Comparison of patients undergoing enhanced external counterpulsation and spinal cord stimulation for refractory angina pectoris

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Introduction **As more patients survive coronary events, the prevalence of patients with refractory angina pectoris is increasing. The aim was to evaluate the effects of enhanced external counterpulsation (EECP) and spinal cord stimulation (SCS) and compare with optimal medically treated patients with refractory angina.**

Methods **153 patients with refractory angina were treated with either EECP, SCS, or were retained on their pharmacological treatment (control). Glyceryl trinitrate usage and Canadian Cardiovascular Society classification were registered at baseline, 6 and 12 months after therapy.**

Results **Both EECP and SCS reduced the angina as compared with controls ($P<0.001$). Patients treated with EECP showed a more effective reduction as compared with SCS patients ($P<0.05$). Both treatments resulted in significantly decreased glyceryl trinitrate usage at 6 and 12 months follow-up ($P<0.001$). The nitrate consumed was unaltered in the controls.**

Discussion **The results from this study show that both EECP and SCS therapy reduce angina in patients with refractory angina pectoris; the response to EECP was slightly more effective than that to SCS. Thus, EECP can be used as an alternative treatment for patients not responding to electrical stimulation. The beneficial effects in the treated groups were maintained during the 12 months follow-up period.** *Coron Artery Dis* **19:627–634**

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Keywords: angina pectoris, enhanced external counterpulsation, spinal cord stimulation

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Introduction

Many patients with coronary artery disease (CAD) have multiple medical management and several invasive interventions in their history. Despite current therapy, these patients have highly symptomatic CAD and frequent cardiac-related hospital admissions. This group of patients suffers from refractory angina pectoris, which cannot be controlled by a combination of medical therapy and revascularization. Refractory angina pectoris is a clinical diagnosis that is characterized by chronic angina because of coronary artery insufficiency in patients who are refractory to conventional treatments. Refractory angina causes severe impairment in the quality of life of the patients. It has been estimated that 30 000–50 000 of the European population meet the criteria for refractory angina pectoris [1]. As more patients now survive coronary events it is estimated that the number of patients with refractory angina pectoris is increasing [1]. The clinical problem of patients becoming refractory is widespread and there is a need for new therapies, both pharmacological as well as nonpharmacological.

Angina treatment involves several strategies [2]. As a first-line therapy, pharmacological treatment such as β-adrenergic blocking agents are used as these drugs have shown to have cardioprotective and symptom-relieving effects. Other standard treatments include Ca^{2+} channel antagonists and nitrates. The pharmacological therapy often does not provide adequate symptom relief and thus there is a need for alternative nonpharmacological treatments. One such option is neuromodulation therapy using transcutaneous electrical nerve stimulation (TENS) and spinal cord stimulation (SCS) [3]. Other alternative treatments are thoracic epidural anesthesia and enhanced external counterpulsation (EECP) [2]. Little evidence directly comparing these multiple therapeutic methods is found.

SCS is a well-documented technique for patients with refractory angina who respond to and tolerate electrical stimulation. Mannheimer and colleagues (1998) [4] have shown that the survival at 5 years is comparable to bypass for high-risk patients. The method modifies the neuronal

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input and output of the heart by delivering a low dose of electrical current to the dorsal columns of the high thoracic spinal cord. Several hypotheses on how SCS modifies the angina pain are present. It is suggested that SCS may release endogenous peptides into the coronary circulation, which reduces myocardial oxygen demand and enhances vasodilatation of collaterals to improve the myocardial blood flow of most diseased regions of the heart. A more likely hypothesis is, however, neuromodulation based on the gate theory of pain whereby the stimulation of large afferent fibres can block the nociceptive information at the brain stem level [5]. This is supported by findings that the activity in intrinsic cardiac neurons is suppressed by SCS even during myocardial ischemia [6]. It is also of interest that clinical and experimental studies have not shown an effect of SCS on coronary blood flow [3].

Patients not suitable for neuromodulation may be candidates for EECP. The increase in coronary blood flow seen by EECP treatment is mainly owing to diastolic augmentation, which is similar to the effect on the arterial system by intra-aortic balloon pumping, but EECP has an effect on venous return and increased cardiac output as well. These hemodynamic effects lead to increased blood flow in multiple vascular beds, including the coronary arterial circulation. The results from earlier studies show consistently a positive clinical response among treated patients. Benefits associated with EECP and SCS include reduction of angina and glyceryl trinitrate (GTN) usage, increased exercise tolerance, positive psychosocial effects, and increased quality of life as well as prolongation of the time to exercise-induced ST-segment depression [3,7–11].

Aim

The primary aim of this study was to compare the antianginal effect of SCS and EECP with a group of optimal medically treated patients measured by the Canadian Cardiovascular Society (CCS) angina scale and use of GTN. Furthermore, we aimed to compare the two methods to evaluate if EECP is suitable as an alternative treatment for patients with refractory angina pectoris not responding to neurostimulation. The effect of these two treatments was followed up over a period of 12 months. The aim was further to compare the results throughout the study period with a control group receiving the same pharmacological treatment.

Methods

Patients

This study was carried out on 153 patients (44 SCS, 79 EECP, and 30 controls) with refractory angina pectoris in an open label, single-center observational trial (Fig. 1). All the patients were referred to the department of medicine at the Central Hospital in Kristianstad (Sweden) following a refractory angina pectoris round with the Departments of Thoracic Surgery, Cardiology, and Radiology at the Lund University Hospital. The patients included in the study had intractable angina, thereby fulfilling the inclusion criteria: these include angiographically documented significant CAD with verified significant stenoses in at least one major coronary artery, not suitable for further revascularization procedures such as coronary bypass graft surgery or percutaneous coronary intervention, and pharmacologically optimal drug treatment. Optimal medical therapy includes the maximal tolerated use of antianginal medications (long-acting and short-acting nitrates, β-adrenergic blocking agents, or Ca^{2+} antagonists). All of the 153 patients were treated according to implemented procedures and had similar baseline clinical characteristics (Table 1).

