Compression Therapy in Venous Disease

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Clinical Pearls

1. Compression therapy is essential for the treatment of venous disease affecting the lower extremities.
2. Compression therapy promotes healing and decreases recurrence of venous ulcers.
3. Compression therapy decreases the risk of DVT, decreases discomfort after developing a DVT, but does not necessarily decrease the risk of post-thrombotic syndrome.

Introduction

Chronic venous disease (CVD) is a very common condition affecting up to a third of the adult population [1, 2]. It can lead to varicosity, edema, and even intractable leg ulcers requiring prolonged wound care. Regardless of the pathophysiology, reflux, or obstruction, the mainstay of therapy remains compression [3]. Compression stockings are utilized as they are thought to compensate for increased ambulatory venous pressure, for prevention of deep and superficial vein thrombosis, and for reduction in inflammation, swelling, and pain. In addition to various forms of stocking, compression can be provided with bandages as well as pneumatic devices.

Hippocrates (460-370BC) and Aurelius Celsus (25BC-AD14) both utilized compression in their treatment of venous disease [4, 5]. Conrad Jobst made the observation that hydrostatic pressures in a pool relieved venous insufficiency symptoms. The applied pressure was greater with depth. In the 1950s he developed compression stockings to emulate those pressures [6]. This chapter will review some of the evidence behind compression therapy.

Mechanisms of Benefit

The ankle venous pressure represents the weight of the column of blood leading to the right atrium. Low in the supine position, ankle venous pressures rise closer to 80–100 mmHg upon standing. When venous valves are healthy, the use of the calf pump dramatically reduces this pressure. In venous insufficiency, compression stockings can help

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improve venous return and reduce ambulatory venous pressure [7, 8] in part by using a Starling gradient that favors edema resolution [9]. The fluid shift from the interstitium into the lymphatics may also improve conditions for oxygen and nutrient transport.

Compression of a vein can reduce its radius and increase flow velocity [10, 11]. Increased velocity in the microcirculation may lead to endothelial neutrophil detachment [12]. Compression therapy has been shown to reduce elevated levels of the inflammatory cytokines vascular endothelial growth factor and tumor necrosis factor-α in patients with venous ulcers [13]. Ulcer healing seems to correlate with falling cytokine levels.

Two physical laws apply to compression therapy: (1) Pascal's law, external static pressure exerted on a confined fluid is distributed evenly, and (2) Laplace's law, pressure applied by compression is proportional to the tension at the interface with skin and inversely proportional with limb radius ($P \alpha$ tension/radius).

These physical laws have several implications:

1. Each additional bandage layer adds to pressure.
2. Increased applied pressure reduces vessel radius.
3. The same tension applied at the ankle will generate more pressure than if applied at the calf, due to the smaller radius at the ankle (Fig. 5.1).

These laws, however, do not entirely explain how pressure distributes with compression [14]. Chassagne et al. [15] utilized pneumatic pressure sensors in healthy subjects at three locations: the ankle, interface of the Achilles tendon, and the gastrocnemius muscle (where calf circumference is greatest). Interface pressure increased, as expected, with greater bandage overlap. Men demonstrated slightly greater rise in interface pressure with standing than women. As expected, the interface pressure decreased higher up, as leg circumference increased. The relationship between applied pressure and elastic modulus was nonlinear.

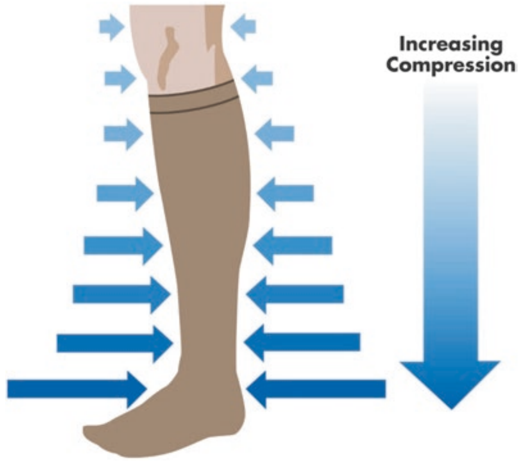


Fig. 5.1 Compression therapy relies on placement of circumferential garments that provide pressure on the leg with maximal intensity at the level of the ankle

Elastic compression hosiery by its very nature demonstrates a degree of hysteresis, i.e., the ability to return to its original length after being stretched. More layers of elastic compression bandaging not only increase compression, but they will also result in a less elastic bandage. This is in part due to friction between the layers. Less elastic bandages exert greater compressive pressure when the wearer stands from a supine position, likely due to muscle expansion [15].

