflux can be eliminated by HL/S or by endovenous ablation.

Elimination of Incompetent Perforators

The role of perforator surgery in PTS is not clearly defined. However, with the introduction of SEPS, there is a renewed interest in this area. In a recent report from the Mayo clinic, in a series of 88 SEPS performed in 81 patients, excellent rates of ulcer healing was reported for patients with primary CVI. The outcome in the

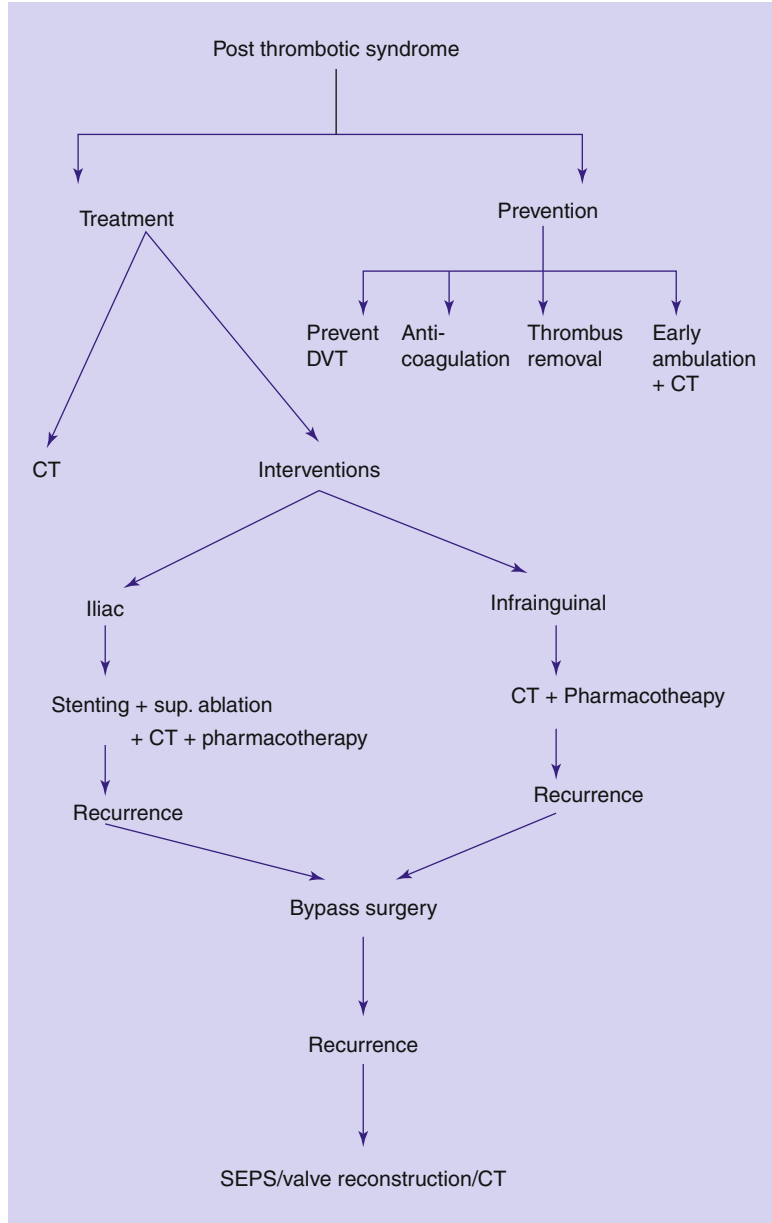

Fig. 14.3 Flow chart for management of PTS

post-thrombotic group was less impressive. At the end of 1, 2, and 5 years, freedom from ulcer recurrence for the primary CVI group was 98, 94, and 85 %, respectively; the figures for the post-thrombotic group were 90, 78, and 50 % [53]. Active smoking has been identified as a risk factor for recurrence [53].

The management strategies are summarized in Fig. 14.3.

Summary

Post-thrombotic syndrome, a late complication of DVT, can impose considerable burden on the patient and the society. It follows a complex interaction between the in vivo thrombus and the vein wall, releasing a number of inflammatory mediators. The final events could be valve damage leading onto reflux in deep veins or

obstruction. Patients presenting with the most severe forms of PTS have a combination of reflux and obstruction.

The most widely accepted risk factor for development of PTS is ipsilateral recurrent thrombosis. This can be identified by persistent thrombus on duplex scan after anticoagulation therapy and elevated levels of D-dimer.

Clinical features result from venous hypertension. Several scoring systems have been evolved to identify the severity of the problem. The most widely accepted system is the Villalta standardized scale. Several modalities of investigations to assess reflux and obstruction are available. For diagnosis of iliac vein occlusion, intravascular ultrasound (IVUS) is supposed to be the most sensitive test.

Several strategies are available to prevent or minimize the severity of PTS. Treatment of established PTS is a major challenge. Several newer methods of treatment are now available. Compression therapy is still the primary modality of treatment, but patient compliance is notoriously poor. Pharmacotherapy with MPFF is reported to improve symptoms and promote ulcer healing. Percutaneous endovenous stenting with or without ablation of the saphenous system is the treatment of choice in patients with chronic iliac vein occlusion. This has almost totally replaced open surgery.

Valve reconstruction in selected patients may be effective, but the results are not as good as in patients with primary CVI. Ablation of incompetent perforators is a debatable issue in the treatment of PTS.

The future tasks in this area would include evolution of newer pharmacological agents, development of dedicated venous stents, and development of non-thrombogenic, non-immunogenic, and flexible implantable venous valves.

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Care of Ulcer and Compression Therapy

15

Subramoniam Vaidyanathan

Contents

Introduction

Care of the ulcer and compression therapy (CT) are the least glamorous but pivotal considerations in the total care of patients with chronic venous insufficiency (CVI). The standard of care for venous ulcers varies widely over different countries and even in different centers in the same country. In this chapter, the standard and ideal care which is feasible on fiscal and logistic grounds would be reviewed.

Ideally, care of the ulcer and CT are undertaken in clinics fully dedicated for such purposes, by trained health-care personnel. This approach would go a long way in improving the total care of these patients. There are many key areas in these services which may be overlooked by an untrained team.

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This chapter would highlight the following aspects:

1. The definition of venous ulcer and the differential diagnosis of leg ulcers
2. Sequential steps in the care of venous ulcer including an overview of different dressings
3. Principles of CT
4. Methods of applying CT in practice
5. Application of multilayer bandaging
6. Complications of CT
7. Alternatives to CT

Local Care of Venous Ulcer

The currently accepted definition of venous ulcer is a full-thickness defect of the skin, located in the lower leg, typically with pigmentation and/or skin change; presence or history of venous disease, documented history of DVT, or documented axial venous reflux or deep vein obstruction; and absence of another condition that could be the essential cause of the ulcer [1]. The duration of the ulcer is accepted as 30 days or more [1]. Venous ulcer is one of the commonest causes of leg ulcer, but there are many other causes also. So it is relevant to differentiate venous ulcer from other pathologies.

Leg Ulcers: Differential Diagnosis

There are many causes for leg ulcer. The common conditions in clinical practice would be considered in some detail [2].

Venous ulcers are located over the gaiter area (area between the distal edge of soleus muscle and the ankle). Varicosity of lower limb veins is a constant finding. They are usually painless unless complicated by secondary infection. The floor contains granulation tissue which may be pale or pink with or without slough. The surrounding skin would demonstrate eczema and features of lipodermatosclerosis. The edge of ulcer is sloping with a thin blue line of growing epithelium.

Ischemic ulcers are commonly located over the forefoot and are painful. The floor is covered with pale granulation. Absence of extremity pulsations would further support the diagnosis. It is important to rule out a *combined ulcer*, having both venous and ischemic components, especially in elderly male patients. Such lesions are designated as ulcers of mixed origin [1]. The venous component may or may not play the dominant role in them. It is important to clearly define the role of each component in this setting.

Diabetic ulcers are observed in patients with long-standing diabetes and are associated with neuropathic changes. They are typically located over the plantar aspect of foot, heel, and leg.

Squamous cell carcinoma is the commonest type of neoplastic ulcer and is easily suspected on clinical examination.

Traumatic and infective ulcers are more often acute in onset.

Some of the less common causes of leg ulcers are discussed below.

Rheumatoid ulcers are very recalcitrant and are typically observed in patients with the classical features of severe rheumatoid arthritis. It is believed to result from breakdown of a subcutaneous nodule. Ulcers are located over lower third of leg and may be single or multiple. They are shallow punched out and are painful lesions.

Vasculitic ulcers are a group of diseases characterized by inflammatory damage to blood vessels. Cutaneous ulceration is common in small- or medium-sized leukoclastic vasculitis (broken leucocytes on microscopy). Ulcers are common in the acute phase of vasculitis. They present as multiple painful purpuric spots in the leg. The overlying skin turns black and the lesions ulcerate. The antineutrophil cytoplasmic antibodies (ANCA) are elevated.

Hypertensive Ulcers (*Martorell Ulcer*). This is a rare condition observed in patients with prolonged and severe hypertension that is improperly controlled. The ulcers are located over the leg above the ankle and are extremely painful. They contain black necrotic areas. The distal pulses are usually normal. They are secondary to increased vascular resistance from hypertensive arteriolar spasm leading onto tissue ischemia. Histopathological study demonstrates concentric intimal thickening and marked hypertrophy of media of small- and medium-sized arteries. Proper control of hypertension,

local wound care, and pain relief are the important principles of treatment. Since beta-blockers can induce peripheral vasoconstriction, they are best avoided.

Table 15.1 sums up the essential features of common ulcers in clinical practice.

The workup would include all the relevant investigations to rule out these conditions. A duplex scan is the gold standard for the confirmation of vascular (arterial or venous) origin. Combined with ankle brachial pressure index, this will help in differentiating arterial and venous pathology. Blood sugar estimation, rheumatoid factor, ANA and ANCA, and biopsy of ulcer edge would help to rule out other common pathologies.

Once the venous origin of the ulcer is confirmed, a well-defined strategy is essential in the overall care of the patient. Ideally, the management should be undertaken in dedicated centers where the personnel are trained for such care. This is more so when CT is combined with ulcer care [3, 4].

The size of the ulcer should be documented on first encounter and subsequently every month. A simple method is by serial digital photography. Smearing the edge of the ulcer with povidone-iodine solution and taking an imprint on a clean graph paper can be a precise method of assessing the surface area of the ulcer.

Sequential Steps of Ulcer Care

The following steps are important in the care of the ulcer. The dressing techniques should be clean and is aimed at preventing cross infection. Strict asepsis is not necessary [3].

1. *Cleaning the ulcer* should be kept as simple as possible. The ulcer can be washed with tap water. No advantage was observed by using sterile saline [4]. The surrounding skin can be washed with a mild soap.
2. *Debridement* can be carried out, if necessary by sharp excision, to reduce the necrotic tissues. But trials have not demonstrated faster healing following debridement [3]. No special advantage was observed with other methods of debridement such as chemical or autolytic agents [3]. Hydrogel and an enzymatic dressing are alternatives to surgical debridement [4].
3. *Biopsy of the ulcer edge* is recommended when there are atypical features such as rolled or raised edge [3].
4. *Topical application* aimed at controlling infection and promoting wound healing is a debatable issue. *Bacterial swabbing and culture* is not routinely needed unless there are evidences of clinical infection [3]. Topical antibiotic applications are best avoided because they can sensitize the skin; same thing holds for topical agents containing lanolin [3]. Topical antimicrobials such as silver-based wound dressings are recommended by some workers [4]. There are conflicting reports regarding the efficacy of topical application of growth factors [3]. *Systemic antibiotics* should be limited to the treatment of obvious infections of the ulcer or surrounding skin such as presence of systemic signs, peri-wound cellulitis, foul odor, or gross purulent discharge [4].
5. *Ulcer dressings*. Generally wound dressings are of three categories: passive (nonocclusive), interactive (semiocclusive and occlusive types), and active (biological types) [4]. *The passive dressings* (*nonocclusive dressings*) protect the wound from trauma and potential infection. An example of nonocclusive dressing is dry gauze with pad and bandage. The *interactive types of dressings* maintain a moist warm wound environment and help to control the amount and composition of wound exudate. They also reduce heat loss and water evaporation. They may be semiocclusive or occlusive type. The common types of semi occlusive/occlusive dressings include hydrocolloids, hydrogels, films, foam, and alginates. *The active or biologic dressings* may be living human dermal equivalent (LHDE), platelet products – autologous or recombinant and growth factors (epidermal growth factor; GMCSF, etc.).

   There is no ideal dressing material for venous ulcers. *The saline wet-to-dry gauze dressing* is a simple and popular form of dressing. It functions as a semiocclusive dressing as long as it is wet, but when it becomes dry, it changes over to nonocclusive

Table 15.1 Common types of ulcers and their features

Type of ulcer	Location	Basic pathology	Pain	Number	Ulcer features	Associated findings	Diagnosis
Venous ulcer	Gaiter area	Venous hypertension	Not prominent	Usually single/ multiple can occur	Sloping edge; floor pink granuln	Varicose veins; eczema and LDS	Duplex scan
Arterial ulcer	Forefoot	Ischemia	++++	Single/multiple	Pale floor	Cold extremity; absent pedal pulses	ABPI less than 1; duplex scan
Diabetic ulcer	Sole of foot; heel	Multifactorial; neuropathy	+/−	Single/multiple	Extensive sloughing and local tissue damage	Sensory, motor, and autonomic neuropathy	Hyperglycemia and local features with slough and tissue loss
Rheumatoid ulcer	Leg	Autoimmune	+++	Multiple	Ulcerated nodule	Poly arthritis	Rheumatoid factor; ESR elevated
Vasculitic ulcer	Leg	Multifactorial/autoimmune	+++	Multiple	Shallow multiple, surrounding skin black	Systemic features fever, joint pains, and stomach upset	ANA; extractable nuclear antigen (ENA) and ANCA

type [4]. No extra benefits were observed between the occlusive and semiocclusive dressings [3]. The use of human skin equivalents or the growth factors has not reported to confer any extra benefit [3].

The frequency of dressing changes would depend on whether CT is combined or not and the amount of exudate. Along with CT, the frequency would be once or twice weekly. More frequent change of dressings would be needed if the exudate is heavy. If not combined with CT, dressings could be changed daily or on alternate days.

6. *Management of pain*. Venous ulcers are generally considered to be painless unless complicated by infection. In the event of severe pain, it is important to rule out other causes of ulceration especially ischemia. Fifty percent of pure venous ulcers can be painful [3]. In such situations, an opioid analgesic would be useful. Promoting healing by CT can reduce pain considerably. Pain can be precipitated during dressings, debridement, and other interventions. The use of Eutectic Mixture of Local Anesthetic (EMLA) as a cream is recommended in such situations [4].
7. *Skin grafting for venous ulcers*.
   Split-thickness skin grafting should be considered for large ulcers requiring extended time to heal. Pinch graft is considered better since it can be carried out as a day case without hospitalization [4].

Along with the local treatment measures, it is important to provide optimal general nutritional support for these patients.

Compression Therapy for Venous Ulcers

Definition and General Considerations

Compression therapy (CT) is defined as the direct application of external pressure to the limb with the idea of improving the signs and symptoms of chronic venous insufficiency. This is the primary modality of treatment in patients with venous ulcers. It is an ambulatory form of therapy and has replaced the time-honored method of treating venous ulcers by absolute bed rest and limb elevation. CT is practiced in combination with other interventions, and not in isolation. Such a combined approach would improve the outcome and minimize ulcer recurrence [5]. The time taken for ulcers to heal with CT is approximately 3 months [6]. Noncompliance is the stumbling block in the effective execution of CT.

In simple terms, CT works by squeezing the limb, thereby reducing the edema and aiding venous return toward the heart. The main effect of compression is to lower the venous pressure. The optimum external pressure required to achieve therapeutic effect is debated. It has been demonstrated that in the erect position, an external pressure of 35–40 mm of Hg can narrow the leg veins. When the pressure exceeds 60 mm the veins are occluded [6]. From this, it has been deducted that the effective external pressure for compression would be 35–40 mm of Hg. A safe upper limit of sustained pressure would be 60 mm of Hg [6]. Compression therapy provides several beneficial effects on the venous system, microcirculation, and the lymphatic system [7, 8].

1. *It improves venous pump function*.
2. *It improves microcirculatory hemodynamics favoring resolution of edema*.
3. *The levels of inflammatory mediators such as vascular endothelial growth factor and tumour necrosis factor alpha, responsible for tissue damage in CVI, are lowered by compression*.

Not all patients with CVI respond to compression therapy. The nonresponders include elderly and obese patients, patients with combined venous and arterial ulcers, and those with large ulcers and with multiple recurrences [6].

Methods of Providing Compression Therapy

There are several methods for providing CT. The common methods used in clinical practice include the following [6]:

1. *Compressive bandages – multilayer bandaging*
2. *Compression stockings*

3. *Intermittent pneumatic compression* (*IPC*)
4. *Unna's paste boots and velcro – band devices* (*legging orthosis*)

The most popular and probably the most effective method among these would be CT by multilayer bandaging. This technique will be described in detail.

Compression Therapy by Multilayer Bandaging

Multilayer bandaging is the most widely practiced technique of CT. For a proper understanding of compression therapy, the clinician should be familiar with the various types of bandages and their properties.

The Properties of Bandages [5]

There are several properties for a bandage. A working knowledge of these is necessary in choosing the appropriate materials for providing CT. *Tension* is the amount of force applied to the bandage during application. This is supported by the elastomeric properties of the materials used. *Extensibility* is the ability to increase in length (stretch) in response to an applied force. *Power* is the amount of force required to cause a specific increase in length. *Elasticity* is the ability to return to original unstretched length when the tension is reduced. *Stiffness of bandage* is defined as the increase in pressure applied per centimeter increase in leg circumference [6].

Classification of Bandages

The simplest method of classification is based on the degree of in vitro extensibility of the bandage [6]. This decides their ability to maintain a predetermined level of compression. Based on this property, two types of bandages are recognized: inelastic bandages and elastic bandages.

The inelastic bandages are of two types:

1. The rigid bandage. Type I bandage; retention/conforming bandage – extensibility 0–10 %
2. The short stretch bandage. Type II bandage/supporting bandage – extensibility is 10–100 %

The elastic bandages. Type III; *long stretch/compression bandage – extensibility over 100 %*

Another system of classification is also popular [8]. The details are provided in the following table (Table 15.2).

Dynamics of Compression Therapy

1. *Sub-bandage Pressure*. This is defined as the amount of pressure exerted by the bandage on the tissues. This is calculated by the *Laplace's Law*: Pressure = $N \times T \times 4{,}620/C \times W$

   N = number of layers applied; the more the layers, the greater the pressure.

   T = bandage tension; the greater the force, the greater the tension.

   C = limb circumference; the smaller the circumference, the greater the pressure.

   W = width of bandage; the narrower the bandage, the greater the pressure.
2. *Resting Pressure*. This is the sub-bandage pressure with the patient in the supine position.
3. *Working Pressure*. This is the higher peaks of pressure developing during exercise, such as walking, with the bandages on.
4. *Static Stiffness Index* (*SSI*). This is the difference between supine and standing pressures measured at B 1 point (medial aspect of leg where gastrocnemius tendon turns into muscular part) [9, 10]. A higher stiffness indicates relative inelasticity of the bandage.

Table 15.2 Classification of bandages

Type of bandage	Use
Type I	Retention/conforming bandage
Type II	Light support bandage
Type III	Compression bandage
III A	Light – 14 to 17 mmHg
III B	Moderate – 20 to 40 mmHg
III C	High – 40 to 60 mmHg
III D	Extra high – over 60 mmHg

Adapted from Hopkins and Worboys [8] and Moneta and Partsch [6]

(The long stretch bandage has an SSI less than 10 mm while the short stretch has a value more than 10 mm. It is now known that the SSI is maintained when multiple layers of elastic bandage are applied over each other.)

The Long Stretch (Type III/Elastic Bandage)

This can exert a high resting pressure. But it changes shape with the limb when edema resolves or when the muscles contract from within. Hence, the working pressure does not peak much [8]. The high resting pressure is sustained till 1 week. Long stretch bandages are easy to apply but the high resting pressure induces a feeling of tightness [6].

The Short Stretch (Inelastic/Type II Bandages)

Their stretch is caused by the weave of the bandage. Since type II bandage cannot change shape with the limb, the sub-bandage resting pressure is low in the supine position. When the patient walks, the increased pressure exerted by the muscles from within is resisted by the stiff bandage. This results in high working pressure. This increased pressure is redirected back to the deep veins, squeezing them better and improving the venous drainage [8]. When edema subsides, the bandage cannot conform to the smaller limb size and so it becomes loose. Frequent reapplications may be needed till the edema has resolved. It is useful for patients who have bandage-related pain at night because it cannot exert a high resting pressure [8]. Calf muscle pump function can be improved with this bandage because it exerts a higher working pressure. Overcompression is rare. Loss of bandage pressure after application and the cumbersome application techniques are drawbacks [6].

It is not recommended to apply high compression with a single elastic compression bandage since it can produce considerable pressure damage [6]. Several layers of elastic bandages applied over one another will reduce the elastic property and make it increasingly inelastic [8]. The same is true when two stockings are applied over each other or if several components of different materials are used. This effect results from increased friction between the different layers, which opposes the expansion of the limb [6].

Initiating Compression Therapy Using Bandages

Multilayer bandages are much superior to single-layer compression [8]. The advantages of the multilayer system are sustained compression for longer period of time, uniform distribution of pressure, and better absorption of exudates. The sub-bandage pressure can be measured by several instruments [10]. Based on the interface pressure measured at B1 point, compression systems can be light, moderate, high, and extra high (See Table 15.2). The usual practice is to provide a pressure around 40 mm of Hg at the ankle.

The Compression Systems and Components

A compression system is an aggregation of several parts which jointly provide the required pressure support. Each member of the system is called the *component* [5]. This can be orthopedic wool, a layer of inelastic supporting bandage, or one or more layers of elastic cohesive or noncohesive bandages (Fig. 15.1).

Usually a system consists of either long stretch or short stretch components. Certain systems have combined both components. It is recommended to use the term component than the term layer [5]. In practice, the two most popular systems are four-layer bandage (4LB) compression system and short stretch bandage (SSB) compression system [9]. The former is more popular and would be considered in some detail.

The Four-Layer Bandage Compression System

This is a multicomponent *elastic system* and provides a high compression of 35–40 mm of Hg at ankle, for patients with ankle circumference

Fig. 15.1 Components: four-layer bandaging. (*1*) Orthopedic wool, (*2*) supporting bandage, (*3*) type 3A elastic bandage, (*4*) type 3B cohesive elastic bandage

ranging from 18 to 25 cm [5]. This was developed by a clinical group at Charing Cross Hospital, London, and is known as *the Charing Cross Hospital Bandage* [2, 11]. The components of the system include padding (orthopedic wool), a crepe bandage (inelastic) to provide a support for compression, and two layers of mild to moderate elastic compression bandages [5].

The Pre-bandaging Workup

1. Detailed history and clinical examination including evaluation of arterial system.
2. Correcting ankle skin changes.
3. Recording the ABPI. A reading of 0.8 or more is acceptable for CT [12].
4. Measurement of the ankle circumference. The general guidelines are suitable for ankle size of 18–25 cm [8, 12]. The technique needs to be modified if the ankle measurement is less than 18 or more than 25 cm [8].
5. Assessment of limb size and shape. In limbs with altered shape, there is increased risk of unequal pressure distribution, slippage of bandage, and higher risk of pressure damage. Reshaping of the limb can be achieved by padding with foam or orthopedic wool [5, 8, 12]. Slippage of bandage is minimized by using a cohesive layer.
6. Difficult location of ulcer. Reshaped by padding [5].
7. Heat intolerance and footwear problems – minimized by reducing padding [5].
8. Restricted ankle movement. In such settings, elastic materials are better than short stretch bandages. Intermittent pneumatic compression (IPC) is a better option in such patients [5].

Technique of Four-Layer Compression Bandaging

The leg is washed, cleaned, and dried. A corticosteroid cream is applied in patients with itching as a problem. The ulcer area is covered with a separate dressing as per the preference and choice (Fig. 15.2a).