The clinical procedure was the following: TENS was used in all participants for testing the tolerance to electrical stimulation in all the patients with refractory angina, except those patients contraindicated at unipolar pacemaker. Thus, 44 patients responded with total symptom relief after 30–60 s of high-intensity TENS to electric stimulation and thus subsequently underwent SCS surgery. The pulse generator was programed with two preset stimulation strengths, one stronger that was used in case of establishing angina pain and one weaker that was used as prophylactic treatment.

Seventy-nine patients did not respond to TENS and were therefore included in the group of patients that received EECP therapy. EECP is a noninvasive method of assisting the circulation, which enhances diastolic augmentation and systolic unloading by means of pressurized air cuffs around the patient's legs that are maintained at approximately 260 mmHg during diastole. Patients with deep vein thrombosis, fast irregular rhythms, severe hypertension, peripheral vascular disease, or severe aortic insufficiency did not receive EECP.

A third group consisting of 30 patients did not receive either SCS or EECP owing to contraindications or unwillingness to undergo SCS or EECP treatment. These patients were retained on their pharmacological treatment and were followed up as a control group. Baseline characteristics in the three groups of patients are shown in Table 1. They were of comparable mean age, sex, medical history, and angina status (all $P > 0.05$). All the patients had a history of CAD with earlier revascularization. All medications (Table 2), except for GTN, were unchanged during the entire study period. The patients' medication could, if needed, be adjusted during the study. All patients suitable for this observational study approved their inclusion and signed an informed consent. The study was conducted in accordance with the Declaration of Helsinki and ethical guidelines determined by the ethics council at Lund University.

Fig. 1

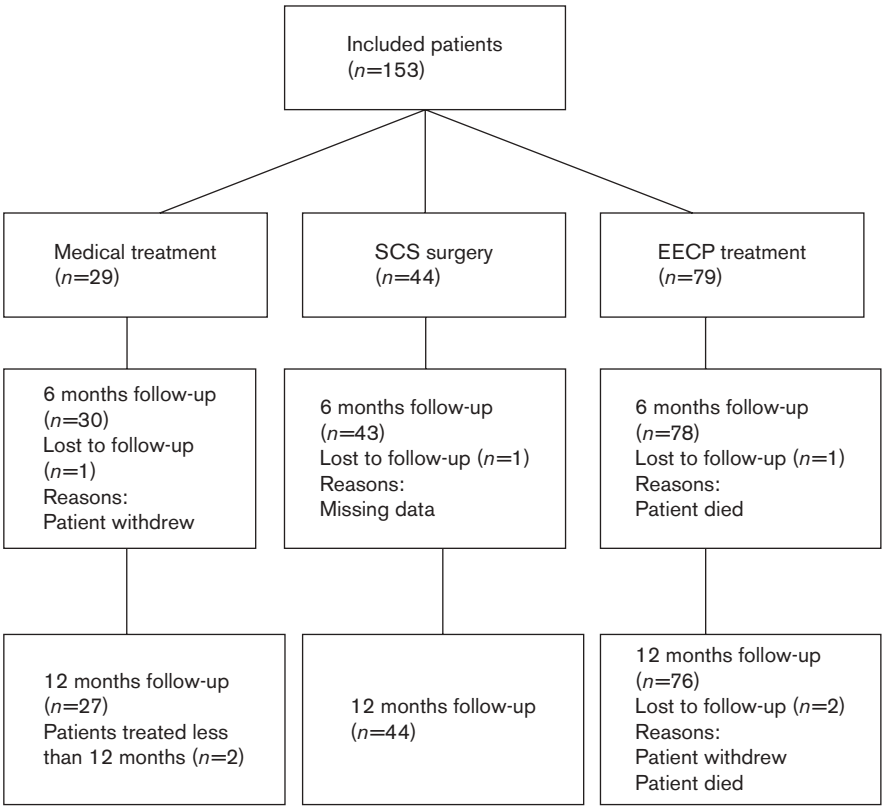


Diagram showing the flow of participants through the study comparing enhanced external counter pulsation (EECP), spinal cord stimulation (SCS), and controls.

Table 1 Baseline characteristics (*n* = number of patients)

	Control (*n* = 30)	SCS (*n* = 44)	EECP (*n* = 79)
Mean age, range (years)	71 (52–86)	69 (54–87)	68 (46–90)
Sex (male/female)	22/8	36/8	64/15
Coexisting disease			
Heart failure (%)	37	22	44
Hypertension(%)	27	45	34
Diabetes mellitus(%)	37	20	22
Coronary artery disease factors and revascularization status			
CAD diagnosis (years; mean, range)	15 (4–28)	13 (2–32)	15 (3–38)
Prior myocardial infarction (%)	67	60	57
Left ventricular ejection fraction			
$x \geq 50\%$	63	77	57
$40\% \leq x < 50\%$	23	18	28
$30\% \leq x < 40\%$	7	2	13
$x < 30\%$	7	2	3
Prior PCI (%)	50	60	57
Prior CABG surgery (%)	73	73	72
Prior PCI and CABG surgery (%)	37	43	46
Angina CCS-class (% of patients)			
II	7	2	3
III	73	89	82
IV	20	9	15

CABG, coronary artery bypass graft; CAD, coronary artery disease; CCS-class, Canadian Cardiovascular Society classification; EECP, