Sequential compression biomechanical device in patients with critical limb ischemia and nonreconstructible peripheral vascular disease

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Objectives: **Critical limb ischemia (CLI) patients who are unsuitable for intervention face the dire prospect of primary amputation. Sequential compression biomechanical device (SCBD) therapy provides a limb salvage option for these patients. This study assessed the outcome of SCBD in severe CLI patients who otherwise would face an amputation. Primary end points were limb salvage and 30-day mortality. Secondary end points were hemodynamic outcomes (increase in popliteal artery flow and toe pressure), ulcer healing, quality-adjusted time without symptoms of disease or toxicity of treatment (Q-TwiST), and cost-effectiveness.**

Methods: **From 2004 to 2009, we assessed 4538 patients with peripheral vascular disease (PVD). Of these, 707 had CLI, 518 underwent intervention, and 189 were not suitable for any intervention. A total of 171 patients joined the SCBD program for 3 months.**

Results: **All patients were Rutherford category ≥4. Median follow-up was 13 months. Mean toe pressure increased from 39.9 to 55.42 mm Hg, with a mean difference in toe pressure of 15.49 mm Hg ($P = .0001$). Mean popliteal flow increased from 35.44 to 55.91 cm/s, with mean difference in popliteal flow of 20.47 cm/s ($P < .0001$). Mortality at 30 days was 0.6%. Median amputation-free survival was 18 months. Limb salvage at 3.5 years was 94%. Freedom from major adverse clinical events (MACE) at 4.5 years was 62.5%. We treated 171 patients with SCBD at a cost of €681,948, with an estimated median per-patient cost of treatment with SCBD of €3988.**

Conclusion: **SCBD therapy is a cost-effective and clinically efficacious solution in CLI patients with no option of revascularization. It provides adequate limb salvage and ameliorated amputation-free survival while providing relief of rest pain without any intervention. (J Vasc Surg 2011;54:440-7.)**

Critical limb ischemia (CLI) is a serious condition with dire consequences. If left untreated, patients with CLI face the prospect of limb loss. Revascularization is not always an option, however, due to the poor general condition of the patient or to the absence of reconstructible vessels.[1] Occlusion of crural and pedal vessels in 14% to 20% of patients with CLI makes them unsuitable for distal arterial reconstruction.[2] The Bypass Versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial reported that 50% of patients who had a diagnostic angiogram were unsuitable for revascularization.[3,4]

Every effort must be made to identify alternative therapies that would benefit these patients who are unsuitable for revascularization and are deemed to be amputation bound. Sequential compression biomechanical device (SCBD) therapy is one such alternative. SCBD has been shown to achieve wound healing and limb salvage in patients with severe infrapopliteal disease and limb-threatening ischemia who are not suitable for revascularization.[5-7] It increases flow to the lower limbs by generating improved popliteal artery blood flow, implicating collateral circulation enhancement.[5,7-11]

Acknowledging that the evidence available to date on SCBD is anecdotal and comes mostly from feasibility studies, there is still a paucity in the literature on how to care for these inoperable patients with limb-threatening ischemia. We present our 4-year experience with the use of SCBD in the management of patients with severe CLI, who are not candidates for a revascularization procedure.

Mechanism of action. SCBD reduces venous pressure in the dependent foot by forced emptying of capacitance vessels and expelling blood from the foot and calf to the thigh.[12] This increases the arteriovenous pressure gradient and augments arterial inflow. A suggested mechanism is the momentary delay in the local vasoregulation resistance of the venoarteriolar response (VAR) and the transient suspension of the arteriovenous reflex.[13,14]

This SCBD is delivered with the Art Assist Unit (ACI Medical, San Marcos, Calif) at a maximum inflation pressure of 120 mm Hg, minimum deflation pressure of 0 mm Hg, inflation rise time of 0.3 seconds, and inflation time of 4 seconds, followed by 16 seconds of deflation, resulting in

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three compression cycles each minute. Rapid cyclic blood flow induces high shear stress, which promotes the endothelial cells to generate and release nitric oxide (NO), tissue factor pathway inhibitor (TFPI), and endogenous tissue plasminogen activator (tPA).[15-17]

METHODS

Study aim. The goal of our study was to find out the long-term outcome of the use of SCBD as an alternative treatment for patients with CLI who are unfit for revascularization due to the nature and distribution of nonreconstructible peripheral vascular disease (PVD) or to severe comorbidity scores with expected poor intervention outcome.

Primary end points were limb salvage, sustained clinical improvement (defined as improvement to Rutherford category ≤ 3), and 30-day mortality. Secondary end points were hemodynamic improvement (increase in popliteal artery flow and toe pressure), ulcer healing, quality-adjusted time without symptoms of disease or toxicity of treatment (Q-TwiST), and cost-effectiveness.

Patients. From June 2004 to December 2009, patients referred to our tertiary referral center with CLI were selected to receive 90 days of a treatment protocol with an SCBD if they had nonreconstructible arterial disease or severe comorbidity deeming them to be too high risk for revascularization.

Inclusion criteria. Inclusion criteria were:

1. Rutherford category ≥ 4.
2. Patient has been receiving at least 6 months of optimal medical with antiplatelet, statin, and antihypertensive combination, with or without anticoagulant, if necessary.
3. Patient required more than a combination of two analgesic medications, or opiates, to control rest pain.
4. American Society of Anesthesiologists (ASA) grade ≥ 4 and deemed unfit for revascularization by two consultant anesthetists, or absence of any reconstructible distal runoff vessels below the midcalf, with no outflow below the ankle, after diligent arterial mapping (as described below) and by consensus of at least one vascular surgeon and one interventional radiologist.

Exclusion criteria. Twelve patients were excluded for the following reasons:

1. Occluded popliteal artery; however, patients with a stenosed popliteal artery were not excluded.
2. Extensive foot gangrene precluding attempts at limb salvage.
3. A nonviable acutely ischemic limb.
4. Severe infection.
5. Recently confirmed deep venous thrombosis.
6. Congestive heart failure.
7. Inability to tolerate compression.

Patients were assessed on an intention-to-treat basis. Demographic data were recorded according to the *International Classification of Diseases* codes. Patients were assessed regarding cardiovascular risk factors and severity of peripheral vascular disease.

Arterial mapping. Imaging was primarily by duplex ultrasound arterial mapping (DUAM) for all CLI patients, using an HDI 5000 (ATL Ultrasound, Bothell, Wash) or a Phillips IU22 (Philips Medical Systems, Bothwell, Wash) with popliteal artery flow assessment and resting toe-brachial pressure measurement.

If DUAM failed to reveal any reconstructible vessels and the patient was deemed unfit for surgery, then no further imaging was sought. If DUAM failed to show any outflow vessels, yet the patient was deemed fit to withstand a revascularization procedure, then further imaging was done with computed tomographic angiography (CTA) or magnetic resonance angiography (MRA), or both.[18] If neither modalities showed any reconstructible outflow, and the patient had tissue loss and was fit for revascularization, then the presence or absence of any options for revascularization was confirmed with on-table digital subtraction angiography (DSA).[18]

SCBD protocol. After obtaining informed consent, patients were commenced on a treatment protocol that lasted 12 weeks[5] or until they required amputation. The therapy protocol consisted of a minimum of 6 to 8 h/d. Treatment was spread throughout the day at two intervals.[5,7] The SCBD device was applied to the symptomatic leg(s) while the patient was sitting upright in a chair. Patients self-administered the treatment at home by wearing the inflatable cuffs on the foot and calf. At the end of the 12 weeks, if the patient's rest pain was improving, or the ulcer was reducing in size, yet their symptoms had not completely resolved, then a second 12-week protocol was commenced. All patients were treated with aspirin, clopidogrel, amlodipine, and a statin.

Data collection. Data were prospectively collected into a prospectively customized vascular database based on VascuBase 5.9 (Consensus Medical Systems Inc, Richmond, BC, Canada). The generic VascuBase software was customized to allow it to cover any data not routinely collected by VascuBase.

Follow-up. Follow-up was at 30 and 90 days and at regular 6-month intervals. Patients were assessed clinically at each visit for resolution of rest pain, ulcer healing, and improvement of gangrene. Doppler pressure measurements and popliteal duplex scanning were performed.

Cost analysis. Cost data were obtained from the hospital patient accounting database. Total costs included the costs of the SCBD, hospital bed occupancy (during the initial work-up phase or any subsequent PVD-related hospitalizations required by the patient), physician fees, operating room services, imaging and investigations, medication, and other services related to the treatment.

Statistical methods. Descriptive statistics were used for patient demographic characteristics. A paired *t* test was used to compare the arterial flows before, during, and after the application of SCBD. Data were expressed as a mean $\pm$ standard deviation and 95% confidence intervals (CIs).

Table I. Demographics and risk factors in 171 patients with sequential compression biomechanical device therapy

Variable	*No. (%) or Median (IQR)*
Age, years	75 (68-81)
Males	107 (63)
Diabetes mellitus	67 (40)
Hypertension	87 (51)
Ischemic heart disease	82 (48)
Dyslipidemia	87 (51)
Renal impairment[a]	32 (19)
Smoking[b]	114 (67)
Hyperhomocysteinemia	90 (53)

IQR, Interquartile range.
[a]Defined as creatinine >150 mg/dL.
[b]Defined as a current smoker or a smoker who stopped during the past 5 years.

Table II. Clinical presentation of 171 patients with sequential compression biomechanical device therapy

Variable	*No. (%) or Median*
ASA 4	80 (47)
Ulcer duration, months	14 (6-23)
Ulcer surface area, cm^2	28 (19-41)
Rutherford category 5 and 6	126 (74)
Duration of symptoms, months	24 (14-34)
Ankle-brachial index	0.36 (0.11-0.48)
Toe pressures, mm Hg	39.9 (12.4-51.8)
Popliteal flow, cm/s	35.44 (16.1-58.2)

ASA, American Society of Anesthesiologists.

For those patients who died before the study completion at 18 months, the data last accumulated were considered for an intention-to-treat analysis. Data are expressed as median and interquartile range (IQR). The level for statistical significance was set at $P = .05$.

RESULTS

Patients. From 2004 to 2009, we reviewed >4538 patients with PVD. Of these, 707 presented with CLI, 518 had one or more interventions for PVD, and 189 were not candidates for surgery. Only 171 patients (63% men) met the inclusion and exclusion criteria and agreed to join the SCBD program for 3 months at 3 hours bi-daily. Patients were a median age of 75 years. More than half were smokers, hypertensive, with dyslipidemia and hyperhomocysteinanemia (Table I). All patients were Rutherford category 4, 5, or 6, and 47% were classed as ASA grade 4 by two consultant anesthetists. The mean absolute toe pressure was 39.9 mm Hg, and the mean popliteal artery flow was 35.44 cm/s (Table II).

No tibial vessel runoff was documented in 59% patients. All patients had multilevel vessel involvement, 87% had superficial femoral artery involvement, 20% had a diseased popliteal artery, 71% had tibioperoneal trunk involvement, and 83% had at least one diseased tibial vessel (Table III).

Table III. Vessels involved and distal vessel runoff in patients who received sequential compression biomechanical device therapy

Variable	*No. (%)*
Total patients	171 (100)
Aortoiliac segment	19 (11)
Common femoral artery	30 (18)
Superficial femoral artery	149 (87)
Popliteal artery	35 (20)
Tibioperoneal trunk	122 (71)
Anterior tibial artery	130 (76)
Posterior tibial artery	111 (65)
Peroneal artery	126 (74)
Occlusive lesions	142 (83)
No distal runoff	101 (59)
Vessel runoff	
1 vessel	27 (16)
2 vessels	14 (8)
3 vessels	29 (17)

Table IV. Reason patients were deemed not suitable for revascularization

Variable	*No. (%)*
Total patients	171 (100)
Unfit for surgery, nonreconstructible vessels	10 (6)
Unfit for procedure only (ASA ≥4)	70 (41)
Nonreconstructible disease only	91 (53)

ASA, American Society of Anesthesiologists.

