ORIGINAL ARTICLE

Hemodynamic Effects of Supervised Calf Muscle Exercise in Patients With Venous Leg Ulceration

A Prospective Controlled Study

Yuk Man Kan, MB ChB, FRCS; Konstantinos T. Delis, MSc, MD, PhD

Hypothesis: Because more than two thirds of patients with venous ulcer have an impaired calf muscle pump, enhancement of its ejecting ability with physical training may generate an improved hemodynamic milieu sufficient to promoting ulcer healing. This study evaluated the effects of short-term supervised calf exercise on calf muscle pump function and venous hemodynamics in limbs with venous ulceration.

Design: Prospective controlled study.

Settings: University-associated tertiary care hospital.

Patients: The study consisted of 2 groups. An exercise group comprised 10 patients (median age, 72 years) receiving supervised isotonic calf muscle exercise for 7 consecutive days. A control group comprised 11 patients matched with those in the exercise group for age, sex, ulcer size, and ulcer duration (all, $P>.09$). Patients in both groups had perimalleolar venous leg ulcers, impaired calf muscle function (ejection fraction, <60%), and full ankle joint movement.

Interventions: After providing a complete clinical history, both groups underwent a physical examination, venous duplex scanning, and air plethysmography. The venous filling index, venous volume, residual venous volume, and residual volume fraction of the calf on standing were measured plethysmographically at baseline and on day 8, in addition to calf muscle endurance as determined by the maximal number of plantar flexions performed against a fixed 4-kg resistance during 6 minutes (1 flexion/s). Operators were blinded to the subject's group. Exercise in the first group entailed consecutive active plantar flexions using a standardized 4-kg resistance pedal ergometer. Subjects daily completed 3 sets of flexions of 6 minutes each. All patients had short-stretched compression bandaging.

Main Outcome Measures: The ejected venous volume and ejection fraction were evaluated in both groups at baseline and on day 8.

Results: Both groups had a similar hemodynamic performance at baseline for all the variables evaluated ($P>.10$). After 7 days of exercise, patients in the exercise group improved their ejected venous volume by 67.5%, ejection fraction by 62.5%, residual venous volume by 25% (all 3, $P=.006$), and their residual volume fraction by 28.6% ($P=.008$). Changes in the control group within the same period were small (all, $P>.10$). By day 8, the exercise group had a significantly better ejected venous volume ($P<.001$) and ejection fraction ($P<.001$) than the control group. The venous filling index and the venous volume did not change ($P>.50$) in either study group. Calf muscular endurance in the exercise group increased 135%, from a median 153 plantar flexions at baseline to 360 on day 7 ($P<.001$).

Conclusions: By increasing the muscular endurance, efficacy, and power of the calf muscle, isotonic exercise improves its ejecting ability and the global hemodynamic status in limbs with venous ulceration. Prospective evaluations of the clinical effects of calf muscle pump strengthening for the treatment of venous leg ulceration are indicated by the results of this study.

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From the Irvine Laboratory, Department of Academic Vascular Surgery, St Mary's Hospital, Imperial College School of Medicine, London, England.

SUPERVISED exercise is an established treatment in the management of patients with intermittent claudication caused by peripheral vascular disease.[1-3] It is also a standard regimen in the rehabilitation of patients following cardiac surgery.[4,5] Physical training traditionally has been considered controversial in patients with complicated chronic venous insufficiency (CVI). This may be attributable to the potential risks of a segmental rise in the ambulatory venous pressure in vascular beds with venous disease, causing a further deterioration of venous hypertension.[6-8] A significant improvement in several hemodynamic aspects of calf muscle pump function has recently been reported following a brief program of calf muscle strengthening ex-

MATERIALS AND METHODS

Twenty-one patients with chronic perimalleolar venous ulceration ($CEAP_6$), full ankle joint movement, and impaired calf muscle pump function (EF, <60%) were included in this prospective study, consisting of one group receiving supervised exercise (n=10; mean age, 72 years [range, 49-81 years]) and a control group (n=11; mean age, 80 years [range, 69-85 years]). Following detailed clinical history taking and a physical examination, patients who potentially might meet the inclusion and exclusion criteria listed in **Table 1** were invited to the laboratory for further lower limb investigation entailing (1) color flow duplex imaging (HP Sonos 2500; Hewlett-Packard, Palo Alto, Calif) to determine the sites and extent of venous reflux, using the method previously reported[15]; (2) air plethysmography (APG 1000; ACI-Medical, San Marcos, Calif), performed as previously described to assess venous hemodynamics and calf muscle pump function[16,17]; and (3) determination of ankle-brachial pressure indexes using a handheld Doppler instrument and calibrated sphygmomanometer.[18] Fifty-eight consecutive patients attending the ulcer clinic were investigated. Of these, 37 were excluded because of ulcers of mixed origin (n=3), vasculitis (n=2), venous outflow obstruction (n=2), restricted ankle joint movement (n=3), obesity (n=1), mobility-impairing arthritis (n=2), stage IV prostatic carcinoma (n=1), and normal calf muscle pump function (n=23).