Compression Pressure

Compression stockings are available in different grades of pressure (Table 5.1). The classification of pressure varies between countries. One international consensus group, for example, categorized "mild" compression as <20 mmHg, "moderate" as =20–40 mmHg, "strong" as =40–60 mmHg, and "very strong" as ≥60 mmHg, at the ankle [16].

Partsch [8] used ultrasound to evaluate the mid-calf small saphenous vein (SSV) and posterior tibial vein in 14 patients (5 with varicose veins). Narrowing was observed at 30–40 mmHg, occlusion at 70 mmHg, when standing. Lord [17] evaluated 30 patients (13 with varicose veins) who wore waist-high 20–30 mmHg compression

Table 5.1 Grades of compression

United States	German standard	British standard	Pressure (mmHg)[a]	Suggested indication
Light	KK1	3A	<20	Mild C1-3 disease and unable to apply or tolerate class I
Class I (moderate)	KK2	3B	21–30	Mild C1-3 disease
Class II (high)	KK3	3C	31–40	More severe C2-3 disease, C4 disease and higher, PTS
Class III (very high)	KK4	3D	>40	C5-6 disease (if did not respond to class II and if tolerated)

PTS post-thrombotic syndrome
British standards for bandages, German standards for compression stockings [64, 65]. *KK* class of compression
[a]The pressure range for the German standard is different (KK1 = 18–21, KK2 = 23–32, KK3 = 34–46, KK4 ≥ 49 mmHg)

stockings. The great saphenous vein (GSV) was not compressed when standing. Among the varicose vein patients, the GSV was not compressed even when supine. Additional imaging studies utilizing ultrasound and MRI suggest that in order to compress the GSV while standing, 40–50 mmHg compression pressure is required [18–20].

Accomplishment of vein occlusion or compression, however, may not be the ideal outcome to study. Sarin et al. [21] study using duplex found that cuff pressures required to achieve valve function restoration were lower than pressures to achieve occlusion. Some practitioners choose grades of compression based on severity of disease. The CEAP (clinical-etiology-anatomy-pathophysiology) classification system has been widely adopted to standardize research and dialogue in venous disease [22, 23].

In one study, treatment of patients with predominantly C2–C3 venous disease (varicose veins and edema) with 30–40 mmHg compression led to improved pain, pigmentation, and swelling [24]. High pressure compression (>40 mmHg) is better than low pressure compression for venous ulcer healing [25]. For venous ulcer disease, a systematic review [26] showed that 30–40 mmHg compression hosiery is more effective than lower pressures for healing and lowering recurrence. The Society for Vascular Surgery and the American Venous Forum Guidelines suggest 20–30 mmHg stockings for simple varicose veins (C2 disease) [27].

The Role of Compression as Stand Alone Therapy

In a systematic review of stand-alone compression therapy, that is, not after an ablative procedure, in varicose vein patients, symptoms (e.g., pain, discomfort, edema) were improved. However, there was lack of evidence for post-treatment efficacy in reduction of progression or recurrence of varicose veins [28]. A Cochrane review in patients with venous insufficiency (C2–C4 disease) found insufficient high-quality evidence to determine effectiveness of compression [29]. For C5/C6 disease (healed or active venous ulcer), two Cochrane reviews reported lower ulcer recurrence with compression therapy. Furthermore, compression noncompliance is associated with lower ulcer healing and greater recurrence [3, 30]. Various compression lengths are available to adapt to patient needs (Fig. 5.2).

Compression after Sclerotherapy or Ablation

In the 1960s, Fegan described the empty vein technique, where veins would be compressed after sclerotherapy [31]. While the concept sounds logical, evidence for the optimal duration of compression after sclerotherapy or whether it is necessary is scant. Furthermore, there exists a wide variation across the globe on utilization of compression after ablative procedures.