Ten patients (6%) were not suitable for revascularization because they had no reconstructible vessels and a high ASA grade, 70 patients (41%) were deemed not suitable for revascularization due to high ASA grade, and 91 patients (53%) had no reconstructible vessels (Table IV). All patients received optimum medical therapy.

All patients completed at least one 12-week cycle of therapy. Of these, 31 (18%) needed a second 12-week cycle to help completely resolve their rest pain. The median follow-up after the end of the therapy cycle was 13 months, with an average of 18.3 months (range, 1-62 months).

End points. Sustained hemodynamic improvement was noted with an increase in mean toe pressure from 39.9 to 55.42 mm Hg after treatment, with a mean difference in toe pressure of 15.49 ± 30.92 mm Hg (95% CI, 8.06-22.92 mm Hg; $P < .0001$). This increase was sustained at 12 months of follow-up (Table V).

Mean popliteal flow increased from 35.44 to 55.91 cm/s after treatment, with a mean difference in popliteal flow of 20.47 ± 46.22 cm/s (95% CI, 14.02-26.91 cm/s; $P < .0001$). This improvement was maintained at 12 months of follow-up (Table V).

Rest pain resolved in all patients by the end of their one- or two-cycle treatment period. Gangrene remained dry and nonprogressive. Ulceration healed in all but five patients, who required a major amputation. No device-related complications were reported.

Table V. Hemodynamic improvement at 12-months of follow-up[a]

	Pre-SCBD	*Post-SCBD*			
Hemodynamic improvement	*Mean*	*Mean*	*Change*	*95% CI*	P[b]
Ankle-brachial index	0.36	0.50	0.14	0.03-0.26	.018
Toe pressure, mm Hg	39.9	55.42	15.49	8.06-22.92	<.0001
Popliteal flow, cm/s	35.44	55.91	20.47	14.02-26.91	<.0001

SCBD, Sequential compression biomechanical device.
[a]There was a significant improvement in the ankle-brachial index, toe pressures, and popliteal artery flow velocity.
[b]Paired *t* test.

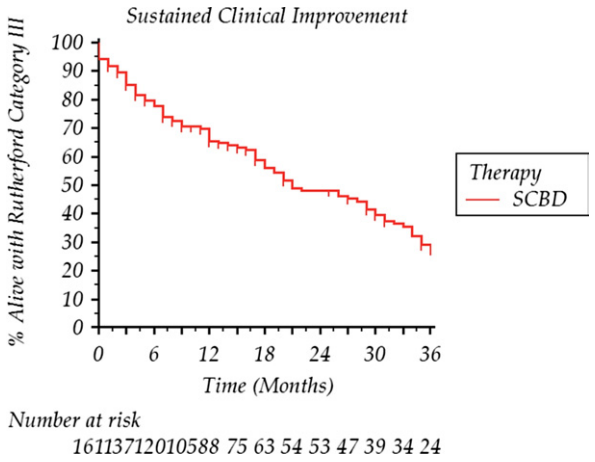

Fig 1. The Kaplan-Meier curve shows the time with sustained clinical improvement (patients alive and in Rutherford category 3) was 30% at 3 years in patients who received therapy with the sequential compression biomechanical device (*SCBD*). The standard error was 10.2% at 36 months.

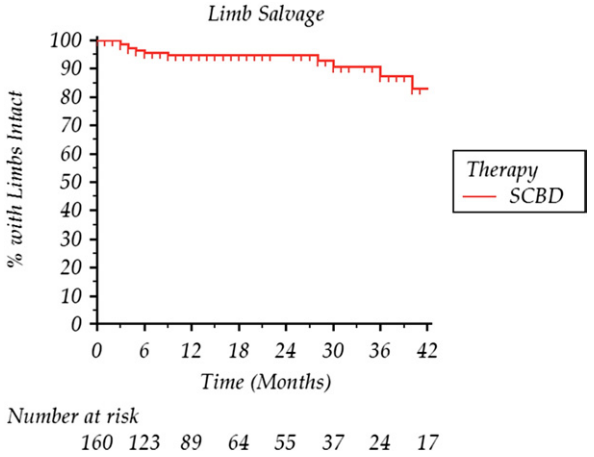

Fig 2. The Kaplan-Meier curve shows an amputation-free survival limb salvage rate of 94% at 3.5 years in patients who received therapy with the sequential compression biomechanical device (*SCBD*). Standard error was 6% at 40 months.