The 2 groups were matched for age ($P>.09$), sex ($P>.10$), median ulcer size (exercise group, 16.5 cm^2 [range, 4-50 cm^2]; control group, 20 cm^2 [range 10 -33 cm^2]; $P>.46$), ulcer duration (exercise group, 24 months [range, 13-52 months]; control group, 29 months [range, 19-41 months]; $P>.59$); and venous hemodynamics (all, $P>.25$). Subjects were consecutively allotted to the 2 groups until the sample sizes were sufficient to enable statistical analysis with the following end points: ejected venous volume (in milliliters) and EF (percentage), which measure the ejecting ability of the calf muscle; residual venous volume (in milliliters) and residual volume fraction (percentage), which measure the residual calf volume after maximal muscle contraction using tiptoe exercise; venous filling index (in milliliters per second), an estimate of the amount of venous reflux; and the venous volume (in milliliters) of the calf on standing. In both groups, these hemodynamic variables were measured at baseline and on day 8, using air plethysmography. The mean of 3 measurements taken and interpreted blindly by the operators was documented for each estimated variable per leg and time point.

Supervised exercise aiming at isotonic strengthening of the calf muscle was offered for 7 consecutive days to the exercise group. The protocol entailed active plantar flexions for 6 minutes using a standardized 4-kg resistance pedal ergometer (Stress'ter, Stu-ert Medical Devices, Frinton-on-Sea, United Kingdom). Patients were seated on an examination couch with their knee in slight flexion resting on a pillow and their heel firmly placed on the backrest of the ergometer pedal as shown in **Figure 1**. Subjects daily completed 3 sets of flexions of 6 minutes each. A 5-minute rest was allowed between consecutive sets. In the first 3 days, each set consisted of three quarters of the maximal number of flexions reached at baseline during 6 minutes at a rate of 1 flexion per second, and up to 360 flexions in the last 4 days. Both groups received changes of ulcer dressings and short-stretch compression bandaging twice weekly, the standard ulcer care at our institution. A synopsis of the investigation protocol used in the present study is depicted in **Table 2**.

Statistical analysis of the data was performed using nonparametric tests. The Mann-Whitney test was applied to evaluate intergroup differences. The Wilcoxon signed rank test was used to determine intragroup differences. The 95% confidence intervals (CIs) of the estimated median differences and point estimates were also calculated (Minitab for DOS, release 8.2; Pennsylvania State University, State College). Differences in proportions were assessed using the χ^2 test with Yates correction.

ercise using heel raises in legs with healed venous ulcers.[9]

Calf muscle pump function deteriorates with clinical class of disease.[10-12] As reported by Araki et al,[12] the ejection fraction (EF), an indicator of the ejecting ability of the calf muscle, is impaired in 60% of patients with varicose veins (Clinical, Etiological, Anatomical and Pathophysiological [CEAP] 2-3[13]), in 76% of limbs with a healed ulceration, and in 90.5% of limbs with active ulcers. The residual volume fraction, which is the common denominator of the power of the calf muscle pump against the refluxing venous blood, is deranged in 63% of patients with varicose veins ($CEAP_{2-3}$) and in 92% of legs with active ulcers. Not only does the proportion of limbs with impaired venous hemodynamics increase with the clinical severity of CVI but also the actual magnitude of the impairment itself increases. The median EF is 52% in limbs with varicose veins and 38% to 47% in legs with ulcers, representing a deterioration of 14% and 21% to 37%, respectively, compared with the upper normal limits. Similarly, the residual volume fraction is 32% to 37.6% in legs with varicose veins ($CEAP_{2-3}$) and 49% to 61% in legs with ulcers, representing a deterioration of 7.4% and 40% to 74%, respectively, compared with the upper normal limits. It has been stated that venous reflux is necessary but not a sufficient cause of ulceration, and that calf muscle pump impairment is required for development of venous ulceration.[12]

Because more than 70% of patients with venous ulcer have impairment of the calf muscle pump,[12,14] enhancing its ejecting ability by physical training may generate an improved hemodynamic milieu sufficient to promote ulcer healing. The aim of this prospective controlled study was to evaluate the effects of short-term supervised calf exercise on calf muscle pump function and venous hemodynamics in limbs with venous ulceration, using air plethysmography.

