Venous Stasis Ulcers: An Answer to the Treatment and Prevention Dilemma

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Abstract: Compression to the lower limb(s) is the gold standard for non-surgical care and prevention of venous stasis ulcers. This specific wound type, occurring annually in greater than 2.5 million Americans, costs approximately 3 billion dollars, recurs predictably, and results in over 2 million lost work days. Although, in motivated individuals, ulcer recurrence can be minimal; these rates are dismal in the majority and, thus, noncompliance with the standard becomes/ is the norm. Noncompliance is currently fueled by difficult to apply, expensive, and poorly reimbursed (most especially once the individual's wound has healed) compression devices. These problems do not even address the different set of issues and costs associated with another category of compression devices, namely those that require ongoing healthcare professional application within a physician office or wound clinic.

A unique, effective, and user-friendly compression stocking/sleeve combination has been developed, which is applied by the individual at home, and can be re-used for extended periods. Following healing, ongoing use of this device, as a preventative therapy, resulted in markedly decreased ulcer recurrence, decreased need for medical intervention, and increased satisfaction on the part of patients, family members and health care providers.

Prior to enrollment in this IRB-approved study, individuals with lower extremity ulcers underwent assessment and documentation of valvular incompetence and simultaneous assessment of the absence of arterial disease. Depending on appropriate compression requirements, subjects could wear either the test stocking (exerting 20-30 mm Hg pressure) or the test stocking/sleeve combination (exerting 30-40 mm Hg pressure). For the most part, study subjects wore the stocking/sleeve combination throughout. Two to six pairs of the test stocking/sleeve combination were used by subjects over the course of the study. Time-to-wound-closure for subjects that healed ranged from one week to slightly under 6

months. Of those with closed ulcers, recurrence was forestalled, in most, with the longest time to recurrence being 11 months after wound closure. The majority of subjects, both those who healed and those who are still in the process of healing, continue to wear the device daily, seven days a week, 24 hours a day, reporting satisfaction with the feeling of the stocking and delight in the outcomes as regards their wound. User-friendly treatments increase adoption and compliance with the gold-standard and have the potential of making inevitable ulcer recurrence become a thing of the past.

Goals: The goals of this study were to:

- Document the effectiveness of the stocking/sleeve compression device.
- Document compliance with the use of the stocking/sleeve compression device.
- Identify issues with use of the stocking/sleeve compression device.
- Obtain user reactions and 'ease of use' information on the stocking/sleeve compression device.

Study Design: Prospective, single treatment, case-series.

Sample: Subjects were sourced from the Principal Investigator's patient population or through referrals from physicians within the community. All enrolled subjects were required to be over 18 years of age, male or female, non-pregnant, and comprehend English. Having met the inclusion/exclusion criteria, individuals to be enrolled signed consent forms prior to becoming a study subject. These individuals also agreed to be compliant with the protocol and scheduled clinic visits. The following list describes more specifically selected parameters of the inclusion/exclusion criteria.

Inclusion Criteria: -One or more wounds of any size on a single lower extremity, where only one wound would be classified as the 'study ulcer'
-An ankle-brachial index (ABI) > 0.75
-Capable of applying the stocking/sleeve compression device daily in the home (alone or with assistance).

Exclusion Criteria: -Individuals could <u>not</u> be enrolled in the study if they:

-Had documented arterial disease of the lower extremity on which the study ulcer was present
-Could be defined as members of the “vulnerable population” or required a legally authorized representative

Design: This IRB-approved, prospective, single treatment, case-series study was undertaken to evaluate a novel compression device on individuals with venous stasis ulcers. The compression device (i.e., stocking/sleeve combination) and Castile soap were provided over the course of the study at no cost to the subjects. No monetary incentives were provided to the subjects. Other than the use of the standardized soap to cleanse the wound surface and peri-wound skin, during the subject’s shower, no topical treatments were applied directly to the wound surface throughout the study; the stocking fabric came in direct contact with the ulcer surface. Clinic staff only applied the test stocking during weekly study visits at the clinic; at all other times the subject or a household member removed and re-applied the stocking at the subject’s residence. Subjects were instructed to wear the test compression device at all times, except during showering. If only the stocking was ordered for the subject, it was worn 24 hours a day, 7 days a week, except during showering. If the subject was to wear the stocking/sleeve combination, both were worn 24 hours a day, 7 days a week, but the outer sleeve was removed at bedtime. Subjects were also instructed to wash the stocking or stocking/sleeve (including within a washing machine and dried in a dryer) whenever they became soiled or whenever they desired. Study subjects received 2 pairs of the stocking/sleeve combination on entry to the study. Having more than one pair insured that one set of clean, dry stocking/sleeve combination was always available. When new stockings were needed, they were provided to the subjects.

