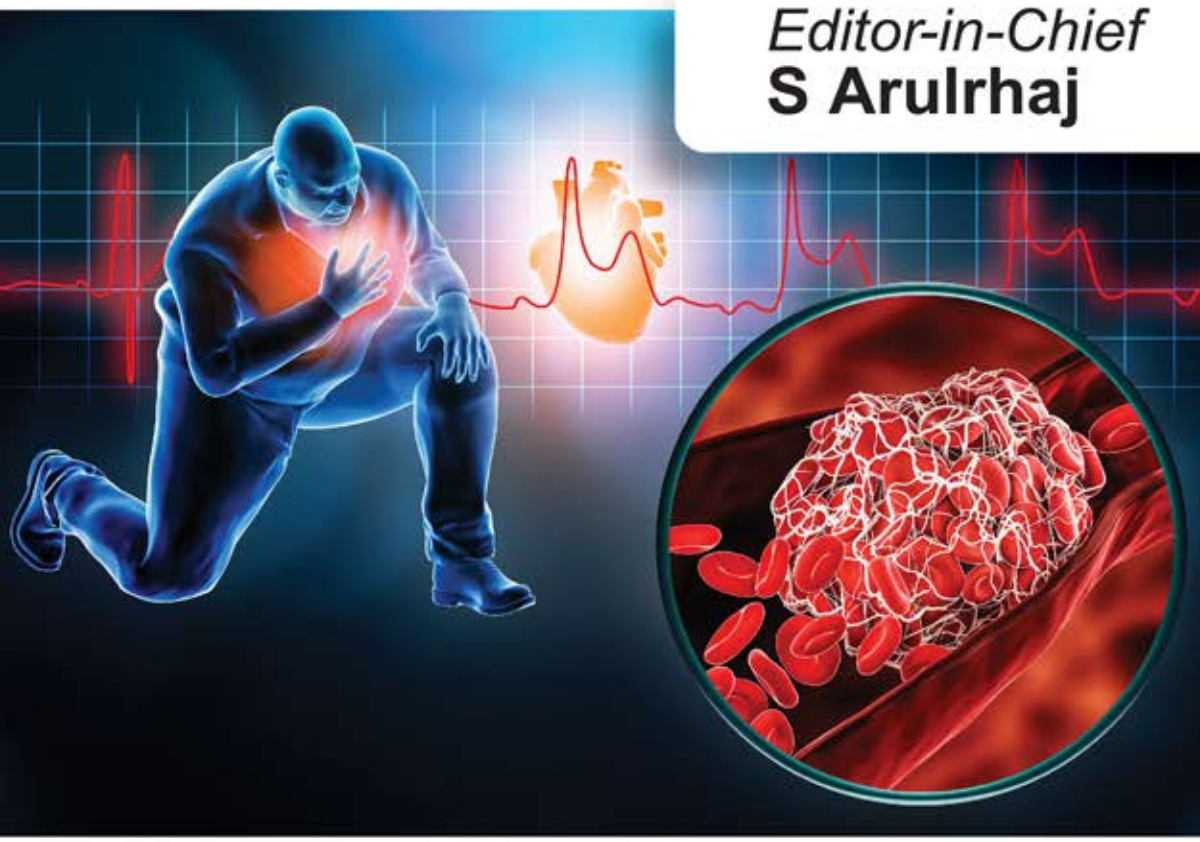
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Clinical Update
Obesity and Cardiology

Editor-in-Chief
S Arulrhaj



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CHAPTER

12

Obesity and Venous Diseases

VS Hariharan, Balamurugan Murugavel

INTRODUCTION

According to the recent World Health Organization data, a quarter of the adult population is obese (body mass index > 30 kg/m^2), while half of this obese adult population suffers from lower limb venous disease (LLVD).[1] Obesity impacts various physiological mechanisms and can affect the development of metabolic syndrome. Excess body weight can impact the coagulation system adversely and alter fibrinolytic activity and endothelial function.[2] Overweight and obesity are one of the best-established risk factors leading to chronic venous disease **(Box 1)**.[3] LLVDs in obese patients comprise a spectrum of clinical presentations including

BOX 1: Obesity and lower-extremity venous disease—pathophysiological mechanisms.[3]

Proposed pathophysiological mechanisms for lower-extremity venous disease in obese patients:

- *Mechanical pathway*:
  - Increased intra-abdominal fat
  - Extrinsic compression of ileofemoral venous pathways
  - Venous stasis
  - Distension of lower limb veins
  - Venous stasis and valve dysfunction
- *Inflammatory pathway*:
  - Alteration in coagulation pathways
  - Alteration in endothelial function
  - Increase in D-dimer, fibrinogen, factor VIII, and factor IX
  - Venous stasis
- *Lymphovenous dysfunction*:
  - Cellulitis causing sclerosis of lymphatic channels
  - Reduced lymphatic drainage causing edema

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varicose veins, chronic venous insufficiency (CVI), a chronic venous ulcer, deep vein thrombosis (DVT), and venous thromboembolism (VTE).