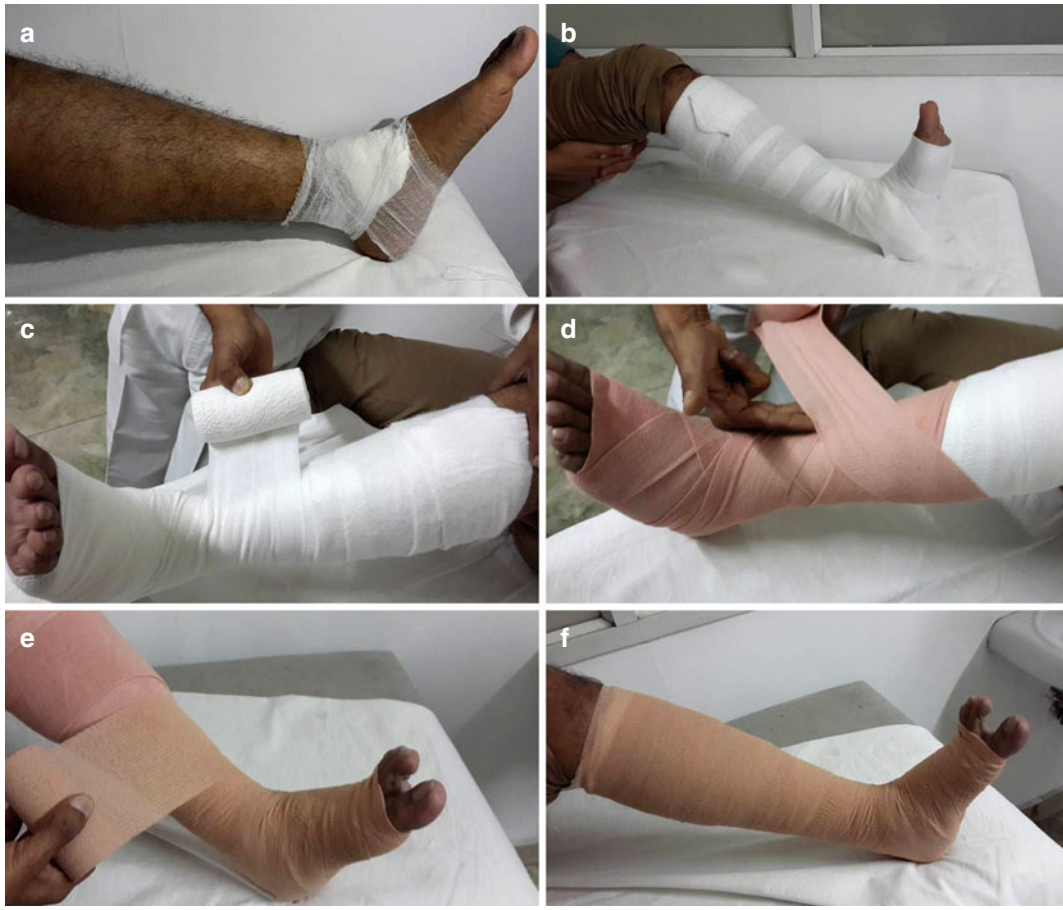

Fig. 15.2 Four layer compression bandaging steps. (**a**) ulcer with dressing in place, (**b**) component 1. Orthopaedic wool, (**c**) component 2. Supporting inelastic bandage, (**d**) component 3. Elastic bandage type III A, (**e**) component 4. Elastic bandage type III B/cohesive, (**f**) Completed four layer bandage

1. *The first component* is sub-bandage wadding with orthopedic wool. This is done in a spiral fashion from toes to knee. It protects the bony prominence and shapes the limb and helps to absorb the exudate. The padding will have to be reduced if the patient has heat intolerance, has fixed ankle, or has problem with footwear (Fig. 15.2b).
2. *The second component* is a crepe bandage (type II) applied in a spiral fashion. This is only a supportive layer and helps to flatten the wadding and aids in the absorption of exudates (Fig. 15.2c).
3. *The third component* is provided by a type III a bandage providing an ankle pressure of 17 mm of Hg. This can be applied with a 50 % overlap or figure of eight configurations. The stretch is usually 50 %. The bandage starts from the base of the toes and extends to 1 cm below knee. The ankle joint should be kept dorsiflexed (toes to nose) or at 90° angle. This step would prevent wrinkling of bandage and pain over dorsum of foot. Bandage pressure can be assessed by slipping two fingers underneath the bandage. It should be possible to slip the fingers easily (Fig. 15.2d).
4. *The fourth component* is a III b bandage with a pressure of 35 mm of Hg over ankle. This is applied in a spiral format, ensuring that the calf muscles are completely enclosed. If the bandage has a tendency to slip, it can be converted to a cohesive type (Fig. 15.2e, f).

On completing the bandaging, check for patient's comfort and whether footwear can be worn properly. The patient is encouraged to walk for about half an hour. The sub-bandage pressure can be objectively documented by placing a probe under the bandage at the B1 point and connecting it to a measuring device [9, 10]. Signs of overcompression include pins and needle sensation, numbness/discoloration of toes, and alteration in the character of the pain from the prebandage settings [12]. In such a situation, the patient is instructed to remove the outermost component and wait. If symptoms improve, they can reapply the top component with less pressure. If there is no relief, they should report to the clinic.

Evaluation and Review

The usual frequency of bandage change is once a week [9]. More frequent changes would be needed if the bandage becomes loose from resolution of edema or if the exudate is profuse. One of the signs of adequate compression is the guttering effect, longitudinal folds in the gaiter area and above, 3–5-mm wide resulting from resolution of edema [8]. During each session, progress of the ulcer is documented and any signs of compression damage noted. The usual healing time is 12–24 weeks (Fig. 15.3). If the ulcer does not heal within this time or if the pain is severe, specialist review is mandatory.

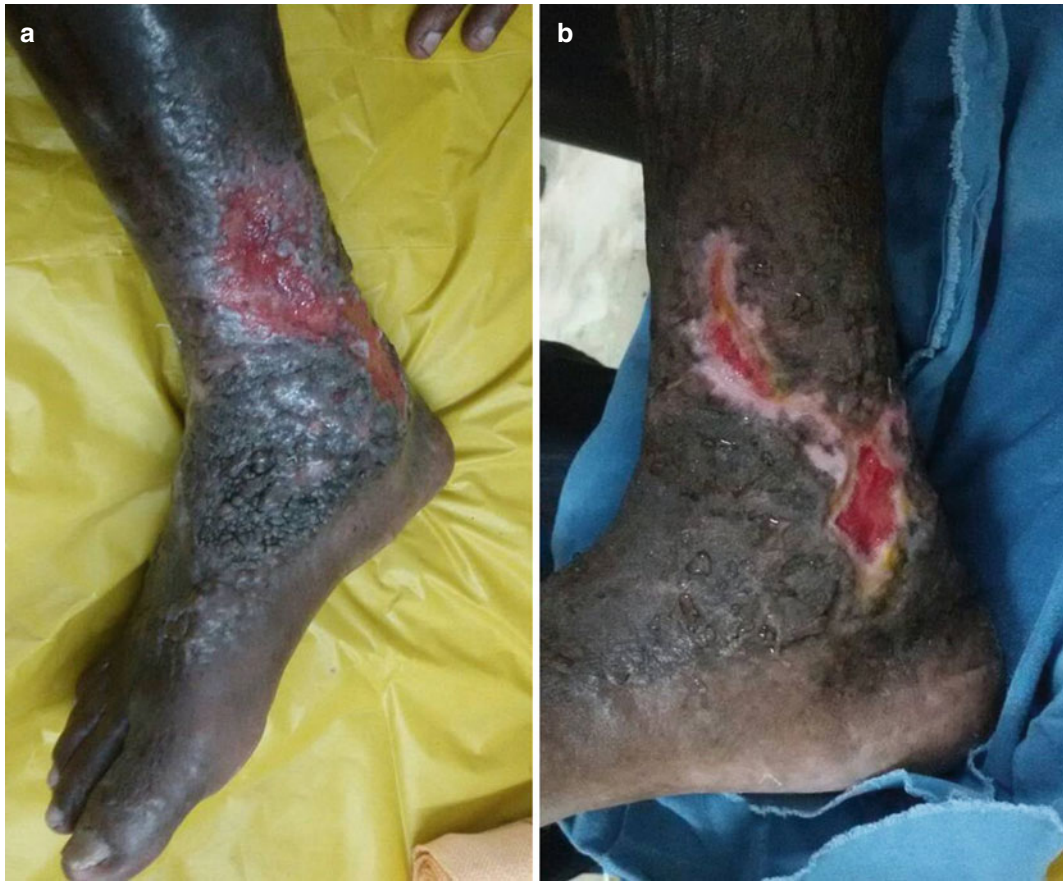

Fig. 15.3 Effect of compression therapy. (**a**) Limb before CT. (**b**) 3 weeks after CT

Maintenance Therapy

Once the ulcer has healed, further breakdown is prevented by fitting a class II below-knee-graded compression stocking after ruling out ischemia. If the patient cannot tolerate a class II system, a twin system consisting of class I stocking inside and class II outside can be recommended. The outer layer can be removed at night.

Contraindications for Compression Therapy

There are certain absolute and relative contraindications for CT [13]:

1. Patients with decompensated heart failure.
2. Patients with severe obliterative arteriosclerosis with ABPI <0.5.
3. Patients with vasculitic ulcers. CT can aggravate damage to microcirculation and induce tissue necrosis.
4. Diabetes mellitus is not a contraindication, but if there is severe neuropathy, the possibility of pressure damage is higher.
5. Ulcers of mixed etiology (venous and arterial) are not a contraindication. Here low compression regime under strict supervision is to be practiced.

Modifications of the Technique Based on Ankle Circumference

The following table highlights the modifications based on ankle circumference, as suggested by Hopkins and Worboys [8] (Table 15.3):

Table 15.3 Modifications of CT based on ankle circumference

Ankle size (cm)	Modifications
Less than 18	Sub-bandage wadding – 2 layers; crepe and 3B bandage
18–25	Sub-bandage; crepe; 3A figure of 8 and 3B bandage
25–30	Sub-bandage wadding; 3C and 3B
Over 30	Sub-bandage wadding; 3A, 3C, and 3B

Adapted from Hopkins and Worboys [8]

Complications of Compression Therapy

Several complications of compression therapy have been documented [5]. Common problems and their possible solutions are suggested below:

1. *Pain*. This is an important reason for noncompliance. Applied properly, compression should relieve pain in CVI. If pain persists, the following options should be considered: appropriate analgesics, recheck the ABPI and if less than 0.5 consider arterial pathology, encourage limb elevation and toe movements, and consider non-stretch bandages.
2. *Pressure damages*. The usual manifestations of pressure damages include erythema and blistering of skin. The risk for pressure damage is aggravated in the presence of impaired circulation, altered limb shape, foot deformities, edema, neuropathy, and rheumatoid arthritis. The common sites for such changes are the ankle, the dorsum of foot, and the calf segment. The strategies in the presence of pressure damage should be prompt and urgent. These include adequate padding over bony prominences and ensuring that the bandage is not too tight and that the overlap is even. In certain situations, short stretch bandage may have to be considered.
3. *Wasting of calf muscles*. This results from reduced activity. The problem could be minimized by ensuring proper movement of knee and ankle joints, use of flat comfortable footwear and supervised exercise program.
4. *Skin problems*. These are different from pressure damages and include skin macerations and excoriations. They are caused by improper control of exudates and persistent allergies. The methods to tackle these problems would be to ensure proper control of exudates, skin-moisturizing agents, and relieving skin allergies and itching.
5. *Difficulty in tolerating compression*. This can result from work settings, choice of clothing and footwear, and bathing practices. Climate and cultural factors are also relevant.

Compression Therapy by Short Stretch Bandages

Selection of the bandages used in CT should be based on the needs of the patient and not on the preference of the treating clinician. Generally, short stretch bandages exert a low resting pressure and peaks of high working pressures during walking. The contracting calf muscles exert rebound pressure over the stiff tubular bandages, compressing the deep veins and improving the venous return [6]. The advantages of the short stretch bandage system include the following:

1. Since the resting pressure is low, the bandages are less painful and more comfortable especially at night.
2. It is more convenient to use footwear.
3. The bandages are applied at full strength and so the risk of overcompression is much less.
4. For an ankle less than 25-cm size, only two components (inner cotton and outer bandage) are needed. The bandages are less bulky and have a better patient compliance in a hot and humid setting. For limbs with larger ankle dimension, additional layers are needed. If the ankle circumference is less than 18 cm, it is better to use the long stretch bandages.

The details of the patient workup are exactly similar to 4LB technique. The limb has to be padded and reshaped. The SSB are to be applied at full stretch, in a spiral fashion with 50 % overlap [14]. Clinicians are warned not to use short stretch bandages in patients who are immobile and in whom the ankle joint mobility is restricted. This is because ambulation is required for effective functioning of this type of bandage. This precaution is not always essential because the calf muscle pump can function even during immobility [15].

Several workers have compared the effectiveness of the two systems of bandaging, the 4LB and the SSB.

1. O'Meara and coworkers have reported that the leg ulcers treated with the 4LB heal faster than those treated with SSB [16].
2. Wong and coworkers found both systems safe and feasible. Significant material cost savings were reported in patients treated with the SSB system [9].
3. Size of the ulcer also has some bearing on the outcome. Larger ulcers took a longer time to heal with elastic bandaging, but complete healing at 26 weeks was no different [6].
4. Stiffer short stretch bandages are considered superior to 4LB in improving deep venous hemodynamics and faster healing of ulcers [6].

Several two-layer systems are available for compression therapy (Coban system and Actico systems). Patients tolerate these systems better than the four layer because they are less bulky and less warm and humid. Use of footwear is much more comfortable with these.

Compression Therapy by Compression Stockings

Medical compression stockings are extensively used in the management of CVD. Their use for CT for venous ulcers is a comparatively recent development. A general review of the different classes of medical compression stockings and their applications are given below.

General Considerations

Medical compression stockings are almost exclusively two-way stretch stockings. It means that they are elastic both in longitudinal and transverse directions. When applied, they limit the extent to which the veins distend. *Graded* (*graduated*) *compression stockings* are specially fabricated support systems exerting higher pressures at the ankle region and progressively less pressures at the knee and thigh. It provides decreasing pressure gradient from distal to proximal part, facilitating proper venous return. Graded compression stockings improve velocity of flow in the deep veins, transcutaneous oxygen pressure on exertion, and expelled calf volume and aid local capillary clearance. Prostacyclin production and release of plasminogen activators are also

improved. They decrease capacity and pressure in veins, visible superficial varicose veins, edema, lipodermatosclerosis, and ambulatory venous pressure [17]. Care and caution must be observed in prescribing stockings. An ill-fitting stocking can do more harm than good. There are several systems of classification of stockings. The simplest system is based on the amount of pressures exerted at the ankle. Based on this, three classes of stockings are identified. Details are presented in the Table 15.4.

Guidelines for the Use of Medical Compression Stockings

There are different systems of classification of the stockings. To avoid confusion, it is recommended that instead of mentioning the class, it is better to indicate the exact pressure exerted by the stockings at the ankle. For optimum outcome, the following guidelines must be adhered to.

1. The use of stocking should be preceded by 2 weeks of compression bandaging. This clears edema and brings the limb back to its normal dimension.
2. Stockings with pressures of 20 mmHg or more can aggravate preexisting ischemia. Hence, it is mandatory that the ABPI should be evaluated in all subjects. If the value is less than 0.8, such stockings are avoided.
3. Below-knee stocking would be sufficient for the ambulant patient. The measurements required areas follows: (a) circumference at narrowest point of ankle, (b) circumference of calf at its widest point, and (c) length from the heel to just below knee.
4. Thigh-length stocking is recommended for bedridden patients. Besides the three measurements mentioned, two more are needed: (a) circumference of the widest part of the thigh and (b) length from the base of heel to the gluteal fold.
5. The stockings are worn during daytime and removed at night (except when used for promoting ulcer healing – see below).
6. If there are skin changes around ankle, the area should be protected.
7. The two signals of overcompression include undue pain over foot and toes and edema of the toes.

Table 15.4 Class of compression stockings and their use in CVD

Class	Pressure at ankle (mmHg)	Uses
Class I	14–17	Varicose veins Mild edema
Class II	18–24	Severe varicose vein, mild edema Prevention of ulcer recurrence
Class III	25–35	Active/healed ulcer. Postphlebitic limbs. CVI

Adapted from Johnson [17]

Medical Compression Stocking: Use in Venous Ulcers

There are several reports of the use of graded compression stocking as the primary treatment modality for venous leg ulcers [17]. The indications for their use are [5] as follows:

1. Patients with small uncomplicated ulcers
2. Patients who need care of skin on a daily basis
3. Patients who would prefer to self-care
4. Noncompliant patients because the bandages are hot/bulky
5. Patients who are at risk for pressure damage
6. Patients unsuitable for surgery

Advantage of this system is that the effect is independent of the operator. Once applied, benefits are obtained as long as the patient is compliant. A technique suggested to improve compliance is the concept of introductory stocking, fitting the patient with a lower strength initially and gradually hiking to higher strength [6]. A two-component system to be worn over the ulcer with dressing is found to be more effective [17]. The first stocking, 10–20 mmHg, holds the dressing in position. A second stocking, 20–30 mmHg, is applied on top of this. The second stocking can be removed at night. Studies have reported complete ulcer healing in 97 % of patients. The mean time for healing was

5 months. At 5 years, an ulcer recurrence rate of 29 % has been reported [6].

Intermittent Pneumatic Compression

Intermittent pneumatic compression (IPC) can be an effective therapy in venous ulcers especially in obese patients with significant edema. This is not a frontline treatment strategy. The effectiveness of IPC is better in combination with CT [5]. IPC improves tissue oxygenation, aids venous return, and accelerates ulcer healing. The current indications for IPC in the treatment of venous ulcers are patients with reduced mobility, wasting of calf muscles, and those with peripheral vascular disease. In the last setting, it is employed without CT. The disadvantages of IPC as a therapy for venous ulcers include disturbance due to noise, excessive exudation, and technical complexity of operating the equipment [5].

Compression Therapy by Paste Boot and Other Devices

Historically the paste boot for leg ulcer known as Unna's boot was introduced in 1896 by *Paul Gerson Unna*, a German dermatologist. Actually, Unna's boot is a form of compression bandage consisting of three or four layers of dressing. This needs a lot of expertise to apply. The first layer consists of a gauze bandage impregnated with calamine, zinc oxide, glycerin, sorbitol, gelatin, and magnesium aluminum silicate. The bandage is applied with graded compression from forefoot to knee. Additional gauze dressing may be needed to retain this. The outer most layer is an elastic wrap, applied with graded compression. On drying, the system becomes stiff and provides compression. The boot is changed usually weekly. The system does not need any involvement from the patient after application and provides effective continuous compression. Because of its heaviness, it is uncomfortable for many patients. Trained personnel are needed for its proper application. Contact dermatitis to components is very common and may necessitate discontinuance of therapy [6].

Legging orthosis is a stiff compression system in the form of a legging, for treatment of venous and lymphatic insufficiency [6, 18]. This consists of a number of unyielding adjustable compression bands fitted with velcro, from knee to instep. This can be applied easily, retained, and removed. It is inelastic and provides compression similar to Unna's boot. It is especially useful for the physically handicapped because of the ease of application and removal.

To sum up, the following basic facts about CT for patients in the C5–6 clinical classes should be clearly appreciated [19]:

1. CT improves healing of venous ulcers compared to no compression.
2. High compression is more effective than low compression.
3. No one form of CT is better than the other.
4. Ulcer healing was faster by 3 weeks with stockings than by bandages.

Alternatives to Compression Therapy in Venous Ulcers

As already mentioned CT is the primary modality of treatment in venous ulcers. Several other interventions have been attempted with limited success.

1. *Skin Grafting and Skin Replacements*
   Split-thickness autologous grafting is commonly performed for ulcer healing. Results are better with excision of the ulcer and grafting [2]. Pinch grafts and ulcer excision with mesh grafting have been shown to provide good long-term results [2]. It has been observed that if the ulcer remains healed 3 months after grafting, the long-term results are likely to be good [20]. Larger and refractory ulcers are the two common indications for grafting [20]. Stimulation of healing does occur even if graft fails [20]. Reasons for failure of grafts include local fibrin deficiency in the ulcer bed preventing sticking of grafts and microthrombi in dermal vessels [20]. Radical excision of the ulcer bed along with all the fibrotic suprafascial tissues and the superficial and perforating veins along with a flap cover

for the large defect has been reported in several patients [20]. A number of biological dressings have been developed including fetal keratinocytes and collagen meshes. They are not effective except in a small subset of patients. Moreover they are expensive.

In summary, there is insufficient current evidence to indicate that skin grafts or skin replacements hasten the healing of venous ulcers. No fiscal benefits were identified for these procedures [3].

2. *Topical Negative Pressure* (*Vacuum-Assisted Closure – VAC*)
   There was no evidence to indicate that the application of topical negative pressure speeds healing of venous ulcers specifically [3, 21]. The technique is useful in preparing the bed of the ulcer before grafting [6].
3. Ultrasound Therapy
   The Royal College of Nursing guidelines indicate a possible benefit of ultrasound therapy in the healing of venous ulcers [3]. Chung and coworkers in a recent survey found no advantage, clinical or economic, with ultrasound therapy [22].
4. *Low-Level Laser Therapy*, *Electromagnetic Therapy*, *and Electrical stimulation*
   None of these interventions have any benefit in promoting the healing of venous ulcers [3].

Summary

This chapter has highlighted two neglected but central areas of care of a patient with venous ulcer: care of the ulcer and compression therapy.

Several sequential steps are involved in the care of ulcer. It is important to pay attention to all these principles. The clinician must be aware of the merits and demerits of different types of dressings and choose the most appropriate one based on the patient's needs and fiscal abilities. Generally, occlusive/semiocclusive dressings are popular in many centers.

CT is the primary modality of treatment for promoting ulcer healing. This is an ambulatory form of treatment based on sound physiological principles. There are several methods of providing CT; the most widely practiced technique is by compressive bandages – four-layer long stretch bandaging or two-layer short stretch bandaging. The choice is based on the patient's needs rather than the preference of the clinician. Alternatives to bandaging include compression hosiery, intermittent pneumatic compression device, and paste boots and legging orthosis.

Several alternatives to CT have been tried but currently none is found to be superior.

Finally, it is recommended that these procedures are carried out in dedicated clinics/centers manned by personnel specially trained for such activities.

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Pharmacotherapy of CVI

16

Subramoniam Vaidyanathan

Contents

Introduction

Pharmacotherapy of chronic venous insufficiency (CVI) and varicose veins is an area which cannot claim significant progress. Several drugs are used to control the symptoms of chronic venous disorders and promote healing of venous ulcers. None of them are effective in altering the course of the disease. The wonder drug in this arena would be one that can completely reverse the underlying molecular pathology of this disease.

This chapter focuses on the following aspects:

(a) Classification and pharmacological actions of commonly used drugs for CVI
(b) Possible future developments

Drugs Used in the Treatment of CVI

Several drugs are used for the relief of symptoms in patients with CVI. They are broadly divided into four groups [1, 2]:

- Venoactive drugs
- Hemorheological agents
- Antiplatelets
- Other agents

Venoactive Drugs

Venoactive drugs (VAD) [1] are also known as phlebotonic agents. They improve venous tone and capillary permeability. They may be naturally

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Table 16.1 Venoactive drugs

Molecule	Drug
Alpha benzopyrones	Coumarins
Gama benzopyrones	Diosmin (micronized purified flavonoid fraction – MPFF)
	Rutin, rutosides
Saponins	Aescin (horse chestnut seed extract)
	Ruscus extract
Other plant extracts	Anthocyanins
	Extract of Ginkgo
Synthetic	Calcium dobesilate
	Benzarone
	Naftazone

Adapted from Perrin and Ramelett [1]

occurring agents or synthetic compounds. The commonly used agents are listed in Table 16.1.

Mode of Action of VAD

- VAD *improve venous tone* by acting through the noradrenaline pathway. Micronized purified flavonoid fraction (MPFF) prolongs noradrenergic activity. Hydroxyethyl rutosides block the inactivation of noradrenaline. Ruscus extract is an agonist of α 1 adrenergic receptors [1].
- *Capillary resistance* is increased and filtration reduced [1].
- *Lymphatic system:* Coumarins are used in the treatment of lymphedema. MPFF is known to improve lymph flow and increase the number of lymphatics. Calcium dobesilate can increase lymphatic clearance [1].
- *Hemorheological changes:* Increased viscosity due to plasma volume reduction and increased fibrinogen content is a common finding in CVI. Another common feature is red cell aggregation. MPFF and calcium dobesilate reduce viscosity. RBC aggregation is inhibited by Ginkgo extract. MPFF improves RBC velocity [1].
- *Anti-inflammatory action:* Venous hypertension induces an inflammatory response in the veins, capillaries, and skin. Experimental induction of venous hypertension in animals by venous occlusion, A-V fistula, and venous ligation confirmed the release of several inflammatory mediators. More importantly, priming these animals by administering MPFF considerably reduced the harmful effects induced by these inflammatory mediators [3]. Only MPFF is known to possess such anti-inflammatory action.