All subjects were encouraged to elevate their legs as often as possible. At the time of the initial visit and at each subsequent clinic visit, the study wounds were photographed and the wound and leg circumference measured until wound closure occurred. Standardized leg measurements, untoward events, and feedback regarding the use of the stocking during the time between clinic visits also were collected weekly. If non-compliance with the study protocol became apparent, this issue was discussed with the subject and, in selected cases, subjects were discontinued from the study. Once wound closure was achieved, the interval between visits could be prolonged at the discretion of the Principal Investigator. Healed subjects were followed prospectively for varying time periods after wound closure.

Although healed subjects did not return to the clinic weekly, many had scheduled appointments and, when seen, reported on whether the study ulcer had recurred during the interval since their last visit, as well as their level of compliance with stocking wear. These individuals were also asked to share any issues that might have arisen with wearing the stocking or with the stocking itself.

Compression Device (See Figure 1)**:** The novel stocking/sleeve combination is composed of a: 1) base-layer, enclosed-toe stocking, extending to just below the knee which exerts 20 mmHg graduated compression, and 2) an outer, toeless sleeve which extends from the malleolus to just below the knee. It also exerts 20 mmHg graduated compression. This outer sleeve is applied (slipped) over the base-layer stocking until it reaches to just below the knee and just below the malleolus. The combination of the base-layer stocking and the sleeve provides 30-40 mmHg graduated compression. The stocking sleeves can be manufactured in a full range of colors and are available currently in foot sizes 6 to16. The largest calf circumference in the current stocking/sleeve is 55 centimeters (~22 inches).

Both components of the stocking/sleeve are knit from a combination of natural wicking fibers (i.e., alpaca and merino wool) along with elastic fibers. Additionally, nano-silver triangular plates are covalently bonded to the natural fibers. This unique incorporation of silver plates into the natural fibers allows the stocking or stocking/sleeve combination to be applied in direct contact with the open wound surface; no other dressings or topical treatments are required. Independent *in vitro* studies have demonstrated that this fiber/nano-silver plate combination down-regulates selected inflammatory mediators, such as MMP-9 and bacterial proteases, thereby killing bacteria protected by biofilm, and allowing epithelialization of the wound without harming keratinocytes. Additional *in vitro* studies also demonstrated that the nano-silver plates do not leach out of the stocking fibers, even after repeated machine washings.(1)

(Figure 1) Test Compression Device

Stocking*
(20-30 mmHg)

Sleeve*
(20-30 mmHg)

Stocking & Sleeve Combination= 30-40 mmHg

(*Stocking/Sleeves can be manufactured in a variety of colors and in sizes 6-16)

Results

Sample (See Table 1)**:** The study duration was 19 months. During this time, 39 individuals were screened with 23 meeting all inclusion and none of the exclusion criteria. The most frequently occurring exclusionary findings during screening were: 1) lack of documented venous reflux (n=8), 2) presence of arterial disease (n=3), and 3) presence of the ulcer on other than the lower limb (n=2). Of the subjects enrolled, 6 were adjudged as non-compliant and discontinued at some point from the study, though, in two cases, the study wound healed prior to them being discontinued. One subject was 'lost to follow-up' and one subject expired. The ulcer in the individual who expired healed prior to their death and it was concluded that death occurred due to conditions unrelated to the presence of a chronic wound or application the study device. All subjects were greater than 18 years of age (range, 43 to 86 years of age, mode 79, median 70 and with the mean age being 67). Seventeen subjects were male and 6 were female; 19 were Caucasian and 4 were African-American. All subjects comprehended English and none was pregnant. The weight of subjects ranged from 155 to 439 pounds; the majority of subjects were retired, two were on disability and one was currently employed, as a truck drive. The range of time on one's feet during a 24 hour period was 4 to 8 hours per day. One subject was followed for eleven months following wound closure; the shortest length of time a subject was followed was ??. Subjects reported washing their study compression device as frequently as every day or up to once a week.

Of the 23 study subjects, trauma was determined to be the etiology of the ulcer in 11 subjects; the etiology in 6 subjects was classified as 'venous disease', one as chronic lymphedema, one as scar tissue from a burn earlier in life, one a lower limb pressure ulcer following orthopedic surgery, 2 as obesity coupled with venous disease, and 1 as 'unknown'. Fifteen of twenty-three of the subjects healed (65%) during the course of the study, with two of those subjects ultimately discontinued due to non-compliance. The range of days to healing was 7 to 171. Of the 6 subjects discontinued from the study for non-compliance, one remained healed at 2 and the other at 3 months prior to being dropped from the study. The individual who expired during the study remained healed without recurrence for 5 months prior to his death.