RESULTS

Supervised isotonic calf muscle strengthening exercise for 7 consecutive days in the exercise group resulted in a significant improvement of the ejected venous volume, EF, residual venous volume, residual volume frac-

Table 1. Inclusion and Exclusion Criteria

Inclusion	Exclusion
Venous leg ulcers	Mixed origin ulcers
Ulcer duration >2 mo	Ankle-brachial index <1.0
Impaired calf muscle pump function (ejection fraction <60%)	Vasculitis
	Collagen diseases
	Steroid therapy
	Immunosuppression
	Venous outflow obstruction
	Restricted ankle mobility
	Pregnancy
	Cancer
	Congestive cardiac failure
	Inability to perform tests
	Uncontrolled diabetes mellitus
	Noncooperative patient

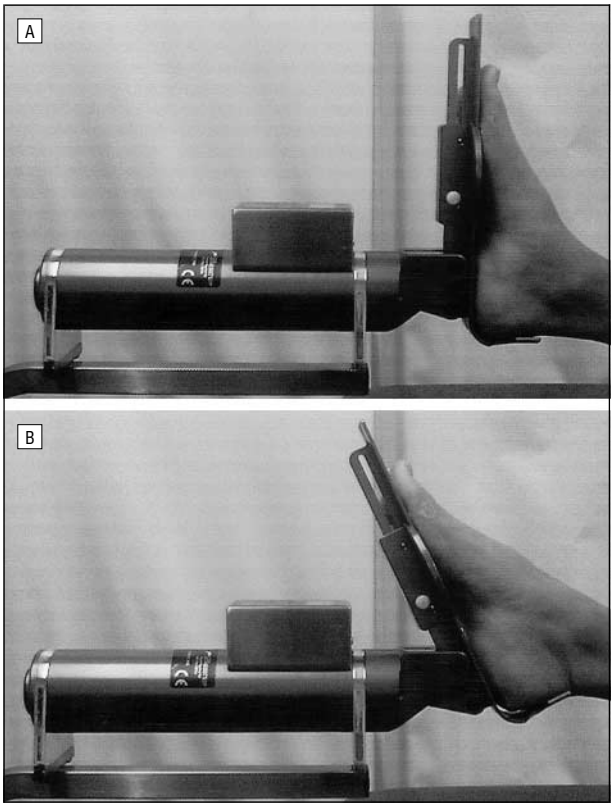

Figure 1. Isotonic plantar flexion performed using a pedal ergometer attached to the edge of an examination couch at resting (A) and on active plantar flexion against a 4-kg resistance (B).

tion, and calf muscle endurance. Changes in the control group within the same period were small and insignificant. An intergroup hemodynamic comparison at the end of the exercise protocol revealed a significantly improved ejected venous volume and EF in the group performing calf muscle exercises.

EJECTED VENOUS VOLUME

The median (interquartile range) ejected venous volume in the exercise group increased by 67.5% during the supervised exercise period, from 40 mL (range, 35-60 mL) at baseline to 67 mL (range, 57-98 mL) on day 8 ($P=.006$; estimated median difference, 28.5 mL; 95% CI, 20.5-35.5 mL) (**Figure 2**). Changes documented in the control subjects were small ($P>.50$; estimated median difference, 0.5 mL; 95% CI, −4.0 to 8.0 mL). By day 8, exercising patients had a higher ejected venous volume than the controls ($P<.001$; point estimate, 30 mL; 95% CI, 19-70 mL).

EJECTION FRACTION

The median (interquartile range) EF in the exercise group increased by 62.5% during the supervised exercise period, from 40% (range, 36%-44%) at baseline to 65% (range, 57%-68%) on day 8 ($P=.006$; estimated median difference, 23%; 95% CI, 18.5%-28.5%). Changes documented in the control subjects were small ($P=.13$; estimated median difference, −4.5%; 95% CI, −8.5% to 3%). By day 8, exercising patients had a higher EF than the controls ($P<.001$; point estimate, 28%; 95% CI, 17%-35%).