Indications for the Use of VAD

- *For symptomatic improvement.* Several RCTs have confirmed that pain, cramps, restless legs, heaviness, and edema are all relieved by the use of VAD [1]. As per the outcome measures, MPFF and Rutosides offer strong benefit, while the other agents have only moderate impact.
- *For healing of venous leg ulcers* as an adjunct to compression therapy and local treatment, MPFF has been recommended [2].

Daflon: Micronized Purified Flavonoid Fraction (Diosmin 450 mg and Hesperidin 50 mg)

This has been in clinical use for quite some time. Several trials have reported significant symptomatic improvement and better healing of ulcers with the use of this drug [2, 4]. The dosage recommended is 1,000 mg daily for 2 months [5]. The drug is reported to be effective in blocking the inflammatory cascade in CVI [4]. It has been reported that MPFF might be a useful adjunct to conventional therapy in large and long-standing ulcers that heal slowly [2].

Calcium Dobesilate

This is a synthetic preparation. Meta-analysis has shown improvement of symptoms of night cramps, paresthesia, pain, heaviness, and malleolar swelling in a dosage of 1,000 mg daily in comparison to placebo. The improvement was better in patients with the more severe forms of the disease [6]. Another trial has demonstrated

that the improvement in symptoms is independent of the concomitant use of stockings [7].

Side Effects of VAD

These drugs have no serious adverse events. Hepatotoxicity has been reported with coumarins, rutin, and benzarone. Transient agranulocytosis is reported with the use of calcium dobesilate [1].

Hemorheological Agents – Pentoxifylline

Pentoxifylline is extensively used in the treatment of peripheral arterial diseases. Its use has been extended to the management of CVI. It inhibits cytokine-mediated neutrophil action. It also reduces white cell adhesion to endothelium and the release of superoxide free radicals [2]. The current opinion indicates that pentoxifylline in a dose of 1,200–2,400 mg could be an effective adjunct to compression therapy for treating leg ulcers [1, 3]. It can also heal ulcers on its own without compression but the level of evidence is much lower [3].

Antiplatelet Agents

Aspirin 300 mg daily had no impact in the healing of leg ulcers [8]. *Ifetroban* is a thromboxane A2 receptor antagonist. It inhibits platelet activation. Oral administration of this drug showed no effect on venous ulcer healing [2, 5].

Other Agents

Oral zinc supplementation. There was no evidence to support that oral zinc supplementation promotes ulcer healing [8].

Fibrinolytic agents – Stanozolol. This is an anabolic steroid with a powerful fibrinolytic action. It has been shown to improve the pain and skin changes in patients with lipodermatosclerosis. It has no effect on ulcer healing [5]. Since the original publication, no further study has appeared on this drug. The drug has been withdrawn from clinical use in many countries [2].

Prostaglandin E1. The effect of PGE-1 on ischemic limbs is well established. There are reports of its effectiveness in the healing of venous ulcers, reduction of edema, and relief of pain [2].

Prostacyclin analogs have fibrinolytic activity and reduce leukocyte aggregation and adhesion to endothelium. The outcome of topical application of this agent in venous ulcers has been disappointing [2].

Common Clinical Applications of Drugs in CVI

In clinical practice, VAD and other agents are used for three purposes: relief of symptoms, healing of venous ulcers, and the control of lipodermatosclerosis.

VAD were found to be useful in the relief of common symptoms such as aching pain, tiredness, heaviness, and cramps [1]. Calcium dobesilate was found to be effective in providing improvement of cramps and night pains [7].

The two drugs used for promoting healing of venous ulcers are MPFF and pentoxifylline. Pentoxifylline is reported to promote ulcer healing with and without compression bandages [1, 3]. Large resistant venous ulcers healed faster with adjuvant treatment with MPFF along with compression [2]. This is the only agent which can block the inflammatory cascade in CVI [4].

Topical therapy for promoting healing of venous ulcer is widely practiced. It is now accepted that topical antibiotics may produce skin sensitization and are best avoided. Growth factor (G – CSF) topical therapy is reported to improve ulcer healing [2].

Venous lipodermatosclerosis is very resistant to therapy. The lesion can present both in an acute and chronic form. Stanozolol is considered to be effective in both acute and chronic forms [9]. But this drug is banned in many countries. Defibrotide (a profibrinolytic and antithrombotic agent) in a dose of 800 mg/day for 3 months along with compression stockings is shown to reduce the extent of lipodermatosclerosis and promote healing of ulcers in post-thrombotic limbs [10]. Topical capsaicin 0.075 % cream for 3 weeks is reported to be effective in the acute stage. This deletes substance P and thus reduces nociceptive pain and neurogenic inflammation [11].

Pharmacotherapy: Emerging Trends

Matrix Metalloproteinases and CVI

MMPs play a role in extracellular matrix turnover. Increased activity of the MMPs, which break down extracellular matrix, is reported in advanced state of CVI. Inhibition of MMPs may represent a novel therapeutic intervention to limit the progression of varicose veins to CVI and ulceration [3, 12]. Inhibitors of MMPs such as doxycycline, zinc chelators, batimastat, and marimastat have been used for diagnosis and treatment in oncology, cardiovascular, and autoimmune diseases. They have several side effects especially on the musculoskeletal system. There are no reports of their use for CVD. Specific MMP inhibitors with fewer side effects generated by the new genetic and pharmacological methods may prove to be effective in arresting the progression of CVD [13].

Statins and Venous Endothelial Protection

Statins are known to protect the endothelium from cardiac events [14]. The endothelium on the venous side also has a major role in the pathogenesis of CVD and DVT. There is considerable venous endothelial damage following DVT. Healthy endothelium is critical in preventing recurrent thrombosis. A randomized trial has proven that rosuvastatin in a dose of 20 mg a day significantly reduces the incidence of venous thromboembolism [15]. It is not known whether statins will reduce the incidence of postthrombotic syndrome (PTS) [14]. The role of statins in protecting venous endothelium is an emerging concept. Further studies are needed to define the role of statins in venous diseases.

Summary

Pharmacotherapy of venous disorders has only a limited role in the overall management of patients with CVD and CVI. Several drugs are available. They include the venoactive drugs, hemorheological agents, and antiplatelet drugs. VAD are widely used in practice. These agents are reported to be effective in improving symptoms such as aches, heaviness, cramps, etc. MPFF and pentoxifylline are proven to help the healing of venous ulcers. MPFF is the most promising drug and is the only agent which can block the inflammatory cascade in CVI. Inhibitors of MMPs may find useful therapeutic application. The role of statins in protecting venous endothelium is an evolving concept. The clinical implications of this hypothesis need further validation.

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Strategies for the Management of Incompetent Perforating Veins

17

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Introduction

Surgery of incompetent perforators is the bone of contention in phlebology. The precise role and significance of incompetent perforators in CVI is not clearly defined. Most of the studies have combined elimination of saphenous reflux with perforator disconnection. Reports of isolated treatment of perforators are very few. Judgement on the relevance of perforators in the pathogenesis of CVI is extremely difficult on account of these limitations.

The association between incompetent perforators and leg ulcer was first suggested by John Gay more than 150 years ago. Robert Linton recommended disconnection of the perforators as an effective treatment for venous leg ulcers. Subsequently Cockett and Dodd and several other workers made significant contribution in this area. In spite of all these, perforator surgery remained in the backseat for a long time. This was because of the high incidence of wound complications following the open technique. There was a renewal of interest in this area when Hauer in 1985 introduced subfascial endoscopic perforator surgery (SEPS). Currently SEPS remains one of the widely practiced surgical interventions for the treatment of venous leg ulcers.

This chapter focuses on the following aspects of the problem:

- Review of surgical anatomy of perforators
- The significance and effects of incompetent perforators

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- The common indications and contraindications for perforator surgery
- Overview of open subfascial ligation
- SEPS – principles, procedure, and outcome
- Comparison of open versus endoscopic perforator surgery.
- Percutaneous ablation of perforating veins (PAPs)

Aspects of Anatomy

Details of the anatomy of perforating veins were presented in Chap. 2. A brief review would be presented here.

The medial calf perforating veins are clinically the most significant ones. Among them, the most relevant ones are the three posterior tibial perforating veins (Cockett perforating veins). They do not arise from the main trunk of the GSV but connect the posterior accessory GSV (Leonardo's vein) to the paired posterior tibial veins. The posterior accessory GSV joins the GSV just below the knee. This anatomical arrangement is important because stripping the trunk of the GSV will not eliminate the posterior tibial perforating veins [1, 2]. During subfascial endoscopic perforator surgery (SEPS), a paratibial fasciotomy is needed to get a complete clearance of all the perforators.

The perforating veins exist as a single trunk below the deep fascia. Extrafascially they divide into several branches. Hence, control of the perforator as a single trunk is easier below the deep fascia. Their identification is also easier in this position. For these reasons a subfascial approach is preferred for control of IPV [2].

Importance of Incompetent Perforating Veins (IPV)

Venous ulcers and skin changes are commonly located over the gaiter area – area between the distal edge of the soleus muscle and the ankle. The media calf perforating veins are clustered in this area [1]. In patients with C6 clinical class, duplex scan has shown multisystem multilevel involvement (superficial, deep, and/or perforator). Incompetency of the calf perforating veins along with superficial or deep reflux has been observed in 56–73 % of patients with venous ulcer [3]. When the posterior tibial perforators become incompetent, there is a high pressure leak of blood from the deep veins to the superficial system during calf muscle contraction – the "leaking bellows" [4].

Objective findings of such "significant" perforators include flow duration over 500 ms and size over 3.5 mm [5]. It is extremely difficult to assess the contribution of incompetent perforator in the hemodynamics. Our AVP studies demonstrated that the venous pressure pattern is unpredictable in the presence of IPV [6]. It is pointed out that when perforator incompetence coexists with superficial reflux, elimination of superficial reflux restores the competency of the perforators [7]. On the basis of this finding, it was recommended not to disconnect such perforators. This concept is challenged by Bergan and Pascarela. They have identified two types of perforators: the exit veins and the reentry perforator veins. The incompetent exit veins permit outward flow from deep to superficial veins. The reentry perforating veins permit drainage from superficial to deep veins especially in presence of saphenous reflux (private circulation). These workers suggested that elimination of superficial reflux reverts the reentry perforators and not the exit veins [8]. Since the hemodynamic findings of incompetent calf perforators are extremely variable, the decision on perforator interruption is often made on clinical basis.

Indications and Contraindications for Perforator Surgery

Interruption of the incompetent medial calf perforators eliminates reflux through them and reduces the ambulatory venous pressure in the critical areas above ankle. The *common indications* for perforator disconnection include [1]:

- Patients in clinical class 4–6 with perforator incompetence along with superficial/deep reflux. It can be combined with superficial

vein surgery or can be performed as a staged procedure.
- Patients with isolated IPV. This is not a common clinical situation.
- In C2–3 classes, perforator surgery is considered only if varices recur after elimination of superficial reflux.

Contraindications include [1]
- Occlusive arterial disease (ABPI less than 0.8)
- Recent DVT/obstructed deep veins
- Infected ulcer and large circumferential ulcers
- Nonambulatory and medically unfit patients

Majority of the clinicians would prefer to have the ulcer in the healed or near healing stage before proceeding with any intervention. This can be achieved by an effective compression therapy. At present, an open ulcer is not a contraindication for surgery [1].

Preoperative Evaluation

Duplex scan has 100 % specificity and the highest sensitivity of all diagnostic tests to predict the sites of IPV [9]. Marking the sites of IPV preoperatively by duplex scan will provide useful guidance during surgery. *Venogram* is considered when deep vein obstruction is suspected or when deep vein reconstruction is planned along with perforator surgery. Hemodynamic studies such as *plethysmography and AVP* are useful to quantify reflux. They are particularly useful in assessing outcome after surgery.

Perforator Ligation: Open Surgery

The open techniques of perforator surgery are mostly of historic relevance now. The procedure of SEPS has totally marginalized all of them. The original operation described by Linton employed a long medial incision along with incisions over the antero- and posterolateral aspects too. Because of high rate of wound complications, this was abandoned. Subsequently only the medial incision was employed through which all compartments are cleared – the modified Linton procedure. In addition to the incompetent perforating veins, it included stripping of GSV and SSV and excision of part of the deep fascia [1]. Cockett then proposed an extrafascial ligation technique again through a medial incision [2]. Incidence of wound complications was higher with the extrafascial approach and hence it did not gain much popularity.

The medial approach of open subfascial ligation was a popular form of intervention for a long period. Several authors have reported good outcome with such an approach. Through the medial incision it is possible to reach the posterior and sometimes even the lateral compartments [6]. The problem with the medial approach was that incision is made over unhealthy skin and subcutaneous tissues. To overcome this problem, Felder proposed a posterior midline approach [9]. In the UK, this approach is known as the Rob procedure [10]. DePalma used parallel incision along natural skin lines to create bipedicle flaps. The perforators were approached through this [11].

Edwards in 1976 described a shearing operation wherein the perforators are interrupted using a curved instrument called phlebotome. This is advanced through a small incision deep to deep fascia at the level of knee and advanced to the medial malleolus [12].

Subfascial Endoscopic Perforator Surgery (SEPS)

SEPS has transformed a formidable open surgical intervention with its risk of wound complications into a safe minimally invasive procedure. SEPS combined with HL/S and compression therapy is now a standard treatment for venous ulcer patients.

Hauer and later Fischer [13] introduced endoscopic subfascial interruption of incompetent perforating veins in Europe in the mid-1980s. They used a single port for both viewing and working. The credit for using modern-day laparoscopic instruments for SEPS goes to O'Donnell, who used water for the dissection of the subfascial space. Gloviczki and Bergan et al. introduced CO_2 insufflation and also used two endoscopic ports [14]. They advo-

cated a thigh tourniquet to obtain a bloodless field and to prevent gas embolism [2]. We follow the two-port technique with CO_2 insufflation.

SEPS Steps

A proper marking of the incompetent perforators by a preoperative duplex scan is a prerequisite for SEPS. The procedure is done under regional block or general anesthesia.

The patient is kept in the supine position with the knee flexed to 90° and gentle flexion and abduction at the hip. A sandbag is kept under the thigh to elevate the knee.

Standard equipment for laparoscopy is used for the procedure. A 10-mm incision for the 0° scope is made about 3 cm below the tibial tuberosity and 3 cm medial to the shin of the tibia (Fig. 17.1).

Use of a thigh tourniquet and Esmarch bandage to exsanguinate the limb is reported by some authors [1]. The deep facia is incised under vision and subfacial plane for the port is developed by blunt dissection. Ten-millimeter port is introduced, CO_2 is insufflated at 30 mmHg and subfacial space is bluntly created using the scope. Alternatively a balloon insufflation can be used to create this subfacial plane [1]. The second port is now placed 3 cm posterior and a little caudal to the first port. The two ports can be interchanged to facilitate dissection later. All the perforating veins along the medial aspect of the tibia, from the entry of the port till the medial malleolus, are identified, skeletonized, and disconnected. This can be achieved by clipping, diathermy, or use of harmonic scalpel (Fig. 17.2).

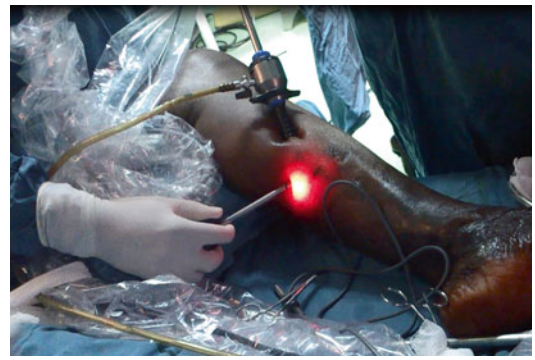

Fig. 17.1 SEPS port placement

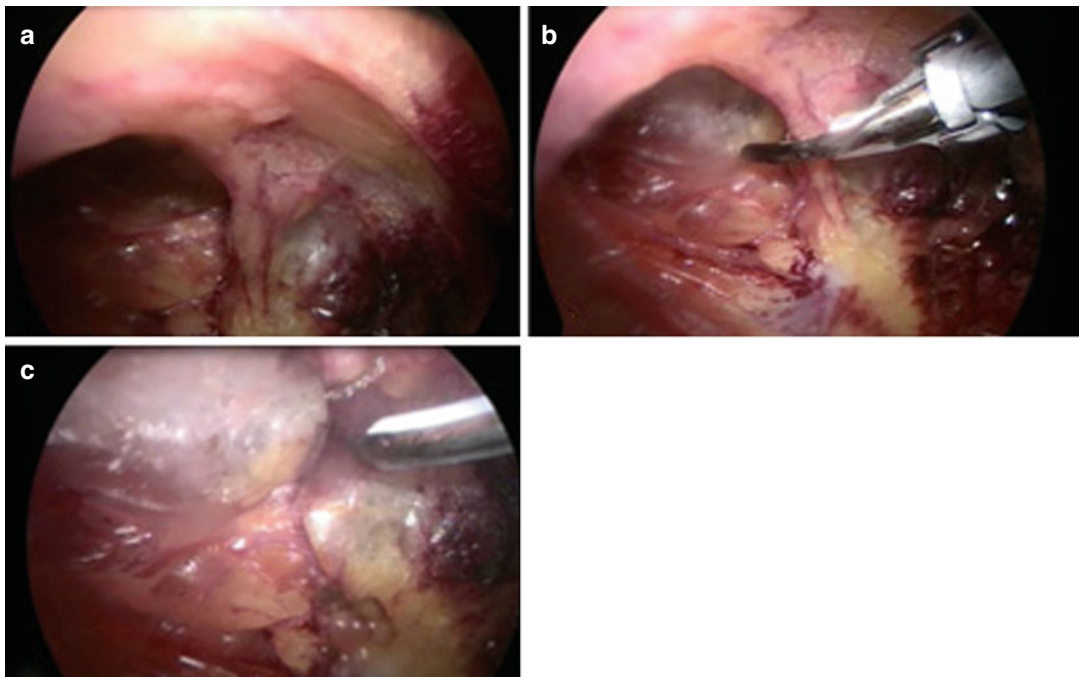

Fig. 17.2 (**a**) Perforator skeletonized. (**b**) Control with harmonic scalpel. (**c**) Disconnected perforator

We prefer to use harmonic scalpel due to less trauma, better occlusion of vein, and less incidence of nerve injury. Dissection at the malleolar area is challenging due to lack of space and difficulty in identifying the perforating veins especially the lateral and anterior ankle perforators and the lower most medial calf perforator. Posterior dissection is continued as far beyond midline as possible.

Ports are interchanged for the next part of the dissection. The intermuscular septum under the tibia is identified and opened to gain access to the lateral perforators (Fig. 17.3).

These are also disconnected. During this step, the upper two medial calf perforators may be encountered passing within the intermuscular septum and need to be controlled before dividing the septum. A survey is done to ensure completion and hemostasis. Ports are removed and wounds closed. Compression bandages are applied and early ambulation is encouraged. Patient is discharged the next day. This procedure can be combined with HL/S or endovenous ablation and phlebectomy if needed.

Postoperative Complications

There are no major complications reported following SEPS and the procedure is considered extremely safe. There are reports of minor events such as bleeding and hematoma in the subfascial plane, infection in the subfascial plane requiring drainage [15], and muscle herniation. Our experience with the technique is extremely satisfying but the numbers are too small.

Comparison of Open and Endoscopic Perforator Surgeries

The advantages of SEPS over the open procedure are obvious. Delayed wound healing, skin necrosis, and wound infections are common after the open surgery. With SEPS postoperative pain is much less and the patient can be mobilized in the immediate postoperative period. All these would result in a significantly shorter hospital stay for the SEPS group. There are several limitations advanced against SEPS [8]:

- Potential risk of injury to posterior tibial artery, vein, and nerve in the distal leg. This is overcome by identifying and confirming the morphology of the perforating veins before dividing them.
- Use of electrocautery in the subfascial space can aggravate vascular and nerve injuries. The perforators are clipped and divided rather than controlling them by electrocoagulation. A better option would be the harmonic scalpel.
- Expanding the subfascial space in the presence of venous lipodermatosclerosis can be difficult. This can result in missing some of the important perforators. A paratibial fasciotomy can overcome the access problem [1].

The advantages of the endoscopic technique in terms of wound complications are very evident, 0 % for SEPS and 53 % for open surgery. In view

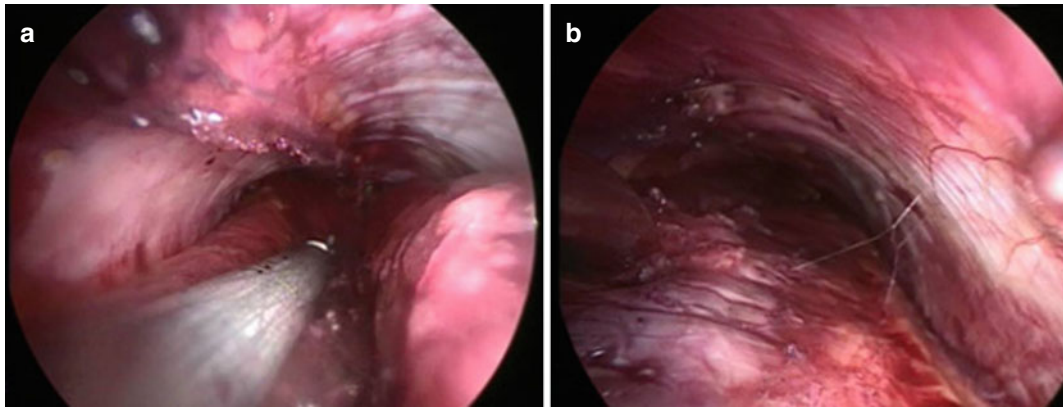

Fig. 17.3 (**a**) Intermuscular septum divided. (**b**) Subfascial compartment on completion

of the unacceptably high incidence of wound complications, in a prospective trial, Pierik et al. had to stop their open surgery arm prematurely [8].

Outcome of Perforator Vein Surgery

The outcomes of perforator surgeries, both open and SEPS, have been reported by a number of authors. The mean ulcer recurrence rate following open surgery was 23 %; for SEPS it was 12%. The most obvious and striking difference was in the incidence of wound complications; for open surgery it was 25 %, whereas for SEPS it was less than 7 % [1, 8]. Since the open surgery is now practically obsolete, these data have no relevance.

Clinical Outcome of SEPS

Since SEPS is emerging as the recommended treatment for incompetent perforators, it would be prudent to compare its outcome in the different clinical classes of patients and also in patients with the post-thrombotic syndrome.

- Several studies have analyzed the outcome of SEPS in patients with the clinical class of C2 patients. RCTs have concluded that at 1 year in class C2 patients, no additional clinical benefits could be observed when SEPS was combined with HL/S of the GSV [5].
- The outcomes in patients of the C3–C6 classes (mostly C5 and 6 classes) are promising. The North American registry reporting on the mid-term results of SEPS (NASEPS) documented a cumulative ulcer healing rate of 88 % at 1 year and a cumulative ulcer recurrence rate of 16 % at 1 year, and 28 % at 2 years [16].

Ten Brook and colleagues in a systemic review in 2004 reported ulcer healing rate of 88 % and recurrence of 13 % in a short-term follow-up of SEPS, with or without saphenous ablation [17].

Ulcer healing was considerably delayed in those patients who underwent SEPS alone, in comparison to the group who had SEPS combined with saphenous ablation. The 90-day cumulative ulcer healing rates for the two groups were 49 and 90 %, respectively. Ulcer recurrence at 5 years was also much higher for the SEPS alone group (53 %) in comparison to the other group (19 %) [1].

Encouraging results were reported from India in two published series. Both authors had good ulcer healing in 6–8 weeks with no recurrence at 1-year follow-up [18, 19].

In the post-thrombotic group, the outcome was not very encouraging. The 5-year ulcer recurrence was 56 % in the PTS group compared to 15 % in the nonthrombotic group. Still the QoL measures and the VCSS have shown improvement in this subset compared to their preoperative status [5].

Hemodynamic Outcome

Since most of the studies have reported hemodynamic outcomes in the group of patients who had concurrent perforator ablation along with HL/S, benefits attributable to the perforator component alone are difficult to assess. Schanzer and Pierce using AVP studies have reported significant improvement of the pressure pattern following isolated perforator interruption in 22 patients [20]. Our studies in patients who had open perforator surgery have shown improvement of the AVP pattern but not normalization [6]. Calf muscle pump function and venous incompetence have improved in patients who have undergone SEPS and saphenous surgery [1].