Protocol Modifications:

1. After the initial 10 subjects were enrolled, the protocol was modified to include completion of a Duplex Scan to validate the presence of valvular incompetence/reflux. Assessment of the Ankle/Brachial Index, to rule out arterial disease, had been and continued to be documented via vascular studies as per the original protocol.
2. Due the large size of a number of subjects' upper calfs, the top cuff of the study stocking and sleeve was modified and increased to 55 centimeters (~22 inches) in circumference.

Discussion: Despite this study's small sample and open-label design, the results mirror the characteristics of the venous stasis ulcer population at large. Herein, even when subjects were afforded the optimal circumstances of being in a study designed to support compliance in order to maximize the potential for healing, some continued to be non-compliant. Put simply, the correlation between compliance and outcomes was blatantly apparent. For the most part, when a subject was compliant, the outcome was positive; when not, the outcome was less positive (but not completely dismal). Given these results, it becomes extremely important, prior to drawing hasty conclusions and assigning 'blame' to non-compliant subjects, to reflect on the fact that 65% (15/23) of these individuals healed. Furthermore, that even some who were discontinued from the study healed and remained healed for months after wound closure. The study results clearly support the strong link between compliance and outcome but they do so in a unique manner. The device tested here begs for the insertion of several key concepts into the compliance maxim. Among the concepts identified in this study that need to be added to compliance to affect outcomes are: *product adaptability and longevity (cost), 'ease of use'* (including the normal-look and care of the product) *and buy-in* from those who must wear such a device (for the remainder of their lives).

Compliance + ***Product Adaptability & Longevity (cost), Ease of Use, and "Buy-in"*** **=** Outcomes

Subjects in this study, the mean age of which was 67, faithfully applied the stocking/sleeve combination for months, perhaps doing so more readily because no additional therapies were required and, most refreshingly because they could actually get the stockings 'on'. Furthermore, they did not have to apply salves and creams or extra dressings. In many cases the addition of these "extra" treatments can become overwhelming and, possibly, decrease compliance. The

literature with regard to venous stasis ulcer recurrence is depressing; it suggests a myriad of recurrence rates following wound closure; they range anywhere from 50-70% within 3 months following healing; to 26-69% within 12 months, and 100% within 3 years.(2) As of this time, no longitudinal studies, using a single, self-applied device to demonstrate healing and lack of recurrence over weeks and months have been reported; many reasons can be proposed for this. Some of them are that, despite the appearance of a growing number of guidelines for the assessment, treatment and prevention of specific chronic wound types, many venous stasis ulcers continue to be treated by health care professionals lacking wound care knowledge and expertise and, more significantly, using outmoded therapies. Devoid of in-depth knowledge of the pathophysiology underlying this wound type, a number of providers espouse the belief that the end-point of treatment is simply wound closure; that preventative therapies are unnecessary. One serious consequence of this thinking leads to the conclusion that ulcer recurrence is solely the patient's responsibility and that further efforts to correct the situation would be pointless. This dismal judgement underlies exasperation on the part of patients and their families; continuous "shopping around" for healthcare providers who might help them; the application of a laundry list of treatments (expensive to the patient and the health care system), and an existence filled with predictable, inevitable and perpetual re-appearance of the same wound (oftentimes in exactly the same place anatomically). Searching for the "magic bullet" becomes the focus of one's existence.

Research and experience have delimited much to upend the inevitability of recurrent venous ulcers. The pivotal goal of non-surgical intervention is to maximize venous return. With sustained (i.e., during and after a wounding experience) use of appropriate compression therapy, edema in the lower limbs is decreased; the dead space, containing third-spaced fluid is reduced, and oxygenation to the local tissue is greatly enhanced. Linked, these effects of continuous compression, greatly reduce, if not, obliterate injury prone skin and ulceration. The key to such success lies not in intermittent application of compression, (when an ulcer appears), but rather, permanent application of appropriate, effective and compliance-prone pressure devices to the affected limb or limbs at all times for the remainder of the individual's life. Though such a plan might sound radical, it is, in fact, no different then treatment of other chronic conditions such as diabetes, hypertension or glaucoma. Once diagnosed, in order to reduce regression and/or progression, treatment must be sustained not sporadic. Perhaps the shock of the thought of wearing continuous compression for the remainder of one's life emerges because wounds, chronic wounds, have never been appreciated for what they really are…chronic; nor have they been explained to patients as such.