Fig. 5.2 Different length of compression garments available on the market: (**a**) knee high, (**b**) thigh high, (**c**) Pantyhose

Kern randomized 100 patients undergoing sclerotherapy for lateral thigh reticular and spider veins to no versus 3 weeks of post-procedure compression (23–32 mmHg). Improved clearance was reported in the compression group at 7 weeks [32]. El-Sheika's [33] systematic review of randomized control trials found seven suitable for analysis. Three studies were surgical; two used sclerotherapy and two endovenous laser ablation (EVLA). Heterogeneity in study quality and duration of compression was found which made meta-analysis difficult. No specific conclusions could be drawn about efficacy or optimal duration of compression therapy.

Two of the evaluated studies suggested that longer compression resulted in less pain. Bakker et al. [34] prospectively randomized patients undergoing EVLA of the GSV to 2 versus 7 days of compression stockings (35 mmHg). Sixty-nine patients were analyzed. At 1-week follow-up, the 7-day compression group reported less pain and better physical function. At 6 weeks no significant difference was found. Another similarly designed prospective study noted a small but significant reduction in pain scores when compression was worn after EVLA [35]. These studies did not demonstrate any difference in procedural success or efficacy.

Compression for Venous Ulcer Disease

Venous ulcers represent the most severe form of venous disease. A 2012 Cochrane systematic review evaluated 48 randomized clinical trials (n = 4321), concluding that compression led to greater ulcer healing compared to no compression. Both ulcer healing and reduction in recurrence are enhanced with compression [3, 26]. Multi-component systems (as opposed to single layer) or those with elastic components appeared to work better. Higher compression pressures appear to heal ulcers better [3]. In another systematic review, Cullum et al. [36] found that multilayered high compression was more effective than moderate compression, in the prevention of ulcer recurrence. Another Cochrane review [30] determined that high pressure compression may work better than medium compression to prevent recurrence. Overall, there was insufficient evidence when comparing types or lengths of compression.

Prevention of Deep Vein Thrombosis

Compression hosiery prevents venous thromboembolism in the perioperative setting. Its mechanism of benefit might be through decreasing venous stasis and stimulating tissue factor pathway inhibitor [37].

A Cochrane database review found 19 randomized controlled trials, 18 evaluating surgical patients, and 1 medical patients [38]. The graduated compression-stocking group developed DVT in 9% compared to 21% among controls ($P < 0.00001$). The incidence of pulmonary embolism based on 5 included studies was 2% in the treatment group versus 5% in controls ($P = 0.04$).

Post-thrombotic Syndrome

Post-thrombotic syndrome (PTS) is a chronic, potentially disabling, disorder that can occur after acute DVT, affecting at least 30% of patients [39]. In the affected leg, skin changes, edema, and ulceration can occur along with pain. It has been postulated that compression may alleviate venous reflux, hypertension, and sequelae, if applied early following a DVT. Subfascial lymphatic function can be reduced with deep vein thrombosis and deep venous incompetence due to a post-thrombotic syndrome but may be treated with compression [40, 41].

Three randomized trials have evaluated compression stockings in the prevention of PTS. Two small randomized trials appear to suggest an approximately 50% reduction in PTS with compression stockings [42, 43]. The SOX trial [44] randomized 410 patients with proximal DVT to 30–40 mmHg below-knee graduated compression stockings versus <5 mmHg placebo stockings. The stockings were mailed to participants within 2 weeks of DVT diagnosis. They were asked to be worn on the affected leg for 2 years, during waking hours. Participants were asked to report frequency of stocking use. At 24 months there was no significant difference in the proportion of patients with PTS. Adherence was recorded as being equivalent.

A number of criticisms have been directed against the study. Compression stockings were not applied immediately upon diagnosis of DVT but rather up to 2 weeks later. In addition, 83% of participants provided a wrong guess or “uncertain” reply as to whether they had been receiving real compression or placebo stockings. This may suggest that a sizeable number had not worn the compression stockings at all. The benefit of compression hosiery post-DVT to prevent PTS is controversial, but in our view, compression hosiery should be applied immediately following DVT, as in the least, it appears to decrease swelling and provide comfort.