Clinical improvement where the patient reverted to Rutherford category 3 was achieved in 161 patients (594%). Sustained improvement at 3 years of follow-up was 30% (Fig 1). Median amputation-free survival was 18 months, with a limb salvage rate of 94% at 3.5 years (Fig 2). Freedom from MACE was 63% at 4.5 years (Fig 3).

The 30-day mortality was 0.6%, and all-cause survival was 31% in SCBD patients at 4 years (Fig 4). All-cause survival was 63% (50 of 80) at 4 years in patients with a high ASA compared with 13% (n = 12 of 91) in patients with nonreconstructible disease only ($P < .0001$). Cardiac or respiratory comorbidities were the cause of death in 54 patients, five of whom required an amputation before death. Vacuum-assisted closure was used in conjunction with SCBD in 75 legs (44%).

Cox proportional hazard modeling showed that smoking, diabetes mellitus, chronic renal failure, hypertension, and hypercholesterolemia did not have a significant effect on limb salvage or toe pressure improvement.

The mean cost of managing a patient with SCBD, including device rental, hospital visits, physician fees, imaging and investigations, medication, and follow-up was €3988 per patient (Table V). Q-TWiST was 38.13 for a total of 606 months of ArtAssist usage (Table VI). Factoring in the cost of those patients who underwent major amputations, the cost per quality-adjusted life year for SCBD was €2,953 (Table VII).

DISCUSSION

CLI affects 765/1 million individuals each year; of these, 30% will undergo an amputation within the first year after diagnosis. The 5-year mortality rate for CLI patients is 70%, and most of these deaths are cardiovascularly related.[19-22] It is challenging to portray the natural history of CLI; therefore, management strategies must be mastered, and the cardiovascular burden should be acknowledged and managed aggressively.

Longitudinal comparison studies for the incidence of amputations signal an increase, ascribed to the cardiovascular atherosclerosis burden, pandemic of diabetes mellitus, and the aging population.[23-25] This is predicted to lead to the number of major amputations being tripled within 2 decades.

Eskelinen et al[26] conveyed that when bypass surgery was meticulously practiced for CLI, 1976 major amputations/1 million were done in contrast to 3177/1 million when bypass surgery was performed as a last resort for limb

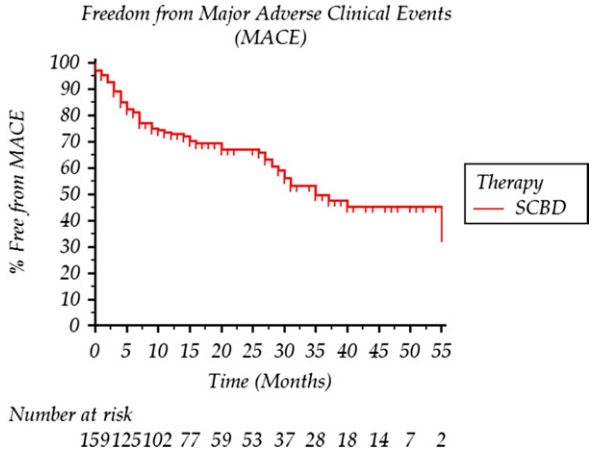

Fig 3. The Kaplan-Meier curve shows freedom from major adverse clinical events was 63% at 4.5 years in patients who received therapy with the sequential compression biomechanical device (*SCBD*). The standard error was 10.7% at 55 months.