Even with the best of intentions and motivation, however, adherence to continual application of compression devices can be discouraging. Critical attributes of compression devices, if they are to be fully adopted are: 1) Easy application of the device by the patient or family members (even when maximal pressure is the goal) within their home, 2) adequate and sustained compression levels over time and multiple washings, 3) ability to absorb and contain drainage without additional dressings, 4) ability to shower during use, 5) ability to wear "normal" shoes with the compression device in place, 6) reasonable cost, 7) appropriate reimbursement, including ongoing reimbursement **once the ulcer has healed,** 8) absence of latex, rubber/irritants in the stocking composition and 9) data to support use, cost, and outcomes. A significant number of these attributes exist in the stocking/sleeve evaluated in this study and the effect was seen in the outcomes and satisfaction vocalized by the subjects.

The compression stocking/sleeve device reported on here meets the following, it is: 1) user friendly and adaptable, 2) composed of wool, alpaca and minimal elastic, thereby reducing irritants, 3) the stocking/sleeve can be used multiple times and easily washed within one's own home washer, thereby reducing cost and the need for frequent replacement; 4) supports normalcy by being able to be worn with normal shoes and is manufactured in a variety of colors. Fifth, the novel stocking/sleeves do not look like a medical device; 6) they are easily removed for showering, and 7) as pressure requirements change, the sleeve can be removed or added without having to purchase a different garment.

Compliance with wear can result in cost savings in many ways, be they financial, for example, in cost of care, lost work days, hospitalization, or in non-measurable ways via the emotional drain and cost of perceiving oneself to be "chronically ill" with an open wound, requiring care from family members, or, at the extreme, withdrawing from socialization completely due to the presence of a draining wound. With the use of the novel stocking/sleeve and ongoing feedback, subjects' compliance increased, their satisfaction with the feel of the stocking/sleeve made them want to wear it because they feel "secure", "better", and had "no problem putting it back on". One healed subject summed up the effect of compliance with this stocking/sleeve combination by stating,"I never thought I would see this day" (referring to his now healed venous ulcer).

There are an increasing number of compression devices on the market, including those for travelers, hikers and those with ulcers. The embarrassment once experienced by having to wear such a garment is quickly becoming a thing of the past but only if the effect of compliance on one's life is fully understood. Wearing compression hose seems like a very logical approach to the treatment of weeping wounds and enlarged limbs, most especially to those who have not had a personal experience of the same. Pulling on a garment with 30-40 mmHg pressure gradient can be nearly impossible even to young and healthy individuals. If the therapy is going to work, if the 'gold standard' is to be adopted and compliance is to be manifested, the compression device must possess the characteristics listed above, it must be adopted by the individual and knowledgeably espoused. He or she must receive feedback on its effectiveness and follow-up must be encouraged. This trinity of factors, namely understanding of the condition by the patient, commitment to wearing compression for the rest of heir lives in order to live without chronic ulcers, and ongoing evaluation of the therapy can change the statistics related to venous stasis ulcers. These ulcers simply no longer need to recur, surgical intervention does not need to be the ultimate course. Quality of life can exist and costs can be reduced for individuals with venous ulcers or worse.

Conclusions:

Though other compression devices may emerge, the stocking /sleeve combination reported herein demonstrated that attention to details affecting the patient's adoption of the device enhanced compliance, reduced ulcer recurrence and inevitably affected cost (i.e., reduction in multiple physician office visits, prescription for multiple medications, potential hospitalizations, and loss of work). A healed chronic wound is also a motivator to maintain that state and reduces the state of discouragement and depression experienced by those who are all too aware that, without satisfactory and sustained treatment, their wounds will remain chronic and predictably non-healing.

1. Venous stasis ulcers are currently a costly and inevitable reality
2. Once valvular reflux has been properly diagnosed, the non-surgical approach requires compression be a life-long, self-applied treatment

3. Compression that provides optimal pressure, ease of use and reuse is the only viable approach to life-long compliance
4. Positive feedback, education and on-going surveillance can reduce the cost of venous ulcers to patients, families, healthcare and society
5. Venous stasis ulcers have the potential of becoming a “wound of the past” with the incorporation of standardized, research-based, and appealing, ‘user-friendly’ treatments.
6. Dollars spent on supporting compliance with compression devices, both during wounding and following healing would greatly affect the expenditure of the health care dollar.

References:

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