Percutaneous Ablation of Perforators (PAPs)

Endovenous thermal and chemical ablations have been extensively practiced for the control of truncal and tributary varices of GSV and SSV. PAPs is the extension of these minimally invasive interventions for the control of perforating veins. The term PAPs was initially introduced in the year 2005. Elias has summarized the basic principles involved in this technique [21]:

- US-guided percutaneous access to perforators
- Intraluminal application of thermal/chemical energy leading onto vein wall contraction and/or occlusion

- Procedure under local anesthesia in an outpatient setting
- Recurrence to be treated by retreatment if needed

Under US guidance direct puncture of the perforating vein is made. The tip of the needle should be at or just below the deep fascia, in the vein. This is to minimize deep vessel and nerve injury. Once an access is obtained, the vessels can be treated by using radiofrequency waves, laser energy, or sclerotherapy. Special RF/laser fibers are now available in the new treating units. Most of the reports use liquid sclerosants; foam sclerosants are advocated in some of the recent reports.

PAPs is a safe procedure. Reported complications include tibial vein DVT, foot drop, and skin burns in the occasional patient [19]. The advantages claimed for PAPs over SEPS are: the procedure is performed without any incision under local anesthesia and can be easily repeated if necessary. There is no separation or expansion of tissue spaces unlike in SEPS. Postoperative pain is minimum or absent. Access to the distal (close to the malleolus) perforators is difficult in SEPS. In PAPs the location of the perforators is of no concern and any perforator visualized on US can be accessed. PAPs can be offered to elderly patients with comorbidities and those with difficult problems like obesity and swollen limbs. The downside of it is that since US can miss many perforators, the treatment may not be complete. PAPs is not a replacement for SEPS. There is a role for both procedures in the control of incompetent perforators [19].

Summary

Surgical disconnection of IPV as a treatment strategy for venous ulcer is a debatable issue. This is because the hemodynamic significance of incompetent perforators in isolation is not precisely understood. Among the perforators the medial calf perforators are clinically the most significant ones. When incompetent, they can generate a high ambulatory venous hypertension in the target areas above the ankle. The open subfascial procedures introduced by Robert Linton and popularized by Dodd and Cockett had an alarmingly high rate of wound complications. They naturally fell into disrepute. Introduction of the technique of SEPS by Hauer in 1985 renewed the interest in perforator disconnection. Currently SEPS is a standard intervention along with HL/S or endovenous procedures for control of venous ulcers. A two-port technique with CO_2 insufflation and a paratibial fasciotomy gives good exposure of all the IPVs. Use of harmonic scalpel is an added advantage. The advantage of the SEPS is so glaring, that the open surgery is abandoned now. No major complications are reported for this procedure. The results in terms of ulcer healing and recurrence are very encouraging in C5 and 6 groups. In the post-thrombotic group, the outcome is less bright. The AVF guidelines do not recommend the procedure for C2 class. PAPs is a natural extension of endovenous procedures. This is emerging as a viable option in certain situations for control of IPV.

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Deep Vein Valve Reconstruction

18

Subramoniam Vaidyanathan

Contents

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Introduction

Axial reflux in the deep veins is a common finding in patients with primary chronic venous insufficiency (CVI). In an attempt to improve the clinical and hemodynamic outcomes, interventions to restore the competence of the deep veins have been extensively reported. Multisystem multilevel reflux is a common finding in primary CVI. In post-thrombotic syndrome (PTS), often there is a combination of obstruction and reflux in the deep veins; both may need correction. Valvuloplasty to correct reflux in the deep veins is an adjuvant treatment option in a subset of patients with primary and secondary CVI. Compression therapy (CT) still continues to be the primary modality of treatment for CVI and leg ulcers [1].

This chapter reviews the treatment options for the correction of reflux in deep veins. The issues presented are:

- Indications for valve reconstructions
- The different options available
- The outcome and complications
- Emerging trends in this area

Reflux in the deep veins due to valvular incompetence is a finding documented in a large number of patients with CVI. Restoring competence in the deep veins would form a rational treatment option in such patients along with control of reflux in the saphenous system. Currently, this is an accepted treatment option in a subset of patients with CVI [2]. Debate continues on the

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optimum technique and site for valve reconstruction and on the issue of single versus multiple site repairs.

Indications

Recurrent Ulcers (C5, 6)

Currently recurrent ulceration forms the commonest indication for deep vein valve correction [3]. Venous ulcers can respond well with less radical forms of surgery. Several reports have confirmed that following ablation of incompetent superficial veins and perforators along with compression therapy, the ulcers remain healed for long periods of time [4–6]. But 33 % of patients with primary deep venous incompetence and 70 % of those with post-thrombotic pathology will experience ulcer recurrence [4].

Intractable Pain

A subset of patients with CVI experience intractable pain (visual analog scale more than 5). Severity of pain with or without other features is considered an adequate indication for deep vein valve reconstruction [3].

Recurrent Cellulitis and Thrombosis

Patients with proximal primary valvular incompetence can develop recurrent cellulitis and thrombosis distal to the refluxing valve in the deep veins [3]. Reflux in deep veins can produce distal thrombosis. Valvuloplasty of the proximal segment has been suggested to break this vicious cycle [3]. This is a less accepted indication for valve reconstruction.

Intractable Edema

This is again a controversial indication [4]. Often, the preexisting edema can aggravate after valvuloplasty.

Reconstruction of the valves in the deep veins is not recommended as a stand-alone procedure. It is complementary to superficial and perforator surgery, forming part of the total/optimal correction [7].

Preoperative Evaluation

This will include clinical and lab studies. The clinical evaluation should consider detailed history including previous episodes of deep vein thrombosis. Coagulopathy workup is mandatory in patients with post-thrombotic limbs. Arterial evaluation and ruling out other causes of leg ulcer are relevant. Duplex scan is the initial tool to evaluate the venous system. It provides useful information on the status of the superficial, deep, and communicating veins. Both reflux and obstruction can be evaluated objectively by duplex studies. Since it is a noninvasive test, it can be repeated without much discomfort to the patient. In many centers, duplex scan has totally eliminated venographic studies. Further venous evaluation would include anatomical studies by ascending and descending venography and MR or CT venograms in selected cases. Ascending venograms are helpful in differentiating between primary CVI and post-thrombotic disease. Descending venograms are practically replaced by duplex scans but it can help to locate the position of valves. Intravascular ultrasound (IVUS) is useful in the diagnosis of iliac vein lesions. Hemodynamic assessment is by the use of the different plethysmographic techniques. Ambulatory venous pressure studies would give information about the functional status of the venous system.

Choice of Anesthesia and Positioning of Patient

The surgical procedures are of long duration. Most surgeons prefer general anesthesia, especially when axillary vein transplantation is being considered. Epidural anesthesia would be a good option for other procedures, but one should be

cautious regarding preoperative heparinization. Prophylactic antibiotics are routinely administered. Intraoperative heparinization and postoperative anticoagulant treatment would be needed for some of the procedures.

Most of the valve reconstruction procedures are performed with the patient in the supine position with the ipsilateral knee joint flexed and supported and the hip externally rotated. The axilla should be prepared in case an axillary valve transplant is needed. Usually the nondominant arm is selected. If the transplant is planned to the popliteal vein, a full prone position is preferred.

Incisions and Exposure of Vessels

The vessels to be exposed are the common femoral vein (CFV), the femoral vein (FV), and the profunda femoris vein in the groin. The popliteal vein needs to be exposed in case of triple valvuloplasty or in axillary vein transplantation to that site.

The femoral veins in the groin are exposed by a standard 6–8-cm vertical incision starting from the level of the inguinal ligament. The femoral artery pulsations are palpated and the incision is cited just medial to it. An "S"-shaped incision is reported to be associated with less wound sloughing since fewer perforating arteries are disrupted in this incision. The incision is deepened to the deep fascia which is also incised. No attempt is made to reflect flaps, for this would result in sloughing of wound edges. The vessels are exposed with minimal handling of the femoral artery to avoid spasm. The GSV and its stump are useful landmarks. The CFV, FV, and profunda are dissected and taped. Exposure of the profunda can be difficult especially in post-thrombotic limbs because of several collaterals. Some of the collateral vessels will have to be ligated and divided and the CFV and FV taped to expose the profunda over the posterolateral aspect.

Above-knee portion of the popliteal vein is exposed by a longitudinal incision made over the lower medial aspect of the thigh in the intermuscular groove between superior edge of sartorius and the inferior edge of vastus medialis. The deep fascia is incised longitudinally. The sartorius, semimembranosus, and the gracilis are retracted posteriorly and the adductor magnus anteriorly. The adductor canal is exposed and the vessels are dissected from the pad of fat.

Below-knee portion of popliteal vein is approached through a long incision starting from 1 to 2 cm below the medial tibial condyle and extending to the leg for about 10–12 cm along the posterior border of tibia. Deep fascia is incised. The semimembranosus and semitendinosus may be divided at its attachment. Plane between the soleus and gastrocnemius is developed. The soleus is retracted anteriorly and the medial head of gastrocnemius posteriorly. The popliteal vessels are located in the loose areolar tissue with the vein lying anterior to the artery.

Full posterior exposure of popliteal vein in the prone position is required for axillary vein transplantation to popliteal vein. An "S"-shaped incision with its transverse portion lying over the popliteal crease is the preferred choice.

Preliminary Exploration and Findings

In post-thrombotic pathology, perivenous and wall fibrosis along with neovascularization and abundant collaterals render dissection extremely difficult. In contrast, in primary CVI, the planes are not scarred and dissection is easy.

Location of the valve apparatus is facilitated by stripping the adventitia to visualize the valve attachment lines from outside. The commissures should be located and the angle between the two cusps noted. In primary valvular incompetence (PVI), this angle is widened. Use of a magnifying loupe (×2) and illumination with a headlight are helpful. The valve located in the femoral vein just below the profunda takeoff is the preferred site for repair. A more prominent valve can be easily located in the common femoral vein, higher up. Technically repair is easier at this site. Repair at the common femoral vein cannot correct the problem totally because backflow of a large volume of blood entering the femoral vein through profunda would still remain uncorrected (Fig. 18.1).

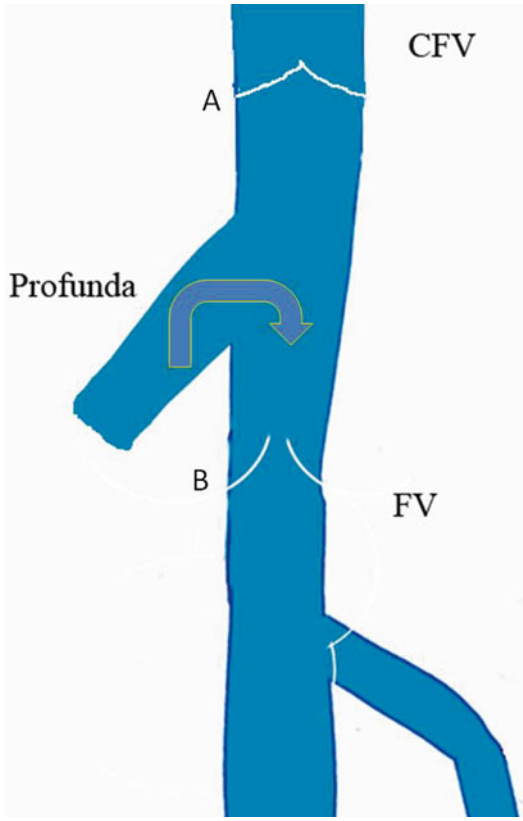

Fig. 18.1 Site of election for valve repair. Valve *B* in FV below profunda takeoff is preferred. Valve *A* at CFV is very prominent and tempting. Repair of this would still permit reflux of blood entering FV from profunda

In the *popliteal vein* valve is located at adductor tubercle level or at mid/distal segment [3]. Preoperative descending venogram and duplex scan can help in localizing the valves precisely.

Reflux in the deep veins is confirmed by the *intraoperative strip test.* The valve apparatus is located first and the infravalvular portion is controlled with a bulldog to prevent inflow. This segment is milked up through the valve to empty all blood. If the valve is competent, the infravalvular portion of the vein will remain collapsed; if it is incompetent, this segment will fill from above. To augment the reflux, the supravalvular portion can also be gently squeezed toward the valve [3, 4].

Techniques of Valve Repair

Several techniques of valve repair are available. The choice depends basically on the pathological process involved. The expertise and preference of the operating surgeon are the other factors that govern the choice of the procedure. The commonly practiced procedures are:

- Internal valvuloplasty
- External valvuloplasty
- Axillary vein transfer
- Segment transposition

Internal Valvuloplasty

The technique is suitable for patients with PVI. It is not feasible for the post-thrombotic group. The valve in the femoral vein just below profunda takeoff is the preferred site for internal valvuloplasty. The technique involves exposure and control of CFV, FV, and profunda in the groin. Venotomy of the femoral vein at the appropriate position is performed after vascular control and intraoperative heparinization. Repair of the elongated valve leaflets are done under direct visualization. The redundant cusps are plicated with 7–0 polypropylene sutures to reduce the redundancy by 20 % and to ensure proper coaptation of the cusps. The knots are tied on the external aspect at the level of commissure. Loupe magnification (×2) and frequent saline irrigation are used to define the cusps. Venotomy is closed with meticulous care and competence is checked again (Fig. 18.2).

Several types of venotomies have been described: Kistner has described longitudinal venotomy starting 10–15 mm caudal to valve attachment line and extending up through the commissural apex [7]. Raju recommends transverse venotomy 5 mm above the commissural apex [8]. Sottiurai introduced T incision, a supravalvular transverse incision with distal extension into valve sinus [9]. Tripathi introduced trapdoor venotomy, two transverse incisions connected by a vertical limb, for optimum exposure [10].

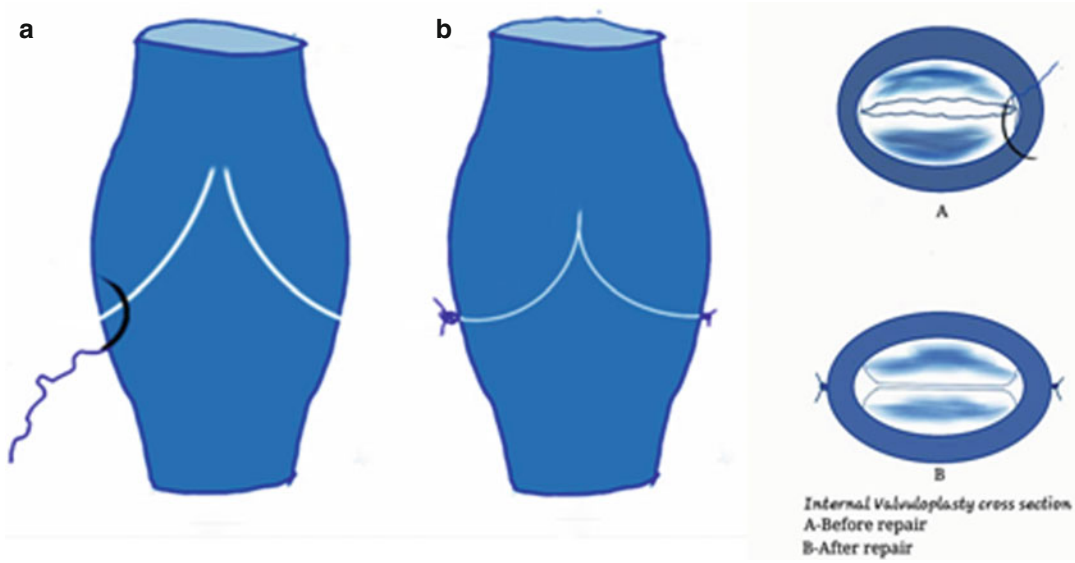

Fig. 18.2 Internal valvuloplasty. (**a**) Valve cusp before repair. Long floppy and incompetent. (**b**) Post repair cusp shortened and competent

The advantages of internal valvuloplasty are that it offers an anatomically precise repair since it is carried out under direct vision and the results are more lasting. The disadvantages of the techniques are that it is time consuming, is not feasible for multiple site repairs, and needs postoperative anticoagulation. The technique is unsuitable for damaged and deformed cusps of the post-thrombotic limb.

External Valvuloplasty

This technique was also introduced by Robert Kistner. It does not require a venotomy and is suitable only for PVI. In this procedure, the valves are repaired by placing sutures transmurally. Widening of the angle between the cusps is considered to be the reason for incompetence. When the angle is narrowed, the valve sinus becomes deepened and prevents reflux. A series of interrupted or continuous sutures placed both at the anterior and posterior valve attachment lines to cover about 20 % of the line. This is sufficient to restore competence. If more narrowing is needed, it is better to abandon the procedure in favor of axillary vein transfer [3] (Fig. 18.3).

Advantages of external valvuloplasty are many. It avoids venotomy and hence postoperative anticoagulation is not needed. The technique needs less time compared to the internal technique. Multiple site repairs can be undertaken: femoral and profunda vein at the groin and the popliteal/posterior tibial vein at the knee level. This is known as triple external valvuloplasty. The major disadvantage is that it is unsuitable for the post-thrombotic pathology.

Modifications of External Valvuloplasty

External banding technique is suitable when venospasm during surgery restores competence. These are cases where the incompetence results from vein wall dilatation. There are two methods.

1. *Prosthetic sleeve*. An external wrap using a Dacron/Teflon graft is wrapped around the vein at the level of the valve with tightness sufficient to restore competence. This acts as a restraint to prevent undue dilatation of the vein wall around the valve. The graft is

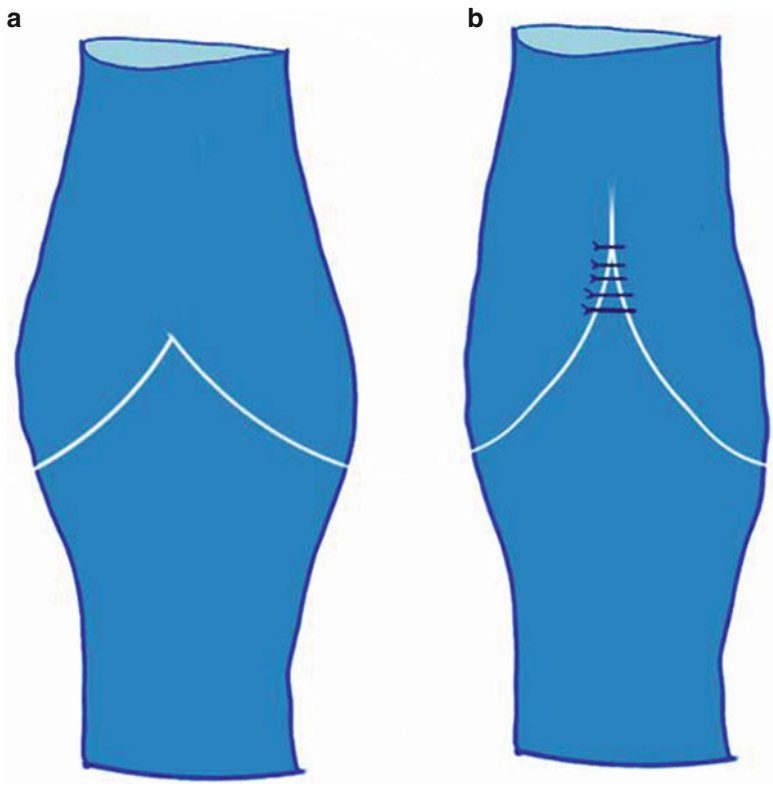

Fig. 18.3 External valvuloplasty. (**a**) Before repair. Note the wie angle between the cusps. (**b**) Post repair. Angle narrowed

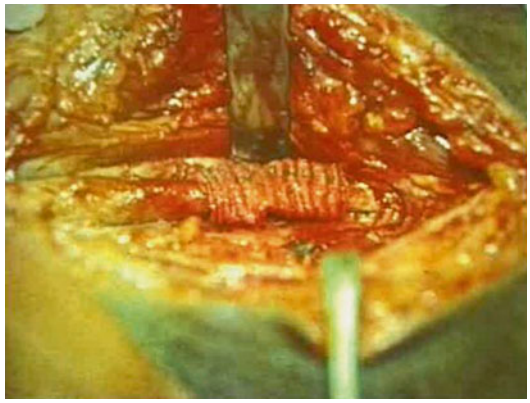

Fig. 18.4 External wraparound with Dacron sleeve

anchored to the adventitia to prevent migration [4]. This method is employed to prevent late dilatation after any technique of valvuloplasty [4] (Fig. 18.4).

2. *Venocuff device*. This is a silicon-reinforced Dacron tube which can be slipped over the vein and progressively tightened to regain competence [11]. The technique is reported to be effective in post-thrombotic limbs also [12].

Angioscopic repair is a modification of the external valvuloplasty. The valve apparatus is visualized through an angioscope passed through a small venotomy above valve station or through a side branch of GSV. The repair is done under vision. The sutures are placed transluminally instead of transmurally, at the level of valve attachment lines to tighten them. The venotomy is closed after repair. The technique was pioneered by Gloviczki and his colleagues from the Mayo clinic [13].

Transcommissural valvuloplasty was pioneered by Raju. Transluminal sutures are placed as in the previous case but "blindly" without the aid of angioscope. Initial suture starts at the commissural angle and is shallow. Each subsequent suture should be placed slightly deeper into the lumen than the previous one and tied. According to Raju, although this is a blind technique, valve competency can be routinely achieved [14].

Limited anterior plication. Circumferential dissection of the vein is reported to increase late post-repair dilatation. The technique of limited anterior plication was introduced to prevent late

dilatation. Both transmural and transluminal sutures with the use of angioscope have been described. The procedure involves dissection of femoral vein over anterior aspect only. Running mattress sutures are placed only at the anterior commissure. The sutures start from a point 3 to 4 mm proximal to angle of valve cusp and extend up to the angle. Combined with high ligation and stripping, this method is reported to provide good long term results [4].

Vein Valve Transplantation (Axillary Vein Transfer)

This technique was first introduced by Taheri and his group in 1982. The procedure is useful in post-thrombotic pathology. The axillary vein is exposed by a transverse incision along the skin crease in the axilla. Two to three cm of axillary/brachial vein bearing a competent valve is harvested. The axillary vein would be a suitable size match for the femoral vein. Ligation of the cut ends of the donor vein does not produce any ill effects [3]. The recipient vein can be either the femoral vein in the groin, just below the takeoff of the profunda or the popliteal vein. The latter site is the "gateway" to control all the proximal reflux. A full prone position is preferred to expose the popliteal vein.

After heparinization, the recipient vein is divided at the appropriate level. The proximal anastomosis is completed first. Interrupted sutures are preferred since continuous sutures can produce luminal narrowing. Valve competence is confirmed by releasing the clamp after proximal anastomosis. Forty percent of the axillary valves may be incompetent [4]. This can be repaired by transcommissural valvuloplasty. The distal anastomosis is completed without reapplying the clamp. This is to allow full distention of the donor segment. The distal end of the recipient vein can be trimmed to achieve optimum tension. Torsion and tension are to be strictly avoided. A Dacron sleeve wraparound helps to prevent late dilatation. In post-thrombotic veins, intraluminal synechiae in the recipient femoral vein could be excised to create a suitable lumen for anastomosis [3] (Fig. 18.5).

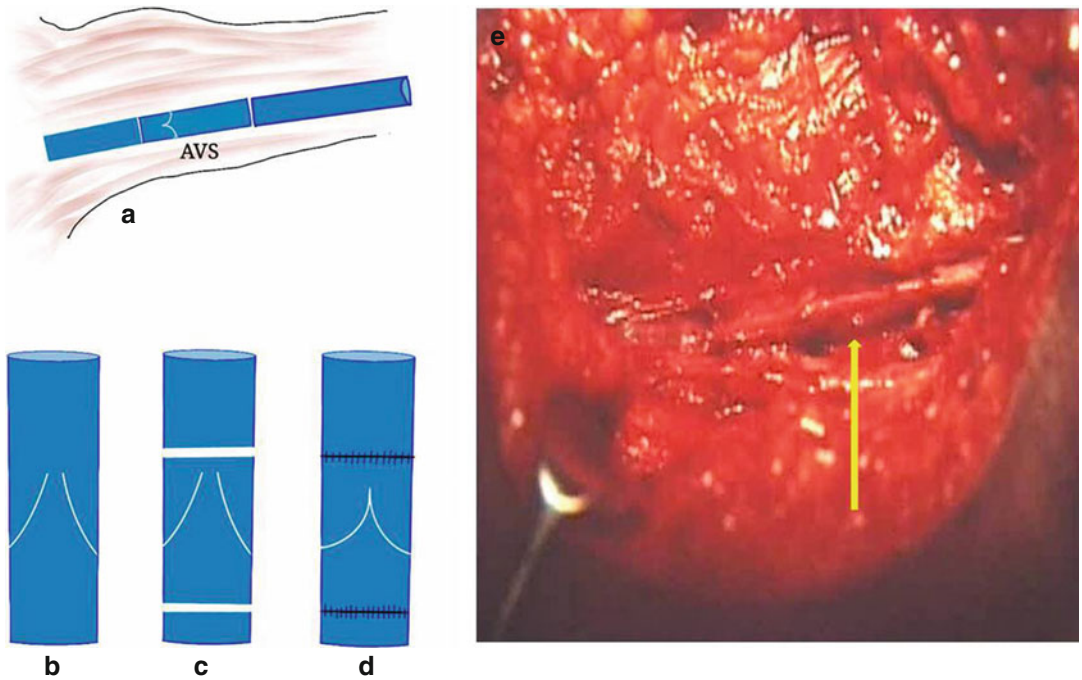

Fig. 18.5 Axillary segment transfer. (**a**) Axillary vein with competent valve being harvested. (**b**) Incompetent FV. (**c**) Segment of FV excised. (**d**) Replaced by axillary vein segment with competent valve. (**e**) Operating photograph axillary vein segment transferred (*yellow arrow*) to PV

The advantages claimed for the axillary to popliteal vein transplant include: [15]

- Size match of the transplanted axillary vein segment to the host popliteal vein.
- Restoring the popliteal valve function at the critical "gatekeeper" position would control all reflux above the calf muscle venous pump.