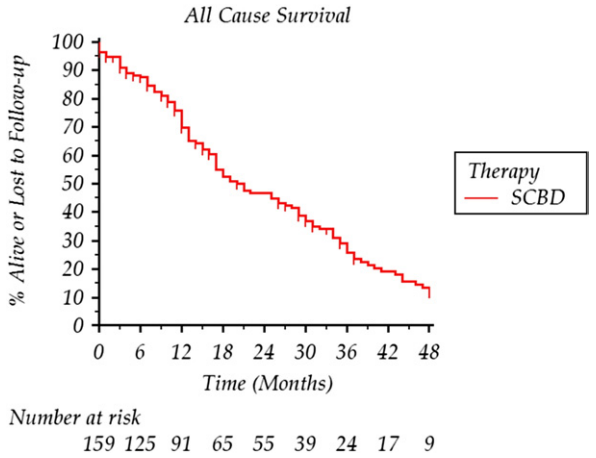

Fig 4. The Kaplan-Meier curve shows all-cause survival at 4 years was 31% in patients who received therapy with the sequential compression biomechanical device (*SCBD*). The standard error was 6% at 4 years.

Table VI. Quality time spent without symptoms of disease and toxicity of treatment (*Q-TWiST*)

Variable	*Outcome*
Toxicity (time with toxicity of disease), months	4.63
TWiST (time w/o symptoms of disease or toxicity of treatment), months	33.03
Progress (time with progression of disease), months	5.56
Q-TWiST	38.13

salvage. There is still a paucity of data in the literature regarding the traditional logic of action when revascularization has been exhausted or is not practical. This provoked us to appraise the clinical efficacy of SCBD in amputation-bound CLI patients.

Table VII. Cost of sequential compression biomechanical device (*SCBD*) therapy

Cost	*Cost, €*
Cost of SCBD rental	
Per patient, 12-week protocol	1600
Total, including second 12-week protocol	323,200
Total cost of medical therapy (not amputations)[a]	358,748
Cost of SCBD rental	
Total cost and hospital visits	681,948
Cost plus hospital visits per patient	3988
Cost of amputation per patient[b]	29,815
Total amputation cost (11 amputees)	327,965
Overall total cost	1,009,913
Cost per quality-adjusted life-year	2953

[a]Includes hospital visits, physician fees, imaging and investigations, medication, and follow-up.
[b]Including hospitalization, surgery, and rehabilitation.

Patient-oriented outcome end points and health-related quality of life and functional status, are entering a new phase by replacing the traditional vascular surgeon–oriented or lesion-oriented outcomes. This new paradigm shift is crucial for the most favorable applicable management opportunities for CLI patients. As gauged by "ideal" outcomes, optimal results in CLI revascularization are seldom achieved. This will become increasingly important from a public health standpoint as the population of CLI patients and the number of treatment alternatives continues to escalate.

Interventions in 14% of CLI patients are typically uncomplicated, with relief of symptoms, complete wound healing, no prerequisite for repeat operation, and maintenance of functional status. For the rest of the 86% of CLI patients, however, repeated hospitalizations will be required for numerous interventions, with declining functional status.[19]

Although limb salvage will persist to be the paramount ambition for most patients referred for vascular surgery interventions, some patients with CLI are undoubtedly better served with amputation. Regrettably, it is not constantly apparent beforehand which patients will gain from primary amputation vs limb salvage endeavor.

Our study showed an increase in the toe-brachial index. This acknowledges the work of Husmann et al[27] on skin blood-flow augmentation with SCBD due to transient suspension of the precapillary sphincter and enhancing skin microcirculation in CLI patients as the VAR is abolished. However, our results contradict the findings of Wahlberg et al[28] and Cisek et al[29] that diabetic patients will not benefit from SCBD, on the assumption that VAR is impaired because of peripheral sympathetic postural auto-vasoregulation. Forty percent of our study was in diabetic patents, and the Cox proportional hazard ratio showed that diabetes mellitus, chronic renal failure, and hypercholesterolemia had no significant effect on limb salvage or toe pressure measurement. We do acknowledge, however, that only 67 patients had diabetes, so the small number of patients needs to be taken into consideration when interpreting this.

Delis et al[30,31] and Husmann et al[32] had established that arterial vascular intervention is associated with a reversal of peripheral vasodilatation with correction of impaired VAR because of the chronic ischemia and decrease in both arterial calf inflow and skin flux on dependency, suggesting readjustment of peripheral resistance.