PATHOPHYSIOLOGY

Research suggests that obesity in adults affects the vascular hemodynamics and flow inside the lower limb venous system. Pathogenesis of venous disease in obesity has been postulated further due to mechanical and inflammatory factors.

Pathogenesis of Lower Limb Venous Disease from a Mechanical Standpoint

Pathogenesis of LLVD from a mechanical standpoint can be ascribed as follows: Obesity is associated with increased abdominal fat, leading to increased intra-abdominal pressure that gets transmitted extrinsically to the lower limb venous system. This elevated hydrostatic pressure leads to stasis inside the lower limb veins and can lead to chronic venous insufficiency.[4]

Pathogenesis of Lower Limb Venous Disease from an Inflammatory Standpoint

Pathogenesis of LLVD from an inflammatory standpoint can be ascribed as follows: Obesity is associated with background inflammatory status, causing vascular endothelial dysfunction, and an increase in D-dimer, fibrinogen, factor VIII, and factor IX creating a prothrombotic state, leading to venous stasis and increased risk for VTE.[5]

Evidence for these postulated theories for LLVD in obesity has been investigated in various research papers.[4] In addition to the increased femoral venous diameter, it was also observed that the peak venous velocity was lower, and the minimum velocity was higher in the obese group. Venous outflow obstruction could explain these observed findings. In addition, the pulsatility index derived from the peak, minimum, and mean venous outflow shows a significant venous outflow resistance in obese patients as compared to non-obese patients. Significantly decreased shear stress might support the development of CVI as described by Bergan et al.[5]

The magnitude of obesity appears to correlate with the relative obstruction to lower extremity venous return, and the severity of venous symptoms due to central *arteriovenous dysfunction*, when combined with increased cardiac output demand.[6] Another potential cause of venous insufficiency could be related to *lymphatic dysfunction,* where repetitive lower limb cellulitis could lead to extensive scarring of lymphatic channels leading to lymphovenous hypertension.

CLINICAL EVALUATION

The diagnostic process begins with a detailed clinical history of the patient focusing specifically on family history, allergies, previous history of any medications, DVT, etc. This is followed by a physical examination where the examiner should try to elucidate clinical signs, such as edema, varicose veins, skin changes, and venous ulcerations.

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Clinical manifestations gradually increase in severity as the disease progresses:
- Lower limb pain especially worsening end-of-day pain
- Malleolar edema
- Dilated superficial veins
- Deep venous thrombosis
- Venous ulcers

LABORATORY EVALUATION

The most widely used diagnostic laboratory test for LLVD involves a thorough lower extremity duplex ultrasound examination including a color Doppler study, while being widely available, noninvasive, and reproducible. The reliability of compression ultrasonography results and its role is questionable in obese patients.[7] Three-dimensional (3D) tomographic ultrasound imaging is on the horizon that can image and help evaluate the superficial and deep venous pathways in a 3D volume while reducing the advanced user "skills" required in ultrasound imaging and improving the scan acquisition time.[8] Plethysmography might be advantageous in identifying pathophysiological mechanisms occurring in patients by distinguishing between venous reflux, obstruction, or both, or conversely, muscle pump dysfunction.

Cross-sectional imaging studies such as computed tomography (CT) venography and magnetic resonance imaging (MRI), may be necessary in complex, persistent venous pathologies including chronic venous obstruction. Recent third-generation CT scanners can perform multiphase CT arteriography/venography and aid in the mapping of deep and superficial venous systems with one single iodinated contrast injection. In patients with renal failure where iodinated contrast agents could not be administered, magnetic resonance imaging with flow sequences, and iron-based contrast agents can provide a good alternative for 3D venous imaging of lower extremities.

DIFFERENTIAL DIAGNOSIS

Various pathologies mimic LLVD in obese patients including:
- Systemic diseases causing lower limb edema such as hypothyroidism, heart failure, and renal failure
- Obstruction due to tumor or fibrosis
- Cellulitis
- Allergic contact dermatitis and eczema
- Dermatologic manifestations of cardiac and renal disease

COMPLICATIONS

Chronic venous disease can be associated with pain, itching, swelling, cramps, and ulcers affecting quality of life, sometimes leading to depression and social isolation in chronic cases. Venous hypertension can trigger inflammatory pathways by activating circulating leukocytes and vascular endothelial cells, leading to an increase in leukocyte adhesion.[5] This proinflammatory state combined with capillary hypertension and edema can lead to skin changes and venous ulcers.

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Research studies have shown a significant correlation between obesity and chronic venous disease while corroborating the negative impact of obesity on the severity of venous disease.[9]

MANAGEMENT

Management of lower extremity venous insufficiency consists of nonpharmacological, pharmacological, and surgical approaches.