Segment Transfer

The technique involves redirection of flow from an incompetent to a competent parallel channel. This was introduced by Ferris and Kistner. The receiving vein, usually the GSV or the profunda, should have adequate caliber and have competent valves. The surgery is usually carried out for correcting an incompetent femoral vein in the groin. The femoral vein is divided just below the incompetent valve. The proximal end is sutured.

Two options are available:

(a) The distal end is anastomosed end to side to GSV below a competent junctional valve.
(b) It could be anastomosed end to side to the competent profunda below its takeoff (Fig. 18.6).

Such a situation of isolated femoral vein incompetence with competent GSV/profunda seldom presents in clinical practice. Therefore, this is the least reported technique [3].

Postoperative Care and Complications

Anticoagulation is continued as per the usual protocol for 2–3 months for all patients undergoing internal valvuloplasty and axillary vein transfer. Early ambulation is recommended. Class II or class III below-knee stockings would be a requirement as long as risk of ulceration persists. Patient compliance is notoriously poor. Patients stand the procedure very well. Mortality after valve reconstruction is rare [3]. The common complications are:

Seroma and hematoma. This is common especially in patients on anticoagulation. Disruption of the groin nodes and lymphatics can aggravate this. Suction drains are useful.

Sloughing of wound edges would result if the flaps are reflected in the extrafascial plain. An "S" incision in the groin can minimize this.

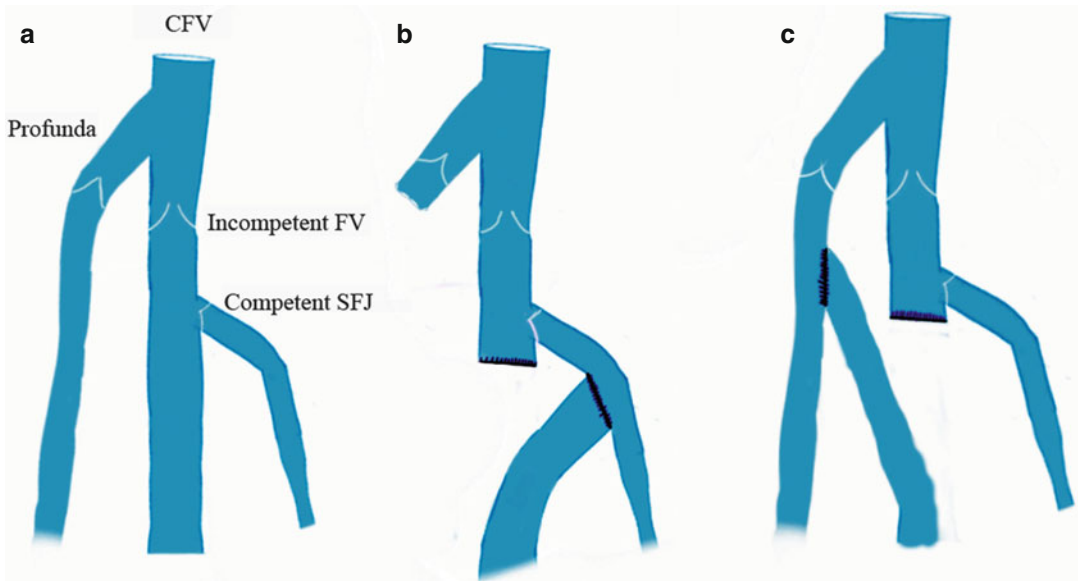

Fig. 18.6 Segment transfer. (**a**) Incompetent FV with competent GSV/profunda. (**b**) FV divided and anastomosed end to side with competent GSV. (**c**) FV to competent profunda

Postoperative deep vein thrombosis occurs in 4 % of patients. The incidence is no different in the post-thrombotic cases after valve reconstruction. But the latter group is reported to be prone for interval recurrent thrombosis [3]. The thrombus is more often encountered at a site remote from the valve repair in the same or opposite limb [3]. Pulmonary embolism can occur but is very rare [4].

Aggravation of the limb swelling. This is observed in the early postoperative period and may be due to disruption of the groin lymphatics. It settles down with compression and elevation.

Valve Reconstruction: Outcome

The literature on this subject is vast and conflicting. Michael Dalsing has reviewed this extensively and the following is a summary of his findings [4].

Clinical Outcome

- In Kistner's series, the 5-year competency of internal valvuloplasty is 60–70 %.
- Tripathi and his team reported a competency rate of 31.3 % and ulcer-free rate of 50 % at 2 years using multiple external valvuloplasties
- Raju reported a competence rate of 63 % at 3 years using transcommissural repair.
- Over 50 % of patients who had undergone axillary vein transfer showed clinical improvement even after 8 years.
- Forty to fifty percent of patients who have undergone transposition showed improvement at 5 years.
- Saphenous surgery combined with limited anterior plication of femoral vein showed a competency rate of over 90 % at 3 years.
- Tripathi has reported his comparative outcome of single versus multilevel repairs. With single-level repair, the competence and ulcer healing at the end of 2 years were 59.4 and 54.7 %; with multilevel repairs, the figures were 79.7 and 72.9 %, respectively [4].

Our experience has not been very encouraging. In a series of 44 patients (3 internal valvuloplasties, 34 external valvuloplasties, and 7 axillary vein transplants), the ulcer recurrence rate was 60 % at 2 years.

Hemodynamic Outcome

Plethysmographic studies, both APG and PPG, are reported to show considerable improvement of the hemodynamics after valve repair [4]. AVP studies demonstrated improvement of the postexercise venous pressure but not normalization, after valve reconstruction in our patients. The AVP pattern is a good predictor of ulcer recurrence after valve repair.

Valve reconstruction is not the panacea for patients with CVI. There is a common belief that the more complex a surgery, the better the outcome. This is far from true in CVI. In fact, simple is beautiful here. Correction of deep vein reflux in isolation is not recommended. Such an approach contradicts the concept of optimal treatment. Valve reconstruction is an adjuvant to conventional surgery. In the post-thrombotic group, it is considered a last-ditch salvage effort. The attempt is worthwhile even if the results are not very promising [3]. No difference in clinical outcome is observed between the various techniques of valve reconstruction [3]. According to Raju, "All things being equal, the choice of technique is largely governed by personal preference and the experience gained with a certain technique" [3].

Newer Trends

Two areas of intense research in this field include artificial valves and endovascular methods of valve deployment.

Artificial Valves

They can be nonautologous or autologous.

Nonautologous Valves [4]

- *Allograft valves*. Cryopreserved valve allograft has been tried in human beings [16]. The tissue is obtained from femoral vein as per the organ donation rules and cryopreserved. ABO compatibility is ensured. In women Rh compatibility is also desirable. Prior to insertion in the recipient vein, the cryopreserved valve is thawed by a four-step procedure. The donor vein could be inserted either into femoral vein or popliteal vein. The outcome is not very bright and the authors recommend this only when all other options have failed [16]. Cryopreserved and decellularized valve allografts have less immunologic reaction [17].
- *Xenograft valves* also have not been found to be sustainable. The use of nonvascular tissue for creation of valve has met with some success in experimental studies. The most promising results were observed in xenograft valve made from small intestinal submucosa (SIS valve) [17].
- *Synthetic valves.* Liquid Pellethane valve and platinum/pyrite carbon-covered titanium valves have been tried in animal models with limited success [17].

Autologous Valves

Dalsing and his colleagues have created autologous valves in experimental animals by invaginating a length of vein into itself as described by Eiseman and Malette. Significant length of vein is needed for its construction and this forms the main limitation of this technique [18]. Tissue engineered bioprosthetic valve has been tried in sheep [19]. Raju and Hardy used autologous venous tissue to make valves in patients. Good results were reported by them but it could not be reproduced by other workers [20]. Plagnol and his colleagues have tried a technique of invaginating a stump of GSV into the femoral vein and fashioning a bicuspid valve from this. Encouraging results in patients are reported by these workers [21].

The Italian valve of Maleti is the most promising option in post-thrombotic veins. A bicuspid or monocuspid valve is created by gently dissecting and layering the intima/media of the thickened wall of the post-thrombotic vein. These sheets are used to form the cusps. Forty neovalve reconstructions in 36 patients (32 post-thrombotic and 4 valve ageneses) have demonstrated encouraging results. DVT was reported as a complication in several patients [22].

Endovascular Approach

Expandable stents with incorporated allograft valves which could be deployed percutaneously would be the least invasive approach for this complex problem. Several trials are under way. But it is too early to predict the widespread application of such a procedure [17].

Summary

Recognition of reflux changes in the deep venous system in patients with chronic venous insufficiency along with changes in the superficial and perforator systems has been a major shift in our understanding. Need for valve reconstruction exists in patients with primary CVI and also in PTS.

Introduction of the technique of valvuloplasty by Kistner opened a new dimension in the therapy of these patients. Currently several techniques of valve reconstruction in the deep veins for correcting reflux are available in selected centers. It is important that the patients for such reconstructions be properly selected. Only a subset of patients who have recurrent ulcers after less major interventions are considered for the surgery.

Several models of autologous and nonautologous valves are under trial. The trend now is a shift from valve reconstruction to endovenous stenting.

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Deep Vein Obstruction: Management Strategies

19

Subramoniam Vaidyanathan

Contents

Introduction

Chronic obstruction of the venous system in the lower limb is commonly encountered in the femoroiliocaval segment and the commonest pathology is post-thrombotic. Nonthrombotic iliac vein lesion, due to extra luminal compression, is now increasingly identified as a cause for chronic venous disorder. In the infrainguinal segment, obstructions result from post-thrombotic pathology.

This chapter reviews the following aspects:

- Causes of outflow obstruction
- Clinical features and evaluation of outflow obstruction
- Technique and outcome of stenting for iliac vein occlusion
- Open surgery for iliac veins occlusion
- Treatment of infrainguinal obstruction

Causes of Deep Vein Obstruction

Thrombotic pathology affecting the iliac vein is the commonest cause of obstruction of the deep veins of the lower limb. This results from poor recanalization after DVT. It is reported that only 20 % of iliac veins recanalize completely with anticoagulation therapy. Typically, lesions involve the common and external iliac veins with irregular stenosis and prominent collaterals.

Nonthrombotic iliac vein lesion (*NIVL*) [1] is being increasingly identified and considered

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significant. It is usually known as May-Thurner syndrome/Cockett's syndrome/iliac vein compression syndrome. There is varying degrees of extraluminal compression along with intraluminal membranes, webs, or bands. It is more common in the left common iliac vein origin where it is compressed by the right common iliac artery. Women in the childbearing age are commonly affected. However, this has been reported in elderly males and on the right side also.

Rare causes of outflow obstruction include neoplasms both benign and malignant, retroperitoneal fibrosis, irradiation, and cysts and aneurysms.

Infrainguinal obstructions can involve the femoropopliteal segments or the infragenicular segments. Majority of these lesions result from thrombotic pathology and patients present with features of the post-thrombotic syndrome.

Clinical Features and Evaluation

Patients with outflow obstruction present with three features: swelling, pain, and discoloration/ulcers over the ankle. In the majority of patients, there is a combination of obstruction and reflux leading onto high venous pressure. Obstruction is responsible for swelling and the typical pain of venous claudication. This is described as an exercise-induced, severe bursting pain requiring rest and elevation for relief. Proximal obstruction can lead onto progressive distal incompetence of superficial, perforator, and deep veins. The reflux-induced venous hypertension is mostly responsible for the changes in the skin and subcutaneous tissues around the ankle, including ulcerations. Clinical examination reveals a swollen limb with varicose veins. Presence of distended supra-inguinal collateral veins is a telltale evidence of obstruction of the outflow tract.

Investigations

Both hemodynamic and anatomic studies are used for confirming obstructions and assessing the severity.

Hemodynamic Studies

Generally, these tests are not very sensitive to identify outflow obstruction [1, 2]. Normal values do not always rule out significant obstruction. The techniques suggested are:

- *Plethysmographic outflow fraction determination*. Air plethysmography is recommended when the duplex scan findings are not very conclusive.
- *Hand-foot pressure differential and hyperemia-induced increase in foot venous pressure*. A negative test does not rule out significant obstruction. This test is reported to be insensitive for the diagnosis of outflow obstruction [3].
- *Femoral venous pressure*. This can be undertaken during venographic or intravascular ultrasound studies. Significant findings are a pressure gradient of 2–4 mm across a stenotic lesion on provocation, with slow return to normal (over 30 s), and a gradient of 2–5 mm on augmentation of flow, compared to contralateral femoral pressure [1].

Anatomical Studies [1]

- *Ascending venogram* is not very sensitive in visualizing the iliac segment. It can provide information on the inflow to the iliac segment.
- *Antegrade femoral venogram in multiple planes* and with the DSA technique can visualize iliac obstruction adequately. Presence of collaterals is supposed to indicate a compensated obstruction. But this is not always true.
- *Intravenous ultrasound* (*IVUS*) is currently the most optimum investigation to delineate iliac vein obstructions. This can effectively visualize intra- and extraluminal compressions. IVUS has recorded more than 50 % obstruction, in more than one fourth of limbs, in whom venogram has been reported as normal [1–3]. IVUS can detect axial collaterals running close to the original vessel, but transpelvic collaterals escape detection. IVUS can demonstrate intraluminal details, trabeculations, and webs that may not be visualized in a contrast venogram. It can clearly delineate deformity of venous lumen due to external

compression. In addition, it can delineate wall thickness, neointimal hyperplasia, and pulsations [3]. Transfemoral venogram significantly underestimates the degree of stenosis by 30 % [3].

Treatment Options

At present, two options are available for the treatment of chronic iliac vein obstructions: percutaneous endovenous stenting and surgery (bypass/open reconstruction). Percutaneous endovenous stenting is the primary treatment for chronic iliac vein obstructions [4].

Percutaneous Endovenous Stenting

This is the method of choice in the majority of patients and has almost completely replaced bypass or open surgery for chronic iliac vein occlusion. Two types of stents are available: balloon-expandable stents and self-expanding stents [5].

The balloon-expandable stents are mounted on a balloon and deployed at the site, through an introducer sheath. The balloon is inflated at the recipient site with the stent on it, which distends to the predetermined size. When the balloon is deflated, the expanded stent remains in place. The diameter of the balloon would determine the diameter of the stent. These stents are not suitable in locations where external physical forces are powerful, such as the groin. They cannot expand, if bent or crushed. They also shorten when expanded. They are useful in locations such as the pelvis where external compressive forces are not prominent. They have to be used with caution in pregnant women since the enlarged uterus can crush them. Balloon expandable stents have a high radial force than self-expanding stents [5]. An example of the balloon-expandable stent is the Palmaz stent (Cordis Corporation, Miami, Florida, USA).

Self-expanding stents are available in greater lengths and larger diameter. They can re-expand if compressed or crushed. They conform to curved vessels, and their deployment is technically easier. Examples of such stents are the Gianturco stainless steel stent and the Wallstent venous endoprosthesis. These stents are usually made of stainless steel [5].

Nitinol-based stents are also available in the market. *Nitinol* is an alloy of *nickel* and *titanium*. This has good shape memory and superior elasticity. They are self-expanding stents. Their size is slightly larger than the target vein. They do not shorten on dilatation or on deployment. But they can be compressed by external forces. To improve the radio opacity of nitinol stents, markers are attached to the stent struts [6].

There is a recent report of use of *fully dedicated venous stents* in a small group of patients. (See later.)

Technique of Stenting [1]

Indications for stenting include symptomatic patients (distressing venous claudication and recurrent ulcerations) with iliac vein occlusion in the presence of adequate inflow and outflow. Ideal indication would be isolated short-segment (12–20 cm) iliac vein occlusions with patent infrainguinal segment and a patent IVC. In our experience such an ideal anatomy is rather uncommon following extensive iliofemoral venous thrombosis which leaves behind long-segment narrowing of the femoral segments and IVC (poor inflow and outflow). In fact during the last 5 years, we could undertake iliac segment stenting in only six patients; four of them had a localized occlusion of iliofemoral segment following femoral vein cannulation, and two had posttraumatic stenosis. We have no data on the prevalence of iliac vein compression among our patients. Contra*indications* for stenting are asymptomatic patients, those with occlusion of femoral vein (poor inflow), and those with occlusion of IVC (poor outflow) [4]. Inclusion of stenting of inflow and outflow areas is now reported to provide good patency [1, 7].

Technical Details

The procedure can be performed under local or general anesthesia. It should be attempted only in fully equipped endovascular or angiographic suite. Administration of prophylactic antibiotic is desirable. Ultrasound guidance for cannulation is mandatory, and the availability of IVUS is an added advantage.

Usually an antegrade approach in the femoral vein or popliteal vein distal to iliac obstruction is preferred. Sheath is passed into the femoral vein, and a guide wire is placed. Transfemoral venogram is performed. IVUS is carried out if available and the extent of obstruction is carefully assessed. Fifty percentage or more reduction in cross-sectional area on IVUS is defined as significant stenosis [3, 7]. Intraprocedural anticoagulation is started. The post-thrombotic vein can usually be easily traversed. If there is difficulty, guide wire recanalization and sequential balloon dilatation of the tract are needed before stent placement. The entire tract is dilated to 14–16 mm width. Veins withstand dilatation well without rupture. Angioplasty alone is not sufficient to treat venous stenosis since recoil is significant in the venous system [8]. Hence, stenting is mandatory.

It is important to oversize the stent by 10–15 % [7]. Self-expanding braided stainless steel stents are used. They are longer, have larger diameter, and are flexible and less liable to deformation by external pressure, arterial pulsations, and the inguinal ligament. The common size used is 16 mm in diameter and 60 mm in length [9]. Adjacent to the confluence of the common iliac vein the stent should be inserted well into the IVC to prevent early caudal migration [1]. With multiple focal stenosis, two or more stents are inserted overlapped by at least 2 cm to avoid any skipped area between the stents. It is important to stent the entire lesion [1]. Post completion venogram and IVUS are performed. Procedure can be carried out as a day case. Patients are discharged with low-dose aspirin (Fig. 19.1).

Post Stenting Complications

Neglen and his colleagues in a series of 982 consecutive patients of nonmalignant obstructive lesions of the iliac segment reported no mortality. The complications reported include [1]:

(a) *Access-related complications*. Hematoma, injuries to femoral vein/femoral artery, retroperitoneal hematoma, etc., are reported. But these events can be minimized by USG-guided cannulation.

(b) *Early thrombotic events* (*less than 30 days*). Neglen and colleagues reported an incidence of early thrombosis of 1.5 %.

(c) *Late thrombotic event*. Twenty-three patients had ipsilateral thrombosis at a median of 13 months after stenting. Seven patients had late thrombosis of contralateral limb.

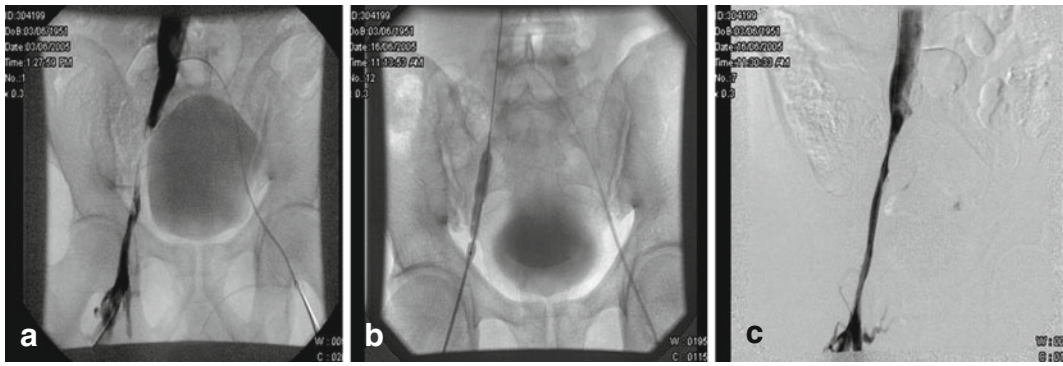

Fig. 19.1 (**a**) Localized block of iliac vein with good inflow and outflow. (**b**) Stenting in progress. (**c**) Post stenting appearance. Stent has to be oversized by 1.5 times

(d) *Stent migration*. This is an unusual complication reported by Mullens and his team. They have reported migration of iliac vein stent for May-Thurner syndrome to the heart [10].
(e) *Stent infection*. This is also an unusual complication reported by Dosluoglu et al. These complications were diagnosed by CT scan. One of the cases presented 6 months after insertion secondary to remote bacteremia. Both cases were treated surgically. A high index of suspicion is necessary to diagnose stent infection. Prophylactic antibiotics should be administered in high-risk situations [11].
(f) *Stent fracture*. There are anecdotal reports of infrainguinal stent fractures. Such events are common with balloon-expandable stents [1].

Results of Iliac Vein Stenting

Stent Patency

The outcome depends on the nature of the pathology, whether thrombotic or nonthrombotic. The overall primary, assisted primary, and secondary cumulative patency rates reported by Neglen and team at 72 months were 79, 100, and 100 %, respectively, for nonthrombotic lesions. The outcome for thrombotic lesions was 57, 80, and 86 % [12]. Cumulative rate of in-stent stenosis (more than 50 %) at 72 months was 1 % for nonthrombotic and 10 % for thrombotic lesions [12]. Patency was much better in patients with NIVL than those with thrombotic disease [12]. Factors adversely affecting stent patency include young age, thrombotic lesions, long lesions requiring several stents, and higher degree of stenosis on IVUS [12]. The intervention side (left or right lower limb), gender of the patient, and thrombophilic state were not associated with increased stent block.

Clinical Outcome [12]

- *Pain and swelling*. In Neglen's series of patients, the rate of limbs with severe pain dropped from 54 to 11 % after the intervention. Gross swelling decreased from 44 to 18 %.
- *Ulcer healing*. The authors reported a cumulative rate of ulcer healing at 5 years of 58 %. Eight patients had recurrence of ulcer.
- *Quality of life*. There was significant improvement in QoL assessment.

Hemodynamic Outcome [12]

Improvement of the venous filling time, venous filling index, and venous volume was observed only after correction of superficial vein reflux also in addition to stenting. AVP and hand-foot pressure differential were shown to improve with stenting alone. When the obstructive component is relieved by stenting, the preexisting reflux is aggravated. This is because the obstructive pathology masked the intensity of reflux.

Iliac vein stenting alone significantly improved clinical outcome in a group of patients with combined obstruction and axial deep vein reflux, even though deep vein reflux was left untreated [13]. A subset of patients presenting with primary CVI with reflux pathology demonstrated presence of significant obstructive NIVL on IVUS evaluation. Iliac vein stenting has shown considerable improvement in this group even when the deep vein reflux is left uncorrected [14]. Neglen and colleagues in a subsequent report recommended elimination of superficial reflux along with stenting for a better outcome [12, 15].

Alerany and team in a report of endovenous treatment of iliofemoral chronic post-thrombotic obstruction in 41 limbs in 36 patients have reported successful outcome with no mortality or morbidity in 39 limbs (95 %) [16]. Nine limbs developed thrombotic events (23 %). At 33 months their primary, assisted primary, and secondary cumulative patency rates were 74, 87, and 89 %, respectively. The main risk factor for stent occlusion in this study was the severity of the thrombotic lesion. Thrombophlia, stent brand used, or extension into common femoral vein were not found to be increased risk factors for stent occlusion. The revised VCSS and Villalta scores showed significant improvement after stenting. It was also observed that the axial reflux in deep veins persisted in many patients; but this did not affect the clinical improvement [16].