Applying the same concept to our SCBD patients demonstrated that rest pain reduction and ulcer healing were witnessed within the first week, because of a transient attenuation of the VAR during SCBD application, and it might be one of the mechanisms that provide blood flow to the lower limb. These findings contradict the traditional assumption that arterioles in CLI patients "maximally dilated," due to peripheral sympathetic autoregulation. This autoregulation is considered to be abolished in CLI, a phenomenon known as vasomotor paralysis, and they are relatively insensitive to vasodilator stimuli.[12,13] Yet epidural anesthesia[33] and the administration of prostaglandins,[34,35] both causing attenuation of peripheral flow resistance with vasodilatation, have been reported to offer an appreciable clinical improvement, thus contradicting the contention of peripheral vasoparalysis in CLI.

Delis et al[30] noted that SCBD increases blood flow, relieves rest pain, and limits tissue damage in CLI patients by generating a threefold to fourfold augmentation in popliteal artery blood flow. This mimics our findings in patients with a normal or stenosed popliteal artery.

We like others documented hyperemia after SCBD, and the pronouncement by Abu-Own et al[36] that SCBD lowers peripheral vascular resistance with the liberation of endothelial-derived relaxing factors is well established. Nevertheless, their effects are not virtuously mechanical and the liberations of biochemical mediators are important.[24]

Our protocol for SCBD of 90 days with 3 hours in the morning and in the evening materialized from the work of van Bemmelen et al,[37] as it was apparent that the greatest improvement occurred in the first 3 months of treatment. Improvement in blood flow was sustained after SCBD usage.[8]

We concur with the annotations of van Bemmelen et al[5] and Montori et al[7] where the relationship between patient compliance and clinical outcome was pragmatic. Those in whom limb salvage was attained made use of SCBD according to the protocol, compared with 11 patients in whom SCBD failed.

Analysis of our hospital inpatient accounting database shows a cost of €17,300 for inpatient hospitalization for CLI for angioplasty and successful distal bypass. Conversely, SCBD offers a cost-effective opportunity in patients who are unsuitable for revascularization. The cost of using an SCBD machine is €3,988 per patient. SCBD can be used to treat four CLI patients for the same cost of operating on one CLI patient. Our figures are comparable to those of Delis et al.[8] Our cost analysis reveals that the price of treating eight patients with SCBD is approximately the same as the cost of one primary amputation. In our institution, the hospitalization cost alone for primary amputation, without home modification and long-term rehabilitation costs, was €29,815.

The cost per quality-adjusted life year for SCBD was €2,953. Q-TWiST was 38.13 for a total of 606 months of SCBD treatment. We managed 171 end-stage CLI patients with impending limb loss, at a cost of €681,948, with a reasonable limb salvage rate.

CONCLUSIONS

SCBD is a valuable tool in the armamentarium of dealing with patients who have CLI with nonreconstructible PVD. It provides ameliorated amputation-free survival, rapid relief of rest pain, and enhanced rates of ulcer healing. This is achieved with reduced hospital length of stay and without any intervention in patients with a limited life expectancy and impending limb loss.

This study provides larger-scale evidence that SCBD therapy is a cost-effective and clinically efficacious solution for treatment of high-risk patients with nonreconstructible lower limb arterial disease with enhanced QALY and better QTWiST.

AUTHOR CONTRIBUTIONS

Conception and design: SS, WT
Analysis and interpretation: WT, SS
Data collection: WT, NaH, ES, AF, NiH
Writing the article: WT, SS
Critical revision of the article: SS, WT
Final approval of the article: SS
Statistical analysis: WT
Obtained funding: Not applicable
Overall responsibility: SS

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DISCUSSION

Dr Alan Dardik (*New Haven, Conn*). Dr Sultan, did you have any other options besides the ArtAssist device for this patient, something like stem cell therapy or growth factor therapy?