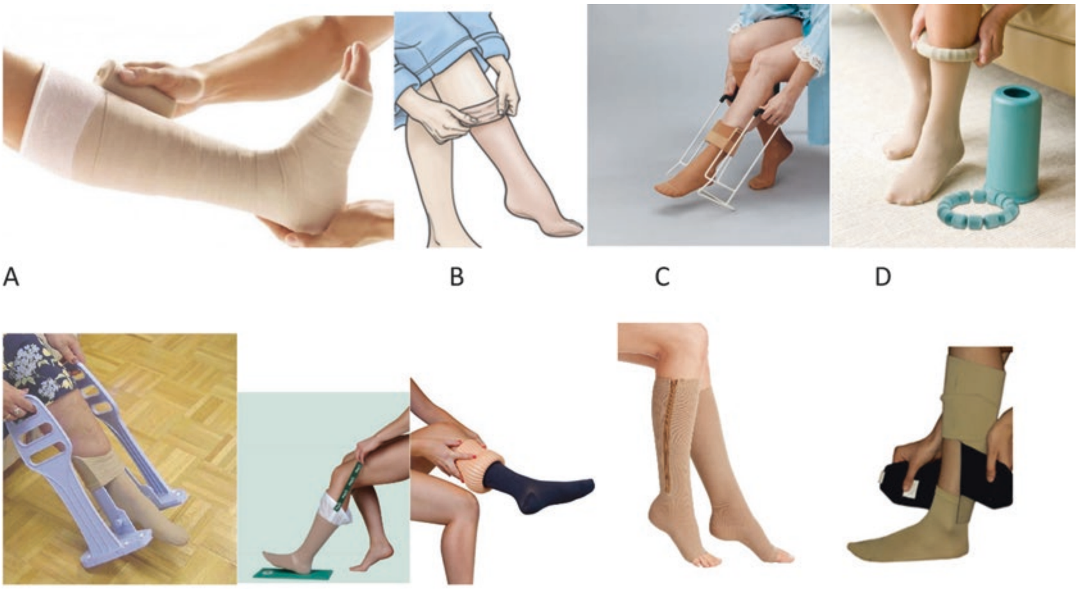
Compression Modalities Compared

A diverse selection of compression modalities exists, from those compressing around the ankle region to those compressing up to the waist. Bandages, stockings, and pneumatic compression devices have been utilized. Single to multilayer bandages have been used. Bandages and stockings can vary in power and elasticity (Fig. 5.3).

Inelastic compression bandages tend to generate lower resting pressures but the pressure increases with walking due to calf muscle expansion [45]. They are therefore not ideal for immobile patients. Inelastic bandages should be reapplied once edema has improved. Increased layers not only augment the pressure applied but also tend to render the compression less elastic.

A small randomized study compared venous ulcer healing rates using five compression modalities: pneumatic compression, multilayer bandages (45–50 mmHg), compression stockings (30–40 mmHg), two-layer bandages (20–30 mmHg), and Unna boots. More patients had superficial than deep reflux. No ablative intervention was performed. At 2 months, ulcer healing rates were best (57–59%) in the groups that received pneumatic compression, 30–40 mmHg compression and multilayer bandages (45–50 mmHg). Ulcer healing rates were lowest in those assigned to Unna boots (20%) and two-layer bandages (17%) [46].

In a randomized trial of 200 patients undergoing EVLA to the GSV, one group wore 23–32 mmHg thigh-high compression stockings. The second group wore the same compression stockings with an added eccentric medial compression band,



A B C D E F G H I

Fig. 5.3 Typical compression modalities and applications. Compression can be provided using an elastic wrap (**a**). More commonly graduated compression stockings can be prescribed that are commonly applied by manual rolling (**b**). For patients who have difficulty using the stockings, several commercial frames and inserts (**c**–**g**) are available to assist in stockings placement. Some stockings have a zipper to enable tightening after the application on the leg (**h**). Finally, Velcro stockings are available also as an alternative compression modality (**i**)

approximating the GSV location. The group with added medial compression reported significantly less post-EVLA pain. GSV closure rates were not evaluated [47]. A 2009 meta-analysis of eight RCTs found faster ulcer healing with purpose-made compression stockings than "diverse" bandages in venous ulcer disease [48]. There was a greater proportion of healed ulcers (62.7% with stockings vs 46.6% with bandages; $P < 0.0001$) and stocking use resulted in 3 weeks shorter mean ulcer healing time ($n = 535$, $P = 0.0002$) and lower pain scores ($P < 0.001$) than with bandages [48].