Most of the workers have used stents designed for arterial tree. de Wolfe and group have reported their experience with the use of *fully dedicated venous stents* (*sinus-Venous stents – OptiMed*, *Ettingen*, *Germany*) [17]. They are longer and broader and have more flexibility and radial force. From March 2012 to July 2013, 48 patients with chronic iliofemoral obstructions (both thrombotic and nonthrombotic) were treated using this stent. At 3 months their cumulative primary, primary assisted, and secondary patency rates were 83, 84, and 97 %, respectively. They have reported no mortality, low morbidity, and no clinically relevant pulmonary embolism. The outcome was better for the nonthrombotic compared to the thrombotic group [17].

These data indicate that venous stenting can be performed with low morbidity and mortality and good long-term patency rate.

Open Surgical Reconstruction of Venous Obstruction

General Considerations

The primary and preferred treatment of venous occlusion of iliac segment is endovenous stenting. The relative safety and simplicity of endovenous stenting have favored this as the treatment option. Currently the indications for open surgery are very limited. The suggested indications for open surgical treatment include patients who are not suitable for endovascular repair and failed attempts at stenting [18]. The procedures can be performed in both thrombotic and nonthrombotic obstructions. It can also be undertaken in patients with iatrogenic or blunt trauma, postirradiation, and retroperitoneal fibrosis and those with benign or malignant tumors producing external compression [18].

The technique of reconstruction is usually a bypass, using either autologous or prosthetic grafts. Anatomical in-line bypass using ringed prosthetic grafts has been performed for femoroiliocaval obstructions [19]. The outcome with open surgery has not been very encouraging because of poor long-term patency. Autologous saphenous vein grafts lose their patency especially with external compression. Prosthetic grafts are inherently thrombogenic. Best results are reported with large diameter (10 mm) PTFE grafts with external support, adjunct use of AV fistula, and meticulous perioperative anticoagulation [18, 19].

Open Surgery for Chronic Outflow Obstructions

The Crossover Bypass: The Palma Procedure (Dale's Procedure)

The original Palma procedure is a femorofemoral crossover graft with autologous saphenous vein. This is performed for unilateral iliac vein occlusion. The following criteria should be satisfied: localized unilateral iliac vein obstruction, patent common femoral vein below block, and healthy contralateral GSV with competent SF junction.

The contralateral saphenous vein is dissected and divided distally at the level of the knee joint. On the affected side, the patent common femoral or femoral vein is exposed below the block. The harvested contralateral GSV is then transposed in a subcutaneous tunnel above the pubis and brought to the affected side. It is anastomosed end to side to the femoral vein below block. It is important to ensure that there is no kink in the GSV. The tip of GSV is excised for optimum length and hooded to ensure a wide stoma. The anastomosis is performed using continuous 6-0 polypropylene sutures (Fig. 19.2).

Indications for creating distal AV fistula are vein less than 5 mm in size and a pressure differential less than 3 mm of Hg between the two femoral veins [18]. A patency rate of 70–83 % has been reported at 3–5 years. Results were better in patients with good inflow and in those with May-Thurner syndrome [18]. In the absence of a suitable saphenous vein, a cross pubic prosthetic bypass using a 8 or 10 mm expanded PTFE graft is a good alternative [18]. For bypass grafts, good clinical and venographic patency, ranging from 44 to 100 %, have been reported on 5-year follow-up [18, 19].

The In-Line Bypass: Femoroiliocaval Bypass

This is an anatomical in-line bypass for unilateral or bilateral iliac, iliocaval, or IVC occlusion. The

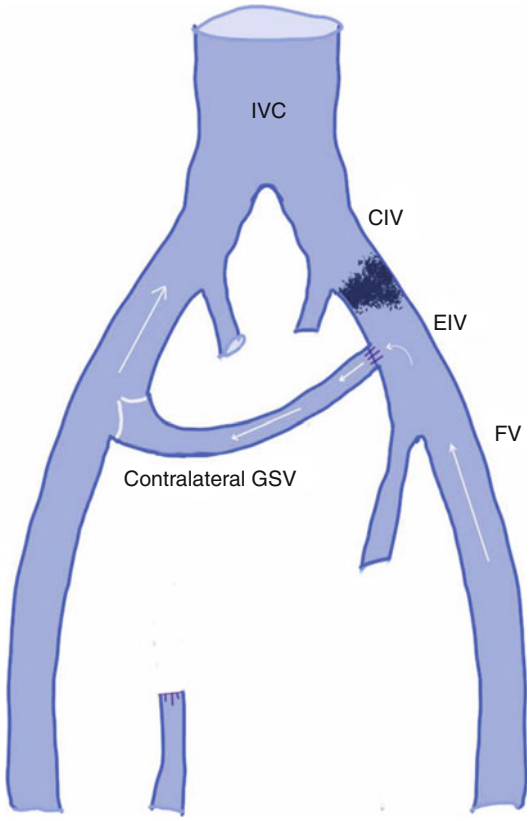

Fig. 19.2 Palma's bypass for unilateral iliac vein occlusion

conduits recommended for such bypasses are externally supported expanded PTFE grafts. The iliac vein and the distal IVC can be approached through a retroperitoneal oblique flank incision. The rest of the IVC is best exposed through a midline or a right subcostal incision. The femoral vein is exposed through a standard vertical groin incision. Conduits used for femorocaval segment is10–12 mm ePTFE graft, for iliocaval segment 14 mm ePTFE graft, and for infrarenal IVC −16 to 20 mm ePTFE graft [18].

Open Surgery for Chronic Infrainguinal Venous Obstructions

Bypass surgeries described for chronic infrainguinal venous obstructions include the May-Husni bypass for femoropopliteal obstructions and perforator bypass for infragenicular obstructions. These procedures are mostly of historical significance and are not very popular in current clinical practice.

The May-Husni Bypass

This procedure is used for obstruction of femoral vein and is basically a saphenopopliteal bypass. The preferred conduit is autologous saphenous vein. Preliminary screening with duplex scan to confirm the competence of the ipsilateral SFJ valve is mandatory. It would be an advantage to map the course of the GSV and to document its dimension in the leg. The ipsilateral GSV is dissected and anastomosed to the patent femoral/popliteal vein below the block. In the upper part, the competent SFJ provides the outflow tract, and no separate anastomosis is needed [20] (Fig. 19.3).

Coleman and his team in a recent report have presented the details of outcome of the saphenopopliteal bypass for chronic femoral vein obstruction in a series of 17 patients [21]. After a median follow-up of 103 months, the primary patency rate was 56 %, primary assisted patency rate was 69 %, and secondary patency rate was 75 %. One patient needed amputation. These authors recommend saphenopopliteal bypass for chronic femoral vein obstruction as "a satisfactory and reliable" procedure [21].

The Perforator Bypass

This procedure described by Raju is recommended for relief of obstruction in tibial vein occlusion. The competent valves in the posterior tibial group of medial calf perforators will not permit blood to flow from the blocked tibial vein into the GSV. Such nonfunctioning perforators are bypassed by anastomosing the divided saphenous vein to the posterior tibial vein below the block [22] (Fig. 19.4). The procedure is not widely practiced now.

Summary

Obstructive lesions of the deep venous system can be located at the iliofemoral segment. The cause of obstruction can be thrombotic or nonthrombotic. The introduction of IVUS and the technique of percutaneous stenting of chronic iliac vein obstructions have simplified the treatment of these lesions.

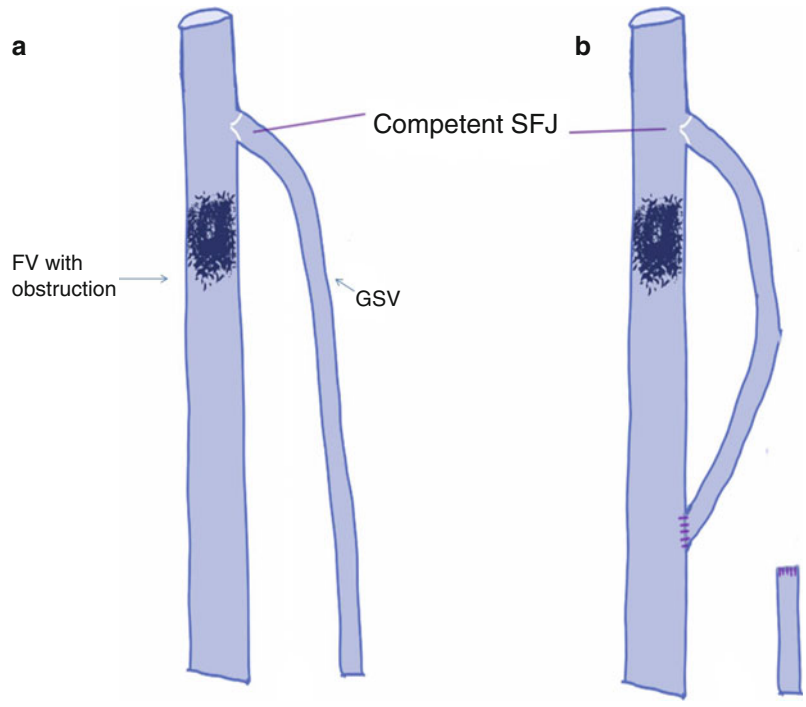

Fig. 19.3 May-Husni bypass for femoral vein obstruction. (**a**) Showing block in the femoral vein. (**b**) Anastomosis of GSV distal to the block

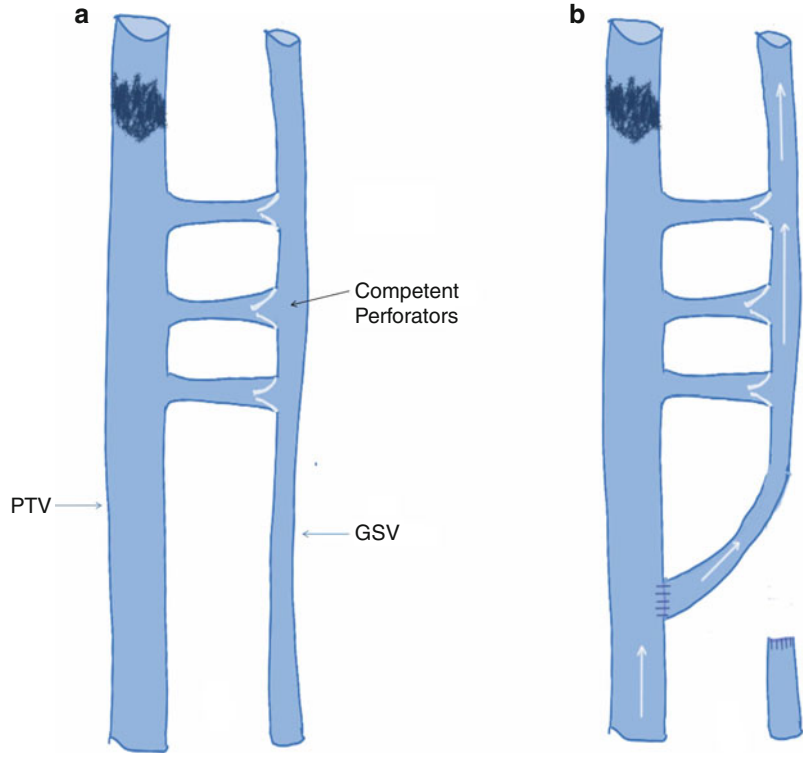

Fig. 19.4 Perforator bypass for PTV obstruction. (**a**) Showing the obstruction. The competent perforators prevent the bypass of blood from PTV to the GSV. (**b**) Post bypass

The procedure can be carried out with low morbidity and mortality. At present, percutaneous stenting is the treatment option in such patients. Open surgeries are practically abandoned.

Infrainguinal obstructions are commonly thrombotic in origin. Bypass for infrainguinal venous obstructions is not practiced widely. Recently there has been a renewed interest in some of these procedures.

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Part IV

Assorted Venous Problems

Venous Telangiectasia and Reticular Veins: Clinical Class C1

20

Subramoniam Vaidyanathan

Contents

Introduction

According to the CEAP classification, reticular veins and telangiectasias come under the C1 clinical class. These lesions are usually associated with truncal and tributary varices. Occasionally, they can present as independent lesions. Till recently, most of the C1 clinical class of patients were overlooked. There is a renewed interest in this subset of patients mainly due to two reasons. A significant number have symptoms of throbbing and pain, out of proportion to the visible extent and size of the varices. More than 80 % of patients with C1 lesions are women and cosmetic improvement is a major concern. With cosmetic dermatology evolving as an independent service, these lesions have assumed greater significance. This chapter focuses on the venous telangiectasias and reticular veins of the lower limbs associated with chronic venous disorders (CVD).

The following aspects are highlighted:

- Definition of reticular veins and telangiectasia
- Classification of small veins based on the caliber of the vessels
- Pretreatment evaluation and workup
- Sclerotherapy principles and practice
- Use of lasers/Intense pulsed light (IPL)

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Definitions

Telangiectasia

Telangiectasia is a confluence of dilated intradermal venules less than 1 mm in caliber. Synonyms include spider veins, hyphen webs, and thread veins [1]. They represent dilatations of preexisting vessels without any new vessel growth [2]. Telangiectasia can develop from several causes [2]: primary telangiectasia presents without any other primary pathology. Examples include: vascular nevi, angiomas and angiokeratomas, hereditary hemorrhagic telangiectasia, ataxia telangiectasia, etc. Secondary telangiectasias are manifestations of other pathologies. These include CVD, radiodermatitis, exposure to sunlight, etc. Telangiectasias in CVD are assumed to result from the rise in venous pressure that stretches the venous end of the capillary or the draining venule [2]. The color of the telangiectasia depends on the caliber of the dilated venule. Large dilatations (up to 1 mm) are dark blue in color; the smallest (0.1 mm) are very superficial and are red in color [2]. They do not empty on limb elevation [2]. It is suggested that the difference in the color of the telangiectasia results from difference in the oxygenation in capillary loops. The red ones represent dilatation from the arterial and the blue from the venous loop of the capillary [3].

Reticular Veins

The reticular veins are dilated bluish subdermal tortuous veins 1–3 mm in diameter [1]. On the lateral aspect of the extremity, they are part of an extensive network of the lateral subdermal venous system, a system that is separate from the saphenous system [4]. The lateral subdermal venous system, a remnant of the embryonic vena marginalis lateralis, is a system of small caliber veins extending above and below the knee on the lateral aspect of the leg [5]. Here, the flow is downward to the perforators. Reticular veins located on the medial aspect of the lower limb will usually be communicating with the saphenous system.

Telangiectasia from Reticular Veins

Telangiectasia can develop from reticular veins due to reflux [4]. Such reticular veins are called the "feeder" veins. They form the type I B telangiectasia of the Duffy/Goldman classification (see below). High-frequency ultrasound and laser Doppler perfusion imaging (LDPI) provide useful information in finding such feeder veins. Controlling the feeding reticular vein by sclerotherapy would treat the telangiectasia effectively [3].

Duffy and Goldman have proposed a classification of the venous system based on size [6].

- Type I veins – telangiectasia, spider veins 0.1–1 mm in diameter; red to cyanotic in color.
- Type IA – telangiectatic matting; 0.2 mm in diameter; red color.
- Type IB – communicating telangiectasia, these are type I veins in communication with saphenous varicose veins.
- Type II veins – mixed telangiectatic/varicose veins without direct connection to saphenous system; 1–6 mm in diameter; cyanotic to blue in color.
- Type III – nonsaphenous varicose veins (reticular veins); 2–8 mm; blue to blue green in color.
- Type IV – saphenous varicose veins measuring above 8 mm; color blue to blue green.

The subdermal network of veins in the lower limbs has been studied extensively. They are considered to have greater clinical significance than was believed till now. On the lateral aspect of the thigh and calf, as already indicated, they belong to the embryological lateral venous system [7]. This has no connection to the saphenous system. It has been reported that venous pressure from the deep veins can be transmitted to telangiectasia through minute incompetent perforators [8]. The reticular veins are considered to be part of an underlying dilated small vessel network [9].

Clinical Presentation and Evaluation

Most of the patients are women and are asymptomatic. Majority seek medical attention for cosmetic reasons. However, some women have

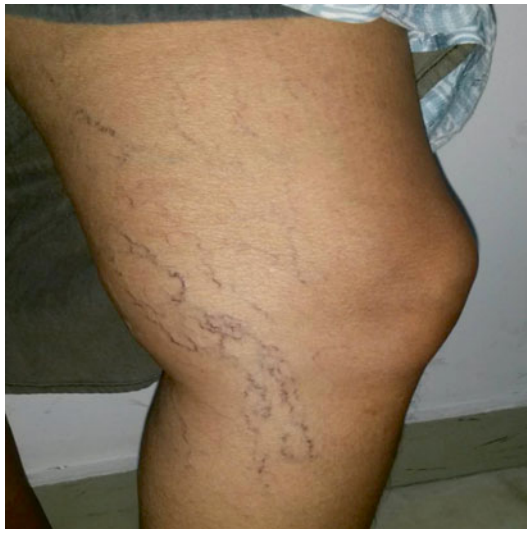

Fig. 20.1 Telangiectasia in the medial aspect of leg and thigh

symptoms of lower extremity throbbing and aches, worse during menstrual periods. The throbbing and pain are aggravated by prolonged standing and sitting and relieved by elevation and compression stockings [4, 10]. It is surprising that the severity of symptoms is totally out of proportion to the size of the involved veins. Minor varices such as telangiectasia can cause more severe leg pain than the larger varices [11].

Reticular veins and telangiectasias localized on the lateral aspect of thigh and leg and are usually asymptomatic [10]. Medial localization is not uncommon and in this location the condition may or may not be secondary to reflux in the GSV [10] (Fig. 20.1).

It is important to rule out other causes of primary and secondary telangiectasias. This is relevant especially if laser treatment is planned, since some of these conditions can be aggravated by laser application [6].

Prior to treatment, a duplex venous scan to rule out reflux in the saphenous, perforator, and deep venous system is necessary. There is general agreement that such pathologies should first be corrected before planning treatment for the smaller veins [6, 10]. The treatment outcome would be unsatisfactory in the presence of a persistent saphenous reflux [10]. No specific imaging modalities are recommended for the small veins. High-resolution US and LDPI are mentioned in some reports [3, 12].

Treatment of Telangiectasia and Reticular Veins

Certain basic issues should be understood by the patient and physician before proceeding with treatment of these conditions.

- C1 disease seldom poses any threat to the life of the patient and does not usually progress to C2 stage [10].
- The commonest indication for treatment is cosmetic. In this setting, there can be a huge gap between the expectation of the patient and the actual outcome of treatment.
- When treatment is offered to relieve the symptom of throbbing and pain in the lower limb, it is important to rule out musculoskeletal and other causes for such pain.
- Treatment of reticular veins is controversial. Reticular veins which are the feeders for type I B telangiectasia should be treated [4]. It is not very clear whether the non-feeding reticular veins should be treated or left alone [10].

Treatment Options

Treatment of C1 disease is a challenge. Surgery has no place since the veins involved are very small. Therapeutic options include sclerotherapy, transcutaneous laser/intense pulsed light (IPL), and cosmetic camouflage, if no interventions are possible [2].

Sclerotherapy for Reticular Veins and Telangiectasia

This is a simple and effective method of treatment of small veins. At present, it is considered to be the gold standard in the treatment of telangiectasia and reticular veins. For vessels less than 1 mm, only liquid sclerosants are recommended in strength of 0.1–0.2 % [4]. Foam sclerosants can be used for vessels of size between 1 and 3 mm. Both sodium tetradecyl sulfate and

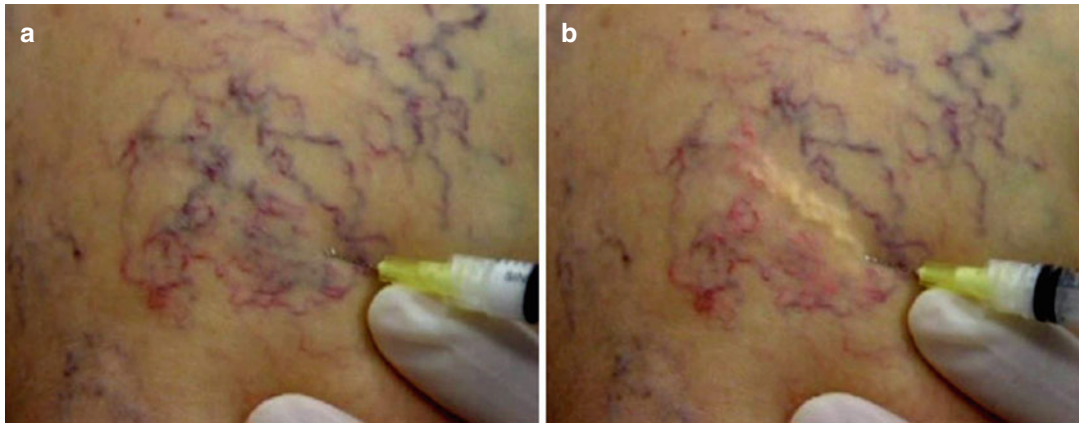

Fig. 20.2 Sclerotherapy for telangiectasia. (**a**) cannulation of the telengiectasia, (**b**) injection in progress. Note the blanching effect

polidocanol are used in concentrations from 0.1 to 0.5 %.

The injection of sclerosant is by the direct cannulation technique. One milliliter syringes fitted with 30-gauge needle is used for cannulation. Good lighting and a magnifying loupe (×2–3) are very helpful. It is always better to "test treat" a small area first, to assess the response and patient compliance [4].

For feeder reticular veins, the cannulation is done with the patient in the recumbent position. The technique of air block is useful in cannulating small veins. The tiny air bubble loaded into the syringe will produce immediate blanching of the vein if the needle is correctly placed [13]. At each site 0.25–0.5 ml of liquid sclerosant is injected [13]. Sometimes, the sclerosant can be seen to pass from the reticular vein into the telangiectasia; it is not necessary to inject the telangiectasia if this happens [4]. Soon after the needle is withdrawn, local pressure is applied by a pad and plaster. The total volume of the sclerosing agent is limited to 2–4 ml/sitting [13].

For telangiectasia the technique is almost the same. Here, only liquid sclerosants are used and the volume is only 0.1–0.2 ml/site. The injections are made at the point of convergence of the venules (Fig. 20.2a). This produces a blanching of 2 cm radius from this site [4] (Fig. 20.2b). The injection has to be performed very slowly.

After injection, the area is massaged and compression pads are applied. Extravasation can produce skin necrosis and should be avoided. If there is resistance to injection or if a bleb appears, it is stopped immediately. Application of 2 % nitroglycerine cream can minimize necrosis by producing vasodilatation [4]. Thigh-length compression stocking is applied for 3–4 days. Patient is encouraged to walk and be active. Ideal treatment interval is between 4 and 8 weeks [4]. After the initial treatment, a gap of 4–6 months is recommended before a fresh course of treatment is planned. This is to settle the skin coloration [4].

The adverse events include skin necrosis/ulceration and insufficient sclerosis. Thrombosis of the vessels is not uncommon and is treated by needle aspiration and evacuation of the clot. The technique of decompressing thrombosed 1 mm veins is called "microthrombectomy" [13]. It is performed by multiple punctures with a 22-gauge needle or by mini incisions at multiple sites [13]. An uncommon event is "matting" – presence of a fine reddish network of small veins [13].

Transcutaneous Laser Treatment

Lasers and intense pulsed light (IPL) are not replacements for sclerotherapy in the treatment of telangiectasia. Sclerotherapy is a more effective method of eradicating cannulable vessels and is the gold standard in treatment. Indications for laser treatment are non-cannulable vessels, telangiectatic matting, sclero-resistance, and needle-phobic patients [6, 14]. The advantages claimed for laser treatment are many. It is a fast and

simple noninvasive technique, requiring no wound dressings and posttreatment compression stocking. The treatment can be completed in one session since there is no maximum total dose unlike in sclerotherapy [6]. Laser treatment is contraindicated in tanned skin, pregnancy, use of iron supplements, photosensitivity, and patients prone for hypertrophic/keloid scarring [14].

Laser treatment works on the principle of *selective photothermolysis* [14]. This is based on two factors – selective absorption of light energy by the oxyhemoglobin in the leg vein and use of suitable pulse energies and pulse widths (pulse duration). The energy should correspond to the thermal relaxation time of the target. Thermal relaxation time indicates the time taken for transfer of heat, from the heated-up target tissue to the cooler surrounding tissues. To ensure optimum outcome, the following basic principles should be observed [14]:

- Appropriate wavelength better absorbed by the hemoglobin than the surrounding tissues.
- Penetration to reach the full depth of the target tissue.
- Increasing the beam diameter can increase the penetration depth.
- The energy must selectively act on the target tissue.
- No damage to the surrounding tissues and overlying skin.
- The exposure time should be such that it should slowly coagulate the vessel.