RESIDUAL VENOUS VOLUME

The median (interquartile range) residual venous volume in the exercise group decreased by 25% during the supervised exercise period, from 52 mL (range, 42-71 mL) at baseline to 39 mL (range, 35-69 mL) on day 8 ($P=.006$; estimated median difference, 12 mL; 95% CI, 5.5-32.0 mL). Changes documented in the control subjects were small ($P=.68$; estimated median difference, 2.0 mL; 95% CI, −14.0 to 13.5 mL).

RESIDUAL VOLUME FRACTION

The median (interquartile range) residual volume fraction in the exercise group decreased by 28.6% during the supervised exercise period, from 56% (range, 51%-59%) at baseline to 40% (range, 31%-49%) by day 8 ($P=.008$; estimated median difference, 12%; 95% CI, 5.5%-21.5%). Changes documented in the control subjects were small ($P=.94$; estimated median difference, 0%; 95% CI, −8.0 to 11.0%).

VENOUS FILLING INDEX AND VENOUS VOLUME

There were no significant changes in the venous filling index ($P=.54$; estimated median difference, 0.1 mL/s; 95% CI, −0.40 to 1.75 mL/s) or the venous volume ($P>.50$) in the exercising patients at the end of the study (**Figure 3**). This was also true of the venous filling index ($P=.72$; estimated median difference, 0.22 mL/s; 95% CI, −1.05 to 0.65 mL/s) and venous volume ($P=.96$; estimated median difference, 0.25 mL/s; 95% CI, −13.0 to 13.5 mL/s) in the control patients.

MAXIMAL NUMBER OF PLANTAR FLEXIONS (CALF MUSCLE ENDURANCE)

The median (interquartile range) maximal number of plantar flexions during 6 minutes (1 flexion/s) against a fixed 4-kg resistance pedal ergometer in the exercise group increased by 135% during the supervised exercise pe-

Table 2. Synopsis of Investigation Protocol*

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
History	×	...	...	...	...	...	...	...	×
Examination	×	...	...	...	...	...	...	...	×
Air plethysmography	×	...	...	...	...	...	...	...	×
Duplex	×	...	...	...	...	...	...	...	...
Exercise	...	×	×	×	×	×	×	×	...

*× Denotes protocol component was performed on that day; ellipses, not performed.

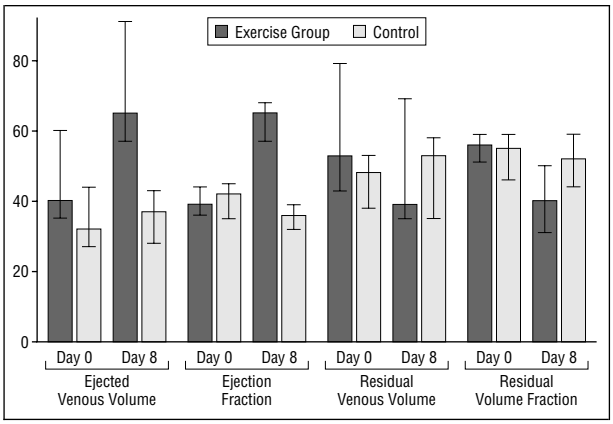

Figure 2. The ejected venous volume (in milliliters), ejection fraction (percentage), residual venous volume (in milliliters), and residual volume fraction (percentage) at days 0 and 8 expressed as median and interquartile ranges. Differences in the ejected venous volume, ejection fraction, residual venous volume (all 3, $P=.006$), and residual volume fraction ($P=.008$) between days 0 and 8 in the exercise group were significant. Differences in the control group were nonsignificant (all, $P>.10$). Differences between groups were significant for ejected venous volume and ejection fraction (both, $P<.001$) at day 8.

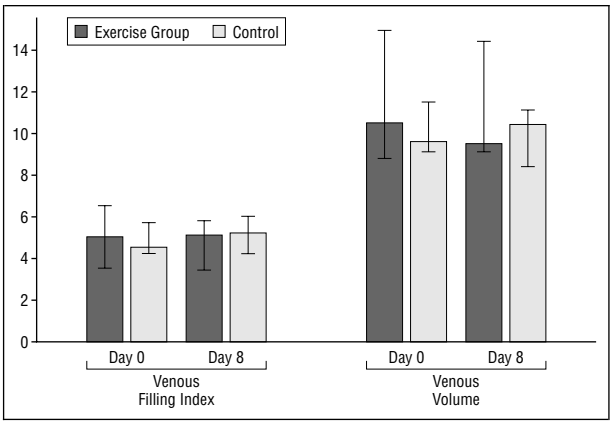

Figure 3. The venous filling index (in milliliters per second) on the left and the venous volume (in milliliters × 10) on the right expressed as median and interquartile ranges. Differences between the exercise and control groups at days 0 and 8, as well as intragroup differences between days 0 and 8, were nonsignificant (all, $P>.50$).

riod, from 153 (range, 74-185) at baseline to 360 (range, 300-360) on day 7 ($P<.001$) (**Figure 4**).