The nonpharmacological approach consists of external compression therapies such as compression stockings targeting venous hemodynamics. This mode of treatment acts by increasing interstitial pressure, thus decreasing both superficial and deep vein caliber which eventually leads to decreased venous pressure. One contraindication to such approaches would be preexisting peripheral arterial disease, where external compression could interfere with arterial blood inflow to the ischemic lower limbs and worsen the underlying condition. Weight reduction by various strategies such as bariatric surgeries including gastric sleeves, and laparoscopic techniques should be attempted.

The pharmacological approach consists of administering vasoactive agents that act by decreasing venous permeability, ameliorating the inflammatory response, and by increasing vascular tone. Pharmacological agents range from saponins, flavonoids, pentoxifylline, a micronized purified fraction of flavonoids, and acetylsalicylic acid.[3]

TABLE 1: Management strategies of lower-extremity venous disease in obese patients.[3]

Management strategy	*Level of evidence and recommendation*	*Consideration in obese patients*
Compression therapy (stockings, bandages, and compression wraps)	1A: Increases the efficacy after interventional procedures	Achieving adequate compression using stockings or pneumatic compression devices is challenging
	1B: Initial therapeutic method of CVD	
Pharmacological therapy	IIaA: Venotonics to ameliorate early symptoms	Lack of evidence in obese patients regarding drug pharmacokinetics
	IIaB: Flavonoids and derivatives as complement therapy	
Sclerotherapy	1A: Second-line therapy for patients who are not eligible candidates for endovenous ablation or surgery	Endovenous therapies are technically more difficult in obese patients
	IIaB: First-line therapy in patients with recurrent CVD and fragile patients with venous ulceration	Compression ultrasound imaging to assess therapy may be challenging
Endovenous thermal ablation (laser or RF energy)	1A: First-line therapy for patients with CVD and great saphenous venous reflex	Need to address obesity using weight loss measures before performing endovenous therapies

(CVD: chronic venous disease; RF: radiofrequency)

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Surgical approaches include interventional sclerotherapy, saphenous junction ligation and stripping, and more recently, endovenous laser ablation and radiofrequency ablation therapies are being considered. Surgical therapies such as endoscopic perforator surgery aimed at improving venous reflux, when performed earlier in the course of chronic venous disease, can aid healing, and help in preventing the recurrence of venous ulcers **(Table 1)**.[10]

CONCLUSION

Obesity and lower-extremity venous diseases are so often coexistent and several epidemiological studies have described it as a risk factor; however, their exact pathophysiological link has not yet been studied thoroughly and proven. The selection of appropriate diagnostic tests for LLVDs and the interpretation of their results in obese patients need to be addressed with due diligence. From a treatment standpoint, nonpharmacological measures such as compression therapies tend to be challenging, and less predictable in obese patients. While endovenous therapies are emerging, their techniques, evaluation, and durability have to be examined in obese patients with due diligence. While obese patients typically have been excluded from most pivotal clinical studies, further detailed research studies on the impact of obesity on venous hemodynamics and treatment pathways for chronic venous disease have to be performed, in this critical, yet rapidly evolving patient population that is under-represented in clinical studies.

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- Will have practical value to doctors around the world who treat patients with obesity every day
- Language of the textbook has been made in such a way that it will be of interest to undergraduates, postgraduates, physicians, general practitioners (GPs), practicing cardiologists, and researchers

S Arulrhaj MD PhD DSc FRCP(Glasgow and London) MBA is a distinguished Professor (Honorary) at Dr MGR Medical University, Chennai, Tamil Nadu, India. He is a Dr BC Roy National Awardee, the highest professional award in India and the Founder Chairman, Chief Physician, and Intensivist of Sundaram Arulrhaj Hospitals, Tuticorin and Founder and Chairman for "ARULS Group". He has been the National President of Indian Medical Association and Association of Physicians of India (API). Dr S Arulrhaj is the Founder Chairman of the Commonwealth Medical Association Trust and Commonwealth Medical eVarsity, UK. He is the Founder and Past Chairman of Commonwealth Health Professions Alliance, UK; Founder and Chairman of Indo Global Cardio Diabetes Academy, India; Past President of the Commonwealth Medical Association, Honorary National Professor of Medicine, IMA and IMACGP, India; and Chief Patron of IMACGP and IMA eVarsity, India. He has published Diabetes Update 2011, Clinical Medicine Update Book 2016, Cardio-Diabetes Medicine 2017 and 2018. He is regularly contributing for Medicine Update, and API over 20 years. He is a postgraduate teacher in Internal Medicine over 20 years—DNB Medicine and has addressed acute medicine on various national and international platforms. Dr Arulrhaj's medical interests are nonintensive cardiology and intensive care. His public health interests are prevention and control of noncommunicable diseases, cardiodiabetic medicine, digital health, rural health, and prehospital trauma and emergency care. He has organized several conferences—national, international and state API, IMA, and conferences of GCDC and ISECON.

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