Generally the 532-nm wavelength penetrates less deeply than the 1,064-nm wavelength.

Cooling of the skin is an essential requirement to minimize thermal injuries to skin structures during laser therapy [6]. Traditionally, ice and cooling gels were used for this purpose. More effective techniques are contact cooling devices (sapphire handpieces), dynamic spray cooling with tetrafluoroethane, and low-temperature air-cooling devices [6].

Several types of laser energies are used in clinical practice for treatment of telangiectasias. The most commonly used ones are: *pulsed dye* (585–605 nm), *KTP* (532 nm), *alexandrite* (755 nm), *diode* (810 nm), and *NdYAG* (1,064 nm) [14]. It is important to standardize the different laser parameters (wavelength, pulse duration, dosage in terms of fluence and spot size) for optimum results (Fig. 20.3) [14].

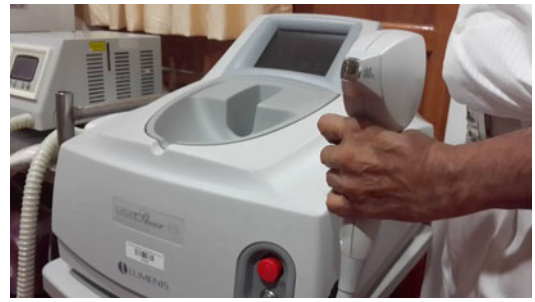

Fig. 20.3 Diode laser 810-nm unit with the probe

Intense Pulsed Light treatment [6]

Intense pulsed light (IPL) devices are nonlaser high-intensity light sources. A high-output flash lamp is used to produce a broad wavelength of noncoherent light, usually in the 500–1,200-nm range [15]. A polychromatic spectrum is emitted. Filters are placed between IPL source and patient to select the correct spectrum [6]. Usually it comes with a collar contact cooling device [6] (Fig. 20.4).

The treatment with lasers/IPL is always preceded by clinical examination to rule out any condition of secondary telangiectasia that would be aggravated by exposure to light. If the lesion is suitable for therapy, major source of reflux is first controlled. A test treatment of a small area is recommended before proceeding with the full session. This is to identify any idiopathic hypersensitivity reactions [6]. Posttreatment compression is not mandatory, but some workers recommend this [16]. Patients should avoid exposure to sunlight before and soon after treatment.

There are several reports of the successful use of laser in the treatment of venous telangiectasias.

- Fournier and team using a 532-nm KTP laser in multipulse mode for red leg telangiectasia of 0.5–1-mm size report a vessel clearance of 53 % after one treatment, 78 % at 6 weeks after two treatments, 85 % at 6 weeks after three treatments, and 93 % at 6 weeks after four treatments. They did not use any cooling [17].

Fig. 20.4 IPL unit

- Adrian has reported satisfactory outcome with a relative lack of patient discomfort in a series of 50 patients with leg telangiectasia using a long-pulse, frequency-doubled NdYag Laser at 532 nm. After two treatments 63 % showed more than 75 % improvement [18].

Neumann and Kockaert have compared the use of sclerotherapy and lasers for leg telangiectasia. According to them, the primary treatment modality is sclerotherapy. But for lesions less than 1 mm, laser or IPL treatment is also effective. They recommend compression for 48 h after both forms of treatment [15].

Many untoward side effects are described after the use of laser for leg telangiectasias. They include [6]:

- Transient or rarely permanent hyperpigmentation.
- Telangiectatic matting from incomplete elimination.
- Treatment-related pain.
- Thrombosis of telangiectasias if size is over 1 mm – this is treated by needle puncture and evacuation of clot.
- Blistering and scarring of skin. This results from overdosage of laser. It can be prevented by proper skin cooling.

The laser-related side effects include purpura for flash lamp pumped lasers, inflammatory skin reaction to long-pulse alexandrite laser and hyperpigmentation to IPL and 532-nm KTP laser.

Combined Laser/Radiofrequency Technique

This is a recent development in the treatment of telangiectasia [14]. In this system, bipolar radiofrequency and optical energy (in the form of diode laser/IPL) are combined. They can act synergistically and produce a better clearance of the skin lesions [14].

Cosmetic Camouflage for Telangiectasia

This is a simple method of concealing the blemishes in patients who do not want any interventions [2]. A liquid camouflage makeup, ColorTration Cover Makeup, is used for this purpose.

Summary

More than 80 % of patients presenting with C1 class of CVD are women. The most important reason for seeking treatment is cosmetic improvement. Symptoms such as throbbing and pain are not uncommon. It is important to control reflux in the major veins before undertaking treatment of the smaller veins. Failure to do so is an important cause for unsatisfactory treatment outcome of C1 class patients. A pretreatment duplex venous evaluation is a must in all these patients. Other causes of secondary telangiectasia should be ruled out. The preferred treatment is sclerotherapy. For smaller vessels which are non-cannulable, laser/IPL techniques can be considered.

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Pelvic Venous Syndromes

21

Subramoniam Vaidyanathan

Contents

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Introduction

Pelvic venous syndromes include a group of poorly understood disorders of the pelvic and gonadal circulation in the female, characterized by chronic pelvic pain. Broadly, two groups of conditions can be identified – pelvic congestion syndrome (PCS) and vulvovaginal varices. Lower limb varicose veins can be an associated feature in patients with PCS. The pelvic origin of these varices is not often suspected by the treating physician. Attempts to ablate the leg veins without controlling the reflux from the pelvis are an important cause of recurrence.

This chapter reviews the following aspects:

- Definition and etiopathogenesis of PCS
- Clinical features and classification
- Imaging in PCS
- Management principles
- Overview of vulvovaginal varices

Pelvic Congestion Syndrome

Pelvic congestion syndrome is characterized by chronic recurring pelvic pain and discomfort of at least 6 months duration, for which no obvious local pathology could be identified. It is experienced typically in the premenstrual phase. The pain is aggravated by prolonged standing, postural changes, or activities that increase intra-abdominal pressure. A classical feature is aggravation of pain after sexual

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intercourse – postcoital ache. It may be associated with dysmenorrhea, deep dyspareunia, and urinary urgency [1–4]. The association of pelvic pain and pelvic varices was first documented by Taylor in 1949 [2]. Apart from PCS, several other terms have been used to describe this entity [2]: pelvic pain syndrome, pelvic venous incompetence, etc. [2]. PCS is the most widely accepted terminology in current clinical practice.

PCS is observed usually in premenopausal multiparous women aged between 20 and 45 years [4]. It is rare in nulliparous women. No case has been reported in postmenopausal women [1]. Prevalence of PCS is around 30 % in patients presenting with chronic pelvic pain in whom no other obvious pathology could be found [5]. The reported incidence of this problem in the USA is one in seven women between the ages of 18 and 50 [2].

Etiopathogenesis

The etiology of PCS is not very clear. Most of the workers attribute the condition to a pelvic venous pathology. This was based on the observations of dilatation, incompetence, and reflux of the ovarian and internal iliac veins resulting in periovarian varicosities. Tubo-ovarian varicoceles have been termed the female equivalent of testicular varicocele [1]. Administration of venoconstrictors or ovarian vein ligation/embolization produced symptom relief in several patients. This is yet another finding supporting pelvic venous pathology as the possible etiological factor for PCS [1]. Several causes are suggested for the pelvic venous pathology in these patients:

- *Incompetence/absence of valves in the ovarian and pelvic veins* is a common finding and could result from congenital or acquired causes. This results in pooling and distention of the ovarian and pelvic venous system [2]. Since the valves are absent more commonly on the left ovarian veins, the pathology is more common on the left side. The incidence on the left side is around 15 % and on the right side 6 % [1]. But incompetence of the ovarian veins is not uncommon in asymptomatic multiparous women [1].
- *Pregnancy exacerbates PCS*. Gravid uterus increases venous return. It can also produce obstruction of the draining veins. Mass effect from enlarged veins in the pelvis can lead to bulk symptoms and irritation [2].
- *Estrogen* has a major role in the pathogenesis of PCS. Estrogens are known to produce venous dilatation. Absence of PCS in the postmenopausal women may be related to the decline in estrogens. Induction of hypoestrogenic state has been attempted as a pharmacological approach in the treatment of PCS [6].
- *Obstruction to venous outflow* can develop at the pelvic or suprapelvic locations. Greiner and group have identified a subset of patients with PCS developing secondary to stenosis or obstruction in a draining vein [3]. The left renal vein could be compressed between the abdominal aorta and the superior mesenteric artery – the nutcracker syndrome [3]. At the pelvic level, iliocaval obstructions, thrombotic or nonthrombotic (May-Thurner syndrome), are reported causes of PCS [7].

Factors that determine the intensity of the symptoms include response of the vein wall, presence of venous drainage routes to the lower limbs (pelvic leakage points), and location of the venous anomaly (ovarian or internal iliac tributaries) [3]. One can identify several subtypes of PCS depending on the above factors [3]:

- Ovarian vein syndrome (the classical type) is characterized by chronic pelvic discomfort and pain, dysmenorrhea, dyspareunia, and postcoital discomfort.
- Neurological syndromes are characterized by pudendal, obturator, sacral, and piriformis muscle neuralgia.
- Visceral syndromes are not very common.

It has been emphasized that pelvic symptoms may be absent or minimal when the pathological veins are effectively drained through escape routes. In this setting, the pelvic transmural pressure is not elevated. Such patients may present with congestive symptoms in the lower limbs [3].

Classification

Greiner has identified three distinct pathological processes responsible for the development of PCS [3]. Recognition of such pathophysiological subtypes would greatly help in the fine-tuning of therapy for this difficult condition.

Type I: Reflux pathology. This results from venous anomalies in pelvis without obstruction to venous flow. The common causes include:

- Congenital/acquired valvular incompetence
- Absence/destruction of valves
- Dilatation of pelvic veins (congenital or acquired)
- Venous malformations

Type II: Obstructive pathology. This results from stenosis or obstruction in a draining vein. The obstruction can be suprapelvic or pelvic. Suprapelvic obstruction can involve left renal vein (nutcracker syndrome) or in the IVC (congenital, extrinsic compression, and thrombosis). Primary causes of obstruction at pelvic level include May-Thurner syndrome and congenital anomalies of the internal iliac vein. Secondary causes include extrinsic compression and thrombosis.

Type III: Local extrinsic cause. Several local pathologies in the pelvis are to be considered and ruled out. These include:

- Endometriosis
- Tumors
- Benign mass
- Secondary uterine retroversion (postpartum)
- Post surgery/infection/adhesions
- Loss of support (Allen-Masters syndrome)
- Non-obstetric trauma

Clinical Features

PCS is common in women in the age group of 20–45 years. The condition has been diagnosed even in girls of 13 years of age [2]. There is no genetic or ethnic predisposition, but it is certainly more common in multiparous women [2]. The symptoms of PCS include:

Pelvic pain is the most common symptom. The duration of pain is more than 6 months [1, 5]. It manifests during or after first pregnancy and is aggravated by subsequent pregnancies [2]. The pain varies in intensity but is usually described as a noncyclical dull ache or heaviness that is worse in the premenstrual phase. Postural changes, prolonged standing, walking, or activities that increase intra-abdominal pressure, all can aggravate the pain. It can be unilateral, more on the left side. It can also be bilateral or shift from one side to the other. The pain is typically aggravated after sexual intercourse – postcoital ache [1–3].

Other symptoms include dysmenorrhea, deep dyspareunia, and urgency and frequency of micturition [1, 4, 5]. Pudendal, obturator, sacral, and piriformis muscle neuralgia are uncommon symptoms in some women [3]. Rectal discomfort is not an uncommon symptom of PCS [4].

Vulvar and lower limb varices. PCS can be associated with vulvar varices. They can be located over the gluteal region, vulva, and posterior aspect of thigh [1–3]. Lower limb varicose veins are common findings in a large number of patients with PCS when there is a pelvic escape route [1, 3, 5]. In a retrospective analysis of 48 women with PCS, Malgor and group have observed that all but three had lower limb varicose veins [8]. Pelvic venous reflux is reported to be a major contributory factor for recurrence of varicose veins in women [9].

Nutcracker syndrome. In this condition apart from the pelvic pain, the patient can experience flank pain along with hematuria, often microscopic than overt [2].

Palpation of the abdomen demonstrates tenderness over the ovarian point (junction of upper 1/3 and lower 2/3 of the spino-umbilical line) [1, 2]. Bimanual pelvic examination demonstrates marked ovarian tenderness, tenderness on moving cervix, and uterine tenderness. A positive history of postcoital ache along with ovarian point tenderness on abdominal palpation is considered to be diagnostic of PCS (94 % sensitive and 77 % specific) [1, 2, 10].

Imaging in Pelvic Congestion Syndrome

The road to the diagnosis of PCS is often long and arduous; it is often established only after excluding other causes of pelvic pain [4]. The

objective of imaging in PCS is to document the presence of the typical pelvic venous changes. The most widely reported finding is incompetence and dilatation of ovarian veins. Presence of dilated ovarian veins is necessary, but not sufficient for diagnosis of PCS [1]. Imaging is also important in ruling out other causes of chronic pelvic pain.

Ultrasound Scan

This is the basic imaging modality in PCS. This is useful in excluding other pelvic pathologies for chronic pelvic pain. Transabdominal and transvaginal scans are carried out. A lower limb duplex scan is also combined along with this. To enhance the sensitivity, the test is conducted in the upright position with the patient performing Valsalva maneuver. If PCS is suspected, the ovarian veins should be evaluated. Dilatation of the left ovarian vein with reversal of flow on USG is diagnostic of PCS [2]. The mean diameter of left ovarian vein in patients with PCS was found to be 7.9 mm; in control subjects, it was only 4.9 mm [11]. However, incompetent and dilated ovarian veins on helical CT scan were observed in 63 % of asymptomatic parous women and in 10 % of nonparous women [12]. Currently, an ovarian vein diameter of 6 mm or more on ultrasound is considered a significant finding supporting the diagnosis of PCS [2, 8]. This is reported to have a 96 % positive predictive value [13].

Malgor et al. have compared mean diameter of the left and right ovarian veins using ultrasonography and compared the findings with venography and concluded that the sensitivity and specificity of duplex ultrasonography to diagnose a dilated left ovarian vein were 100 and 57 % and for the right ovarian vein was 67 and 90 %, respectively [14].

Venography

Selective retrograde ovarian and internal iliac venography is recommended by many workers in patients with symptoms consistent with PCS with or without vulval varicosities [2, 13]. The American Venous Forum guidelines recommend this as the procedure of choice for diagnosis of PCS [13]. The procedure would also facilitate therapeutic transcatheter embolization or sclerotherapy. A percutaneous transfemoral or transjugular route is used to enter the right and left ovarian veins. The diagnostic criteria for PCS by retrograde venography are [13]:

- Abnormally dilated ovarian veins – equal to or more than 6 mm in diameter
- Contrast retention for 20 s or more
- Congestion of the pelvic venous plexus and/or opacification of the ipsilateral or contra lateral internal iliac vein
- Filling of the vulvovaginal and thigh varicosities

Computed Tomography and Magnetic Resonance Imaging

They can demonstrate the pelvic venous congestion effectively. But they are more expensive and do not permit a concurrent therapeutic intervention if needed. They are useful in ruling out other pelvic pathologies. The following diagnostic criteria are reported on MR/CT venography [13]:

- Four or more tortuous parauterine veins
- Parauterine veins, 4 mm or more in diameter
- Ovarian vein diameter of 8 mm or more

Phase Contrast Velocity Mapping (PCVM)

This technique employs flow velocity features to diagnose PCS. The advantage is, unlike venography, it is noninvasive. Meneses and co-workers reported a prospective study of MR phase contrast velocity mapping for diagnosing PCS in a series of nine women. All had MR phase contrast scan and venography. A retrograde or slow (less than 5 cm/s flow) in any gonadal veins was the diagnostic criteria. This related well with venographic findings. These authors recommend PCVM as a useful noninvasive tool for diagnosing PCS [15].

Diagnostic Laparoscopy

Pelvic venous congestion can be visualized during laparoscopy, but very often they are nonspecific findings. Laparoscopy is much less sensitive to venography in the diagnosis of PCS [1]. As with CT and USG, the technique is useful in ruling out other pelvic pathologies. Diagnosis of PCS was negative in 80–90 % of patients with PCS using laparoscopy [1]. Laparoscopic approach is used for treatment of established PCS [2].

Treatment of Pelvic Congestion Syndrome

There is no standardized single therapy for PCS. Treatment should be tailored to individual patient needs. Broadly two categories of PCS patients can be identified from the therapeutic point of view, those without vulvovaginal varices and those with vulvovaginal varices [1].

PCS Without Vulvovaginal Varices

Treatment options available for PCS are pharmacological therapy, interventional radiology, and surgical interventions.

Pharmacological therapy. Hormones, anti-inflammatory agents, and psychotherapy have all been tried in the treatment of PCS [2]. Induced or natural hypoestrogenic states or antagonizing the effects of estrogen by progesterone resolves symptoms of PCS [16]. Such an approach can confer short-term pain relief. Their long-term effectiveness is not yet proved [13]. The drugs used are either GnRH agonists or progesterone. The FDA has not approved these agents for the treatment of PCS. Medroxyprogesterone acetate (synthetic progestin that inhibits pituitary gonadotropins) 50 mg per day is reported to give good response [6]. Goserelin (synthetic long-acting agonist of GnRH) produced clinical and venographic improvement [16]. Etonogestrel Insert Implanon (synthetic biologically active metabolite of the progestin – desogestrel) produced significant improvement with 12 month's treatment [17]. Medical treatment has several limitations. GnRH agonists cannot be used long term, more than 6–12 months. They are not approved by the FDA for treatment of PCS. If treatment is continued for more than 6 months, an add-back therapy with low-dose estrogens is added. Many workers recommend medical treatment as the first-line therapy for PCS [1]. Interventions can be considered in patients who are not responding to medical treatment.

Interventional radiology. Percutaneous transcatheter embolization or sclerotherapy of refluxing ovarian and internal iliac vein tributaries usually as a combined treatment is the standard approach [13]. Following embolization, 76.2 % of patients showed significant improvement of symptoms along with improvement of the associated varicose veins and hemorrhoids [18]. Migration of the coils and thrombophlebitis are possible complications of embolization [19]. Notable improvement in relief of pain is reported in a study involving 127 patients following embolization [20]. Currently therapeutic embolization is the most accepted treatment option for PCS [5]. Pelvic congestion syndrome resulting from iliocaval obstructive lesions (May-Thurner and nutcracker syndromes) has been successfully treated by endovascular interventions [7].

Surgical interventions. Extraperitoneal ligation of the left ovarian vein was first carried out by Rundqvist in 1980 for the treatment of PCS [2]. Since then, many surgical interventions, both open and laparoscopic, have been performed for PCS.

- *Laparoscopic/open ligation of the ovarian veins.* Seventy-five percentages of patients have improved with this measure [1]. Ligation of the main trunk or selectively the anterior branch of the internal iliac vein has been reported to be beneficial [21]. The procedure carries the risk of injury to the ureter and iliac arteries [21]. The reflux in the internal iliac vein can be segmental, limited to few tributaries only [21].
- *Hysterectomy with left/bilateral salpingo oopherectomy*

The procedure is to be considered only in women who have completed childbearing. The beneficial effects are variable. Chung and Huh have compared results of surgery (hysterectomy + unilateral/bilateral salpingo oopherectomy) with transcatheter embolization. Based on the outcome, these workers recommend transcatheter embolization as the preferred treatment option in patients with PCS [22]. Bilateral oopherectomy in women in the reproductive age group has serious drawbacks and should be undertaken only as a last resort [22].

In conclusion the current evidence supports transcatheter embolization as the treatment option for patients with PCS.

PCS with Vulval Varices

In this subset of patients, treatment of ovarian reflux results in reduction of vulval varices, irrespective of the technique used [1, 2, 13]. If vulval varices persist, direct interventions can be considered in those with persistent symptoms usually 4–6 weeks after the original intervention [2].

Vulvovaginal Varicosities

Vulvovaginal varicosities are seen in 4 % of women [1]. Majority of such lesions develop secondary to pregnancy and regress spontaneously after delivery. They are rare in nonpregnant women. Van Cleef reports that vulvovaginal varices occur in 10 % of pregnant women during the fifth month of second pregnancy [23]. They can present as an isolated entity or along with varicose veins of the lower limbs. They can be part of the PCS [24]. When present in the nonpregnant women, they manifest in the second or third decades of life [1].

Etiopathogenesis

Vulvovaginal varices result from a combination of valvular incompetence and proximal venous obstruction. The net effect is increased venous pressure. The common sources of vulvovaginal varices include [1–3, 5]:

- In more than 50 % of patients, vulvovaginal varicosities are associated with an incompetent GSV and varicose veins of the lower limbs. The superficial and deep external pudendal veins and the posterior accessory GSV are involved in that setting.
- Insufficiency of the internal iliac and ovarian veins. This will produce varices involving the internal pudendal (back of the thigh) and obturator veins. They can have extensive connections with the vulval veins and those on the posteromedial aspect of the thigh.
- Rarely, they can arise from the round ligament veins. This condition is similar to varicocele in the male.

Vulvovaginal varicosities are commonly encountered during pregnancy. Several reasons are suggested for this [1]:

- Increased pelvic blood flow during pregnancy which impairs venous return via the femoral veins. This in turn can causes venous congestion in the lower limbs and pelvis.
- Compression of the inferior vena cava/iliac veins by the gravid uterus increasing the distal pressure.
- The hormonal changes causing vasodilatation.

The valvular anatomy of the internal iliac veins has been studied by Lepage and colleagues in a series of 82 dissections [25]. Their studies revealed that only 10.1 % of the main trunk and 9.1 % of the tributaries of the internal iliac vein had demonstrable valves. In addition to scarcity of valves in the internal iliac system, genetic structural changes in the vein wall can cause vulval varicosities. Hormonal and hemodynamic changes occurring during pregnancy are other factors [25].

Clinical Features

The condition is commonly observed in pregnant women. It can remain totally asymptomatic. The symptoms include vulval discomfort and swelling and pressure aggravated by standing, exercise, and coitus. Thrombosis and bleeding are rare

complications [23]. Most of the varices disappear 1 month after delivery [23]. In nonpregnant women, it is usually part of the clinical spectrum of PCS [1].

The diagnosis is confirmed by a simple clinical examination. It is important to examine the patient in both supine and erect postures [1, 23]. The varices usually appear as purple-blue distensible folds in the vaginal mucosa and labia. They can also present as grapelike cluster of veins around the vulva and/or medial aspect of the thigh. They may be isolated lesions or present along with varicose veins of lower limbs. When associated with PCS, there could be varices in the thighs and buttocks. Duplex ultrasound of the lower limbs is useful in ruling out connection to an incompetent GSV. Such information is useful in planning optimum treatment strategies. If vulvovaginal varicosities are associated with chronic pelvic pain, imaging to rule out PCS can provide useful information.

Conditions that can mimic vulvovaginal varicosities include venous malformations, hemangioma, hematomas, Bartholin gland cyst, and AV malformations [1].

Treatment of Vulvovaginal Varicosities

The therapeutic options would be decided by whether the condition presents in isolation or in combination with lower limb varicosities or with PCS.

Presenting as isolated lesion. Such presentation is common during pregnancy and noninterventional therapies are preferred. They include [1, 23]:

- Pelvic support (vulval support and compres sion)
- Leg elevation
- Elastic compression stockings
- Avoiding prolonged standing
- Exercise
- Sleeping on the left side

High doses of phlebotonic agents have been suggested for the relief of symptoms of pain and heaviness during pregnancy [23]. The condition is not a contraindication for vaginal delivery [1, 23]. Theoretically, laceration and massive bleeding are potential risks but are seldom observed in practice. These complications can develop in the event of a vaginal tear or during episiotomy [23]. Rarely thrombosis of the varices can occur during pregnancy. They resolve with conservative treatment. If symptoms persist, thrombectomy through mini incisions would provide relief [1]. If the varices persist for more than 3 months postpartum or if they present in nonpregnant women, they can be treated by sclerotherapy, ligation, or endovenous ablation using laser or RFA. Preferred option is sclerotherapy [23].

Presenting with lower limb varicose veins. The anatomy should be clearly defined. A duplex scan would be very informative in this setting. If the pelvic venous reflux contributes to the lower limb varicose veins, the pelvic veins are treated first. The response is evaluated after 2–3 months. In the majority of cases the lower limb varices regress considerably. Any residual varices in the perineum and lower limbs can be tackled by sclerotherapy [21]. Uncorrected reflux from the pelvic veins is an important cause for recurrence of lower limb varicose veins [9, 21, 26].