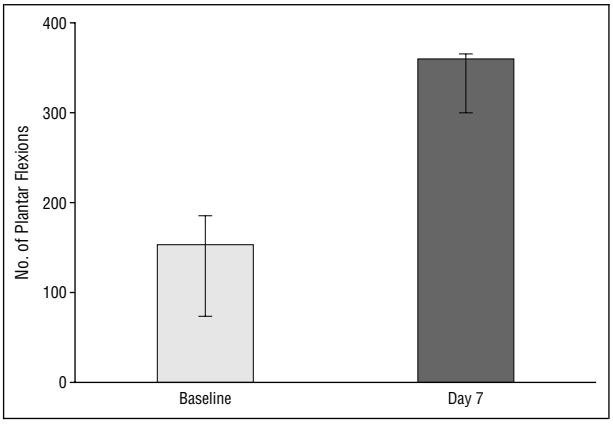

Figure 4. The muscular endurance of the calf muscle pump in the exercise group expressed as maximal number of plantar flexions against a fixed 4-kg resistance pedal ergometer (1 flexion/s) for up to 6 minutes. Data are presented as median and interquartile ranges at baseline and on completion of the supervised exercise protocol on day 7 ($P<.001$).

COMMENT

Venous return is dominated by the action of the 3 natural muscle pumps of the lower limb: those of the foot, calf, and thigh.[6,19,20] The calf muscle pump is the most effective hemodynamically because of its high capacitance,[11,16] the high pressures it can generate,[6] and its positioning in the lower half of the limb, where the venous pressure is maximal.[21] Compartment pressures in the calf during muscle contraction may exceed 200 mm Hg,[6] pumping the venous blood up into the thigh and generating a 60% to 80% decrease in the ambulatory venous pressure.[22-24] The calf muscle pump is characterized by its capacitance and ejecting ability; these can be determined using plethysmographic techniques of which air plethysmography, probably the most accepted, enables their estimation in the form of residual venous volume and EF. When calf muscle pump function is impaired, the residual venous volume in the calf increases immediately after muscle contraction, in the presence of venous valvular incompetence, and causes the ambulatory venous pressure to rise.[25] The clinical severity of CVI is correlated with the amount of refluxing venous blood per time unit[11,26-28]; however, the hemodynamic role of the calf muscle pump in the presence of venous insufficiency is less clearly understood. It has been previously shown that the prevalence of venous ulceration is 2%, 30%, and 41% in limbs with a normal calf muscle pump function and a venous reflux of 2 to 5 mL/s, 5 to 10 mL/s, and 10 to 20 mL/s, respectively; however, in the presence of calf muscle pump impairment, the prevalence of venous ulceration rises to 32%, 63%, and 71%, respectively.[10] This increase in the prevalence of ulceration suggests that patients with normal calf muscle pump function partially compensate for the venous hypertension, or that the effects of venous reflux are further complicated by an abnormal calf pump.

This study shows that a short course of supervised calf muscle exercise, in persons whose ankle joint mobility is normal, can significantly improve the venous hemodynamics of patients with venous leg ulceration caused by venous valvular incompetence and impaired calf muscle pump function. Patients undergoing isotonic strengthening of the calf for 7 consecutive days by means of active plantar flexions using a 4-kg pedal ergometer demonstrated a significant improvement in their calf muscle endurance, which was associated with a marked enhancement in the ability to eject calf venous blood, as shown by the increases in our study in the ejected venous volume and EF by 67.5% and 62.5%, respectively (both, $P=.006$). As expected, the amount of venous reflux, which represents the state of venous valvular incompetence, did not change (95%CI, –0.4 to 1.75 mL/s). However, the conditioning of the calf muscle pump resulted in greatly improved residual venous volumes and residual volume fractions, by 25% and 28.6%, respectively (both, $P=.008$). Previous validation studies[16] show that the ambulatory venous pressure in CVI is linearly correlated with the residual volume fraction; therefore, its improvement in the exercise group may be interpreted as an equivalent attenuation of the venous hypertension.