Inelastic compression stockings typically require application by a trained individual. Adjustable devices may present a better future alternative while also being easier to apply. Mosti et al. [49] demonstrated efficacy in edema reduction among C3 patients when comparing an adjustable Velcro compression device to inelastic bandages. They randomly assigned 20 limbs to multi-component multilayer inelastic bandages versus 20 to the Velcro device for 7 days. The Velcro group was instructed to tighten the device if it felt loose, whereas the inelastic bandage group was asked not to adjust theirs. At baseline the inelastic bandage exerted a supine mean pressure of 63 mmHg versus 43 mmHg with the Velcro device. However, the inelastic bandage pressures fell >50% over 7 days whereas remained stable in the Velcro group. Furthermore, there was greater limb volume reduction in the Velcro group (26 versus 19% at 7 days; $P < 0.001$), without a significant difference in patient discomfort.

Concurrent Peripheral Arterial Disease

In patients with concurrent arterial and venous disease, some authors have advised caution with compression therapy, as it may further decrease skin perfusion [50]. Some investigators have recommended avoidance of compression for ankle brachial pressure indices (ABIs) <0.5 [51].

In a small study on mixed arteriovenous ulcer disease with ABI >0.5 and ankle pressure

>60 mmHg, inelastic compression stockings (more specifically pressure range 20–40 mmHg) did not appear to impede arterial flow while improving venous pump function [52]. However, no longer-term clinical follow-up was made. Ladwig et al. [53] studied a relatively inelastic 2-layer bandage system in 15 subjects with ABIs 0.5–0.8. Average standing sub-bandage pressures measured at the junction of the calf muscle with the Achilles tendon were 30 mmHg. Over 14 days of follow-up, the compression appeared well tolerated and safe.

It may be the case that carefully fitted inelastic compression hosiery are more appropriate in peripheral arterial disease (PAD) as they produce higher working pressures. Regardless, we recommend prompt follow-up and examination of patients fitted with compression hosiery. Some PAD patients have calcified pedal vessels and falsely elevated ABIs. Relying on the ABI alone, therefore, is not advisable. Toe or skin perfusion pressures can therefore be evaluated [54, 55].

Compliance Issues

Ideal compression should compensate for elevated pressures when standing [8, 11] while allowing for the patient to remain ambulatory and comfortable. Patients with obesity, frailty, or arthritis will struggle to apply elastic compression stockings. Even light compression (<20 mmHg) hosiery can be uncomfortable after application. In one report at least 15% of elderly patients could not apply stockings [56]. In a study of post-sclerotherapy compression, only 40% were compliant with daily posttreatment compression, mainly due to discomfort [57]. Noncompliance is noted even among those with ulcer disease [58]. In Coughlin's study of pregnant women with varicose veins, 33% refused to participate once randomized to compression [59]. After 6 weeks follow-up compliance was only 32%.

Non-adherence with compression is associated with reduced and slower ulcer healing, as well as greater recurrence [60]. So-called donning devices that assist in the wearing of compression hosiery are available, although their efficacy in improving adherence is unclear. Individuals unable or unwilling to wear compression hosiery may find pneumatic compression devices easier to tolerate, though the data is limited. In a small controlled study ($n = 28$), females with painful varicose veins received sequential pneumatic compression therapy for 30 min, 5 days a week, totaling 6 weeks. The treatment group reported improved symptoms and quality of life [61].

Conclusion

Despite the paucity of data, compression remains the mainstay of treatment for chronic venous insufficiency, in particular for venous leg ulcers. Higher pressures are required to maintain compression when standing. Before prescribing compression hosiery, a careful evaluation of the target limbs must be performed. Delicate and friable skin, bony prominences and the presence of neuropathy can increase risk of damage. Compression grades, as a guide, can be based on severity of disease and the patient's ability to comply.

Discomfort and poor compliance remain a major barrier. Currently in the United States, compression stockings are not typically reimbursed by health insurance and can be costly. We recommend below-knee compression hosiery rather than thigh high, in general, as the latter can be even more uncomfortable [62]. With thigh-high hosiery, there can be popliteal discomfort particularly during sitting, and slippage can occur [63].

At least a week of compression therapy after ablation procedures may minimize patient discomfort though there is scant evidence that compression improves ablation outcomes such as vein closure. For venous ulcer disease, long-term and higher pressure compression stockings (30–40 mmHg) are advised [3, 30].

Compression reduces the risk of perioperative DVT, but its role in prevention of PTS is controversial. The authors recommend against compression stockings in ABI <0.5 or ankle pressure <60 mmHg and suggest prompt follow-up and examination of PAD patients fitted with compression hosiery.

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