Presenting as part of the PCS. This has been considered in detail already.

Summary

The pelvic venous syndromes include both PCS and vulvovaginal varices. PCS is characterized by chronic pelvic pain especially postcoital pain along with tenderness in the ovarian point. The initial screening test is transvaginal and abdominal ultrasonography in the erect posture. An ovarian vein diameter of 6 mm or more is suspicious of PCS. The diagnosis is confirmed by retrograde ovarian and internal iliac venography. Treatment options include pharmacotherapy and various interventions. Most of the workers support transcatheter embolization with or without sclerotherapy of the incompetent ovarian and iliac veins. Any residual varices in the perineum or lower limbs can be tackled by sclerotherapy.

Vulvovaginal varicose veins can present as an isolated problem or in association with PCS. When

it presents in isolation, it is usually observed in the fifth month of second pregnancy. The varices usually regress within 1 month postpartum. If they persist and are symptomatic, they can be tackled by sclerotherapy, RFA/laser ablation, or by phlebectomy.

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Nonthrombotic Iliac Vein Lesion (May-Thurner Syndrome)

22

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Contents

Introduction

Symptomatic nonthrombotic iliac vein lesion resulting from external compression of the left common iliac vein usually by the right common iliac artery is known as May-Thurner syndrome. It is considered as a permissive lesion, requiring the superimposition of a second pathology for manifestations of symptoms. Initially it was considered to be a risk factor for the development of left-sided, iliofemoral thrombosis. The introduction of intravascular ultrasound (IVUS) has brought out the relevance of this anomaly in the genesis of primary chronic venous insufficiency. This chapter deals with the following aspects:

- Definition
- Relevance
- Anatomy and classification
- Clinical features
- Investigations – role of intravascular ultrasound
- Management

Definition

Chronic obstruction of the iliac veins commonly follows iliofemoral venous thrombosis. In a subset of patients, this segment of vein can be compressed from outside producing a compromise of the lumen without thrombosis. Such extrinsic compression can involve the left common iliac vein as the right common iliac artery crosses over it (Fig. 22.1).

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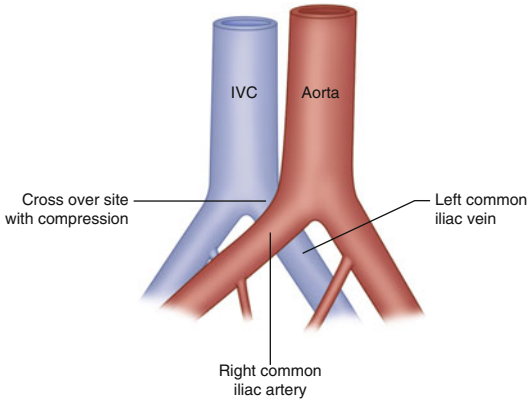

Fig. 22.1 Nonthrombotic iliac vein lesion

This anatomical finding is referred to as nonthrombotic iliac vein lesion (NIVL) and was considered to be of little clinical importance. The external compression can become severe enough to produce thickening and structural changes in the vein wall. It could also be associated with intraluminal pathologies like membranes and webs. Under these circumstances, this anomaly can become symptomatic. Symptomatic NIVL is referred to as May-Thurner syndrome or Cockett's syndrome or iliac vein compression syndrome. Neglen and colleagues in an analysis of 879 patients with iliofemoral venous obstruction identified nonthrombotic compression lesions in 53 %. These patients had no history of DVT and no venographic or ultrasound findings indicating previous DVT. These authors have further indicated that a symptomatic NIVL is an important cause of CVD [1, 2].

Historical overview. The condition was first noted by Virchow in 1851 when he noted that iliofemoral DVT was common on the left side. McMurrich conducted cadaver dissections in1908 and found adhesions in the iliac veins of 35 cadavers, 32 involving the left common iliac vein. He described isolated left lower extremity swelling secondary to left iliac vein compression. The detailed anatomical description of the condition was made by May and Thurner in 1956 using cadaver dissection. The clinical aspects were highlighted by Cockett and Thomas in 1965 [3].

Relevance

Role of NIVL in lower limb venous diseases. Though the anatomical anomaly of NIVL is widely prevalent, it was considered a rare cause of symptomatic CVD, identifiable only in 1–5 % of patients with lower limb symptoms [4]. This was because conventional venography fails to detect many of these lesions. Using intravascular ultrasound (IVUS) as the imaging modality, Raju and Neglen have reported that the incidence of NIVL is much higher in patients with symptomatic CVD [5]. Two basic issues were addressed by these workers in relation to NIVL: Why a silent lesion should become symptomatic? Further, is NIVL an incidental finding in CVD patients?

It is suggested that NIVL is a so called permissive lesion. Permissive lesions are pathologies that may remain silent until additional insult or pathology is superimposed. The triggering factors in NIVL could be trauma, cellulitis, distal thrombosis, decreasing mobility, pedal edema, etc. Very often the cause remains obscure. It was observed that isolated iliac segment stenting in symptomatic patients with NIVL detected on IVUS had produced marked clinical and hemodynamic improvement without correction of the coexisting superficial and deep vein reflux [5]. Stasis changes improved, and leg ulcers remained healed up to 2.5 years of follow-up after stenting. These findings confirm that NIVL can cause symptomatic venous disorder and is not an incidental finding in CVD patients.

Role of NIVL in Lower Limb DVT

It has been reported that lower limb DVT occurs more commonly on the left side than on the right side. Cockett and Thomas suggested that NIVL could be an important factor in the etiology of chronic iliofemoral thrombosis and in its failure to recanalize properly [6].

Anatomy and Classification

The commonest type of NIVL is a compression of left common iliac vein by the right common iliac artery (Fig. 22.1). The further progression of this compression has been evaluated by helical CT. Based on the findings of helical CT, a system of classification has been evolved [7].

- Type 1 is focal compression of the left common iliac vein at crossing point of the right common iliac artery.
- Type 2 is diffuse atrophy of the left common iliac vein between compression site and confluence of the internal and external iliac veins.
- Type 3 is cordlike obliteration of left common iliac vein [7].

Kim et al. [8] reported a sequential progression in the evolution of clinical Iliac vein compression:

- Stage I – Asymptomatic iliac vein compression
- Stage II – Development of a venous spur
- Stage III – Development of left iliac vein DVT

Although compression of the left common iliac vein by the right common iliac artery is the most common finding, several other patterns are also identified [7]:

1. Compression of the left common iliac vein by the left internal iliac artery
2. Compression of the right common iliac vein by the right internal iliac artery
3. Compression of the inferior vena cava by the right common iliac artery
4. Right-sided May-Thurner syndrome with a left-sided inferior vena cava

May and Thurner postulated that the chronic pulsations of the overriding right iliac artery led to the development of a "spur" in the vein wall and that this spur would result in partial venous obstruction. Chronic trauma to the inner side of the vein wall due to adjacent arterial pulsations leads to the accumulation of elastin and collagen, contributing to spur formation. In addition to the chronic arterial pulsations, mechanic compression of the iliac vein by the thick-walled overriding iliac artery leads to extensive local intimal proliferation, impaired venous return, and venous thrombosis [3].

Clinical Features

Patients with NIVL may remain totally asymptomatic. This is because NIVL is a slowly progressive permissive lesion. An additional pathology has to be superimposed for clinical manifestations to develop.

Symptomatic patients can present in two ways:

- With chronic venous disorders and its different degrees of manifestations
- As acute DVT

The disease is common in young women on the left side. But it can develop in both genders, at any age and on the right side too. In elderly patients, atherosclerotic changes in the overriding arterial wall can exert extra pressure on the vein. Ulcers are reported to occur in NIVL without venous reflux but are more common in the presence of reflux [5]. It is rare in nullipara and is commonly seen in multiparous women. In a subset of multiparous women, May-Thurner syndrome can present with features of pelvic congestion syndrome [9]. Many patients are asymptomatic especially when in stage I. With the development of spurs, patients become symptomatic and develop lower limb edema. The compromised blood flow often causes collateral blood vessels to form. These are most often horizontal transpelvic collaterals, connecting both internal iliac veins, thus creating outflow through the right common iliac vein. Sometimes vertical collaterals are formed, most often paralumbar, which can cause neurological symptoms, like tingling, numbness, etc.

DVT is not an uncommon occurrence in patients with NIVL. The narrowed turbulent channel predisposes to thrombosis. Pregnancy and pressure of the gravid uterus seem to be required for the development of DVT in patients with iliac vein compression. In many cases of iliofemoral thrombosis especially on the left side, May-Thurner syndrome is overlooked due to the lack of awareness of this condition.

Investigations

Conventional Venography

The traditional gold standard for diagnosis of May-Thurner syndrome used to be transfemoral venography. One-third to half of cases could be missed by venogram if frontal projection alone is used for diagnosis [5]. Multiple projections are recommended to improve the diagnostic yield in venography. Venogram could be combined with transfemoral exercise pressures. A negative result does not rule out an obstructive lesion.

Duplex Scan

Doppler ultrasound will detect if a DVT is present in the iliac vessels. But it is not sensitive enough to visualize iliac vein compression and spurs.

Foot-Arm Pressure Differential

This test is not considered to be very sensitive in the detection of obstructive lesions. A negative test does not rule out an obstructive pathology.

Intravascular Ultrasound (IVUS)

IVUS is the most useful tool in the diagnosis of NIVL. It can visualize extraluminal compression, pulsations, and intraluminal pathologies. Most importantly, IVUS can easily differentiate between NIVL and post-thrombotic (PTS) pathologies. PTS lesions are segmental, irregular, and multiple with wall fibrosis and lumen stenosis. NIVL on the other hand are subsegmental and focal. They occur at or near arterial crossover points, and the rest of the vein is normal [5].

On the basis of the IVUS findings, Raju and Neglen have identified multiple arterial crossover points leading onto to venous compression. The lesion was found to be commonest at the point where the right common iliac artery crosses over the left common iliac vein. This is called the left-sided proximal NIVL. Distal to this site, in a small percentage of patients, the left hypogastric artery can abruptly cross the left common iliac vein. This is the left-sided distal NIVL. On the right side, compression of the right common iliac vein by the right common iliac artery can occur but is much less common. Proximal right NIVL can develop in about 22 % of patients, as the right common iliac artery courses over the right common iliac vein for a considerable distance. A distal NIVL on the right side can develop when right iliac artery crosses the right common iliac vein at or near the origin of the external iliac vein [5] (Fig 22.2).

IVUS imaging can be combined with the definitive treatment by endovenous stenting.

Other diagnostic strategies include helical abdominal computed tomography (CT), CT venography, and magnetic resonance venography (MRV).

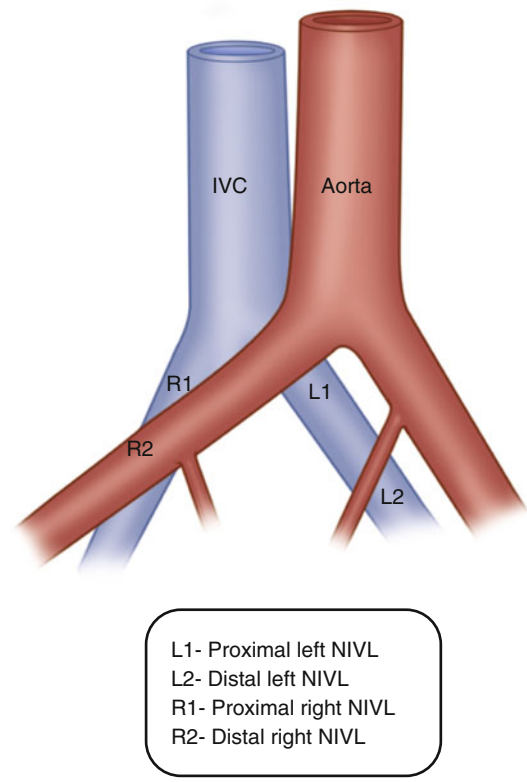

Fig. 22.2 IVUS classification of NIVL [5]. *L1* proximal left NIVL, *L2* distal left NIVL, *R1* proximal right NIVL, *R2* distal right NIVL

Management

Most patients with May-Thurner syndrome are asymptomatic and consequently require no treatment. Treatment of symptomatic May-Thurner syndrome has evolved over the years from traditional open repair to less invasive endovascular repair. The main goal of treatment is to correct the compression over left common iliac vein.

Venovenous bypass with autologous vein, creation of a tissue sling to elevate the overriding right iliac artery, retro positioning of the iliac artery, and excision of the intraluminal spur with patch venoplasty are all historic procedures.

Endovenous stenting. The first known report of treatment of May-Thurner syndrome solely by endovascular means was by Berger et al. in 1995 [10]. The treatment for patients with symptomatic NIVL without DVT is endovenous stenting. Patency rate of iliac venous stenting was much better in patients with nonthrombotic iliac vein lesions than those with thrombotic disease [11]. The overall primary, assisted primary, and secondary cumulative patency rates reported by Neglen and team at 72 months were 79, 100, and 100 %, respectively, for nonthrombotic lesions. The outcome for thrombotic lesions was 57, 80, and 86 % [11]. Cumulative rate of in-stent stenosis (more than 50 %) at 72 months was 1 % for nonthrombotic and 10 % for thrombotic lesions [11]. Stenting of the NIVL has shown considerable improvement even when the associated reflux in superficial and deep veins were left uncorrected [5]. But abolition of superficial vein reflux along with stenting is now recommended by this group [11, 12]. Persistent deep vein reflux has not adversely affected the clinical outcome after iliac vein stenting in patients with NIVL [12]. Valve reconstruction of the deep veins is recommended only in recalcitrant cases [11]. Pelvic congestion syndrome resulting from May-Thurner syndrome has been successfully treated by stenting [13]. Treatment of a patient with NIVL and acute thrombosis is on the usual lines. Initial thrombolysis followed by stenting of the iliac vein has shown long-lasting results [7].

Summary

Symptomatic NIVL is referred to as May-Thurner syndrome. This is identified to be a permissive lesion requiring another superimposed pathology for clinical manifestations. It is identified as an important cause for CVD and CVI. Although the left common iliac vein in young women is the common site of compression, lesion has been identified on both sides in either gender and at any age. Apart from symptoms of CVD, it can predispose to the symptom of pelvic congestion syndrome and acute iliofemoral thrombosis. The ideal imaging modality recommended is IVUS. Percutaneous endovenous stenting can totally correct the pathology.

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Klippel-Trenaunay Syndrome

23

Riju Ramachandran Menon

Contents

Introduction

Klippel-Trenaunay syndrome is a rare sporadic complex congenital abnormality characterized clinically by the triad of capillary malformations (port-wine stain), soft tissue and bone hypertrophy or hypotrophy of one lower limb, and lateral varicosity with or without deep vein anomalies. It is a mixed vascular malformation with predominant capillary, venous, and lymphatic components [1]. It is often mistakenly identified as AV malformation. This chapter deals with the following aspects of this disease:

1. Historical information
2. Embryology
3. Clinical features
4. Pathophysiology
5. Investigation
6. Management
7. Forums

Historical Information

French physicians Maurice Klippel and Paul Trénaunay in 1900 [2] reported a patient with asymmetrical hypertrophy of the soft tissue and bone and hemangiomatous lesions of the skin, using the term "naevus variqueux osteohypertrophique." The classic triad of dermal nevi, bone and soft tissue hypertrophy, and varicose veins was described by Parkes Weber in 1907 [3]. Klippel-Trenaunay syndrome became Klippel-Trenaunay-Weber syndrome when

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Weber in 1918 added the additional component of arteriovenous fistulae [4]. In 1965, Lindenauer proposed that when arteriovenous fistula is present, the term "Parkes Weber syndrome" be used instead [5].

Embryology

In early intrauterine fetal life, the limb has two main vascular systems: the ventral and the dorsal or sciatic system. The dorsal system atrophies and disappears by second month of uterine life. It is represented in the adult as the internal iliac, inferior gluteal, and vessels of the sciatic nerve. Sometimes the old embryonic sciatic system can persist and present as marginal/sciatic/lateral embryonic veins. Persistence of the embryonic sciatic system represents the venous malformation component of Klippel-Trenaunay syndrome [6, 7]. Occasionally, a "sciatic vein" will remain as the only main draining vein of the lower limb. As embryonic vein, a persisting marginal vein, is always "valveless" and can cause severe reflux resulting in chronic venous hypertension with stasis changes, there is a high risk of venous thrombosis and subsequent pulmonary embolism among patients with Klippel-Trenaunay syndrome.

Causes and Risk Factors

Most cases of Klippel-Trenaunay syndrome occur for no apparent reason. However, a few cases are thought to be inherited as an autosomal dominant trait. Wang et al. demonstrated that translocation t(8;14)(q22.3;q13) arose de novo and suggest that a pathogenic gene for a vascular and tissue overgrowth syndrome (KTS) may be located at chromosome 8q22.3 or 14q13 [8]. Common angiogenic factor gene *AGGF1* variants confer risk for development of KTS [9].

Clinical Features

1. Capillary hemangiomas or port-wine stains on the lateral aspect of the limb usually present first [10]. They do not cross the midline.
2. Varicose veins. The Klippel-Trenaunay vein is a large, lateral, superficial vein sometimes seen at birth extending from the foot or the lower leg to the thigh or the gluteal area. Varicosities become obvious when the child begins to ambulate [11] (Fig 23.1).
3. Deep venous abnormalities include aneurysmal dilation, hypoplasia, aplasia [12], and absent or incompetent valves. The popliteal and femoral veins are most frequently involved [13].
4. Bony and soft tissue hypertrophy is the third sign of KTS. Limb hypertrophy can be secondary to increased length (bony involvement) and/or increased girth (soft tissue involvement). Hypertrophy may be appreciated at birth. It usually progresses during the first years of life. Although lymphedema is also seen in patients, true hypertrophy of the affected soft tissues is almost always present. Occasionally, the involved limb may be atrophied rather than hypertrophied [13].
5. Leg bone circumferential hypoplasia was significantly related to the presence of intramuscular lesions. A single subcutaneous venous malformation was linked with subcutaneous hypertrophy [13].
6. A high association of malformations of the lymphatic system and veins in the affected limbs were noted in patients with KTS [14].
7. The venous malformations can produce hemorrhage and thrombosis. It can also lead to chronic venous insufficiency, stasis dermatitis, poor wound healing, ulceration, thrombosis, angiosarcoma, and emboli [15].

Other possible symptoms include:

1. Bleeding per rectum.
2. Hematuria.
3. Other systems can be involved with features of lymphatic obstruction, spina bifida, hypospadias, polydactyly, etc.
4. A greater degree of hypertrophy can be seen in patients with coexisting arteriovenous malformation. Klippel-Trenaunay-Weber syndrome (KTWS) generally affects a single extremity, although cases of multiple affected limbs have been reported. The leg is the most common site, followed by the arms, the trunk, and rarely the head and the neck [16, 17].

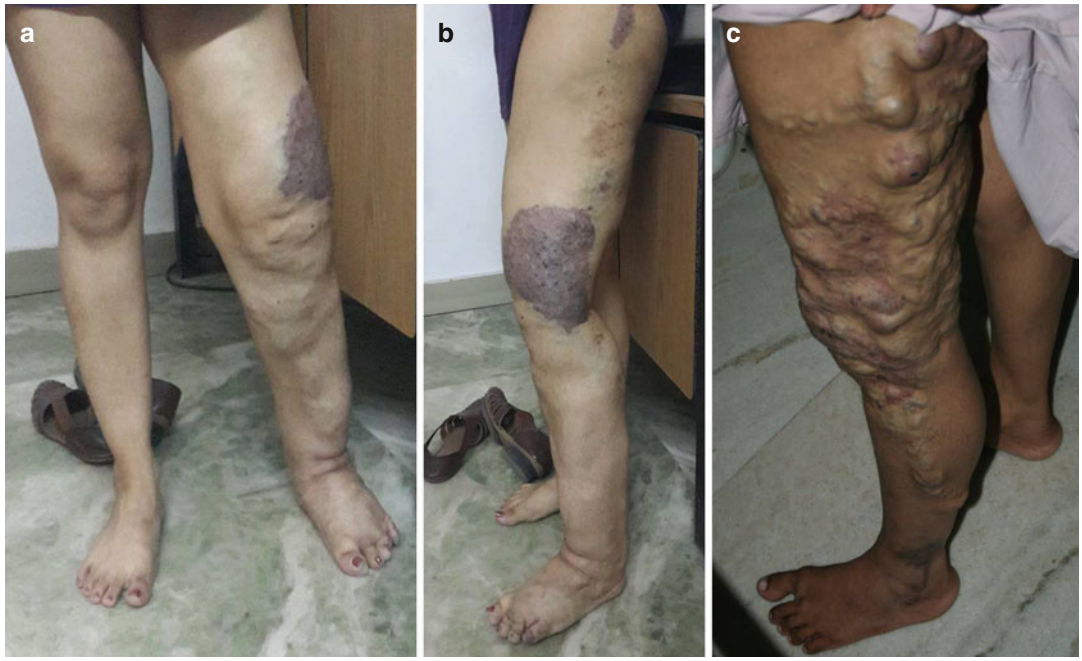

Fig. 23.1 Klippel-Trenaunay syndrome. (**a**) Localized hypertrophy. (**b**) Capillary hemangioma. (**c**) Lateral varicose veins

Investigations

In many instances, a thorough history and physical examination are all that is required to diagnose Klippel-Trenaunay syndrome. However, when complications are present, imaging studies can be useful. CT venography is a useful modality for demonstrating abnormal superficial veins or aberrant lateral veins or sciatic veins along with the extent of the draining system. It is also useful for identifying the presence or absence of pelvic and abdominal extension with unilateral limb hypertrophy [18]. Duplex ultrasound is an accurate, reliable, and noninvasive way to evaluate patients with possible KTWS. MDCT angiogram may be of value in the preoperative assessment of patients with KTWS [19]. MRI is also helpful in imaging the soft tissue hypertrophy. In addition, magnetic resonance angiography can be very helpful in identifying and defining vascular malformations. In patients with associated lymphatic system abnormalities, lymphoscintigraphy can be done to exactly assess the defect in the lymphatic system and plan treatment. Colonoscopy and CT of the abdomen may be necessary to rule out rectal vascular malformations in patients with per rectal bleed.

Treatment

Treatment for Klippel-Trenaunay syndrome is conservative and symptomatic. Compression garments are useful in the management of pain and swelling. Referral to a pain clinic and/or a multidisciplinary team including a pain management specialist is recommended [10]. Debulking has been the most widely used treatment for the syndrome and has been used for decades.

In a large series from Mayo Clinic, the following procedures for KTS have been performed [15].

1. Surgery for varicose veins – open as well as endovenous
2. Excision of vascular malformation
3. Debulking operations
4. Bone deformity and limb length correction

All the procedures demonstrated high recurrence rate in the follow-up. Mayo clinic studies demonstrate that primary surgical management of KTS has limitations and nonsurgical approaches

need to be developed in order to offer a better quality of life for these patients. Major surgery including amputation and debulking surgery does not seem to offer any benefit on a long-term basis. Ultrasound-guided foam sclerotherapy is the state-of-the-art new treatment which could potentially close many large vascular malformations [20]. Endovenous laser therapy has been used alone and in combination with other surgical interventions of the greater saphenous vein. It is gaining support for the management of varicosities in the general public and in patients with KTWS [21]. Laser treatment is also available to lighten or remove the port-wine birthmark in children and adults.

During the last 12 years, we had managed 12 patients with KTS. The treatment strategies followed include : ablation of superficial veins in 4 patients (HLS-2 and thermal ablation-2), debulking in two patients, sigmoid resection in one patient for lower GI bleed and haemorrhoidectomy in one patient. All patients were offered compression therapy. None of the patients had an ulcer.

Support Groups

It may be helpful to join a support group in which members share common problems and concerns.

The following organizations provide further information on Klippel-Trenaunay syndrome:

1. The Klippel-Trenaunay Syndrome Support Group – www.k-t.org
2. Vascular Birthmarks Foundation – www.birthmark.org

Summary

Klippel-Trenaunay syndrome is a rare congenital anomaly presenting with a triad of capillary malformation, limb hypertrophy, and lateral varicose veins. It results from persistence of the marginal/sciatic embryonic venous system. They can present with bleeding, thrombosis, and problems related to overgrowth of the extremity. Involvement of other systems is possible. Rectal bleed and hematuria are not uncommon. Associated with AV malformation it is called Parkes Weber syndrome. Imaging to rule out deep vein anomalies is important. Treatment is multidisciplinary and predominantly conservative. Ablation of varices, debulking, and orthopedic procedures have all been attempted. But the results are not very satisfactory.

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