In ambulation, the venous pressure in limbs with venous valvular incompetence is determined by the intensity and frequency of muscular contractions within the volume-restricted calf compartments in the presence of unhindered retrograde venous flow. Therefore, a weak calf muscle in a frail and malnourished elderly patient with walking difficulty will be far less effective in counterbalancing the refluxing venous volumes of the lower limb veins than that of a robust, well-nourished individual with strong muscles. This study shows the hemodynamic benefits that can be gained in a short period if emphasis is placed on the function of the calf muscles and their improvement. It also confirms preliminary uncontrolled data of previous work[9] reporting that poor calf muscle pump function in limbs with CVI could be improved by physical exercise. Tiptoe exercise performed for 6 weeks, with the patient standing and the balls of the feet at the edge of a 5-cm-high step, improved the EF and the residual volume fraction of 20 patients with recently healed venous ulceration by 12% and 34%, respectively (both, $P=.001$). However, as in our study, this did not produce any significant effects on the amount of venous reflux. Having evaluated the calf muscle pump power at baseline and on completion of the exercise regimen, the authors[9] were unable to detect statistically significant improvements in the calf muscle strength or its endurance. This is not in keeping with our findings that, after the 7-day supervised exercise program, our subjects were able to perform timed isotonic plantar flexions against a standardized 4-kg resistance for twice as long as at baseline. A significant improvement in the ability of patients with CVI grades I through III to perform isometric plantar flexions and dorsiflexions has also been reported by Klyscz et al[29] after an intensified 6-week training program, entailing supervised walking and ergometric exercise for 1 hour twice weekly. Using transcutaneous oxygen tension, they identified a significant increase in the partial tension of dermal oxygen among subjects receiving exercise. They failed, however, to identify significant improvements in the venous hemodynamics, based on phlebodynamometry and photoplethysmography.

Venous hypertension caused by CVI is known to produce 3 types of morphological injuries to the skeletal muscle tissue: (1) atrophy of type 2 muscle fibers, which become angular; (2) denervation (neurogenic atrophy) manifested by grouping of atrophy fibers, target fiber formation, and type 1 and 2 grouping; and (3) myopathic abnormalities, noted by fiber degeneration, inflammation, and necrosis with accumulation of lymphocytes perivascularly.[30] Disuse, denervation, and sustained episodes of ischemia and reperfusion, with subsequent leukocyte margination, pavementing, adhesion, infiltration, sequestration,[30] and kinin production,[31,32] may contribute to this muscle injury. Calf muscle exercise, on the other hand, produces hyperemia and promotes conditioning of the striated muscle cells,[33] resulting in an increase in the skeletal muscle fiber size, capillary density, and succinate dehydrogenase activity, which reflects an enhancement in the cellular oxidative capacity.[34]

Based on published data,[10] the significant improvements in calf muscle pump function with supervised exercise, despite the unchanged venous filling index levels, would be expected in our study to decrease the incidence of ulceration from 63% for a cohort with our 40% baseline median EF to 30% for a cohort with our 65% improved EF reached on completion of the protocol. The clinical data are unavailable to support this anticipated increase in ulcer healing rates prospectively. If these data are accurate, the hemodynamic improvements found in this study could have vast financial and clinical implications. Assuming a prevalence of venous leg ulceration of 1%[35-37] and a mean cost of £400 to £600 million in the United Kingdom[38,39] and $1 billion in the United States[40] for the treatment of venous ulcers annually, the potential increase in the ulcer healing rate with exercise could represent a savings, in a period of cost awareness and containment, of millions of pounds and dollars.

In conclusion, supervised isotonic exercise is able to restore within a week the pumping ability of the calf muscle and to improve the hemodynamic performance in limbs with active ulceration subsequent to severe venous valvular incompetence and calf muscle pump impairment. Active exercise in these patients promotes muscular endurance and the power and efficacy of calf muscular contraction, resulting in an attenuation of the residual venous volume and its gravitational effects on the limb tissues. The clinical implications of supervised exercise on venous leg ulceration merit a prospective assessment, in view of the impact that complicated CVI has on the quality of life and on health budgets.

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Corresponding author and reprints: Yuk Man Kan, MB ChB, FRCS, Irvine Laboratory, Department of Academic Vascular Surgery, St Mary's Hospital, Imperial College School of Medicine, 10th Floor, QEQM Wing, Praed Street, London, United Kingdom W2 1NY.

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