Dr Sherif Sultan. Regarding stem cell therapy, we haven't applied it in our practice yet due to prohibitory national regulations. However, it might soon be an option. But the results from clinical trials that have been conducted have been far from convincing. Stem cell therapy is still in its infancy and it has a long way to go before it forms a cornerstone of our treatment. That said, some of the cultured stem cells are showing some promise but are still far away from applying to clinical practice.

Dr Hasan Dosluoglu (*Buffalo, NY*). Very good results, but I am very confused with the results because it looks not only better than primary amputation but better than those who undergo revascularization. As a matter of fact, the reported survival is better than claudicants in our series. It seems to me that this is a very unique group of patients that we have to better understand the characteristics a little better, because, as I said, it is not your typical critical limb ischemia (CLI) group, just by looking at the 68% 5-year survival rate.

Dr Sultan. First of all, these patients are very high risk. From when you first see them in your clinic, these are the guys that have the sign on them saying "do not touch!" And basically if you don't touch them, they'll survive until they are going to die from their cardiovascular comorbid-laden problems. One of the reasons that we have a good outcome is because these patients die from something else rather than dying from their legs. And this is borne out in the Kaplan-Meier curves. The minute you touch these patients they die, and this is evident from the 12 patients that we did intervene on, all of them are dead. That is the problem. They are very fragile and there is no way back for them.

Dr Hisham Bassiouny (*Chicago, Ill*). Can you elaborate on your strategy to maintain patient compliance for applying the device three times daily for 1 hour during the duration of the study?

Dr Sultan. We use the machine twice per day for 3 hours in the morning and 3 hours in the evening. And some patients use it more than that and are very compliant. One of the major things that we discovered is that when you offer it to the patient, you have to give them at least 2 to 3 days in the hospital to give them the opportunity to build a "friendly relationship" with the machine. If you give them the machine as an outpatient, they're usually afraid of using it. But the minute they get their heads around it, they fare out brilliantly. In fact, some of my patients have already bought this machine and they don't want to give it back to the company.

Dr Peter Gloviczki (*Rochester, Minn*). If I understood your data correctly, the results are as good as with open revascularization. So do you still perform open revascularization in those who are suitable for distal bypass?

Dr Sultan. We are very aggressive with our CLI program and are fully committed to thoracic endovascular aneurysm repair (TEVAR) revascularization, whether angioplasty alone or laser angioplasty. Revascularization remains our prime aim for these patients. We only offer the ArtAssist machine, because of our problem with funding, to patients that are not suitable for TEVAR if they have absolutely no runoff vessel or they are very high risk.

Dr Dardik. So if you can tell us, these patients all had only distal disease or did they have, for example, superficial femoral artery occlusion and then you were unable to revascularize them?

Dr Sultan. These patients, when you do your duplex, there is no runoff vessel traveling from the distal calf to the ankle and the toes. That's the first thing.

The other thing that we have found is that a patent popliteal artery is crucial for the success of the use of this. The inflow-outflow is a problem, but definitely the presence of a patent popliteal is the only way that you can ensure the successful use of this machine.

Dr Dardik. Any contraindications to use of this machine?

Dr Sultan. Severe congestive cardiac failure and deep vein thrombosis (DVT) are two of the major contraindications and that is why we usually keep some of our patients in the hospital initially just to offload a few liters of fluid out of their body before we put the machine on, otherwise you could drive into acute pulmonary edema. DVT is definitely a contraindication.

Dr Samir Issa (*Riyadh, Saudi Arabia*). We passed on very fast the changes in the toe brachial index. Could you please elaborate on the objective change in this parameter? Did you notice any improvement in the toe brachial index after using this device?

Dr Sultan. There is a theory that there is a vascular plegia problem in the precapillary area in these patients, especially in diabetics. Evidence has shown that when an epidural or prostaglandin is given to these patients that there is peripheral vasodilatation and the patients benefit tremendously. We measure the digital pressure and we measure laser Doppler values in these patients. Although we don't have a full set of data from the laser Doppler, we do have a complete set of ankle brachial indices and the digital pressures. The ankle brachial indices have improved significantly in nondiabetic patients. While digital pressures have improved after 90 days in all patients who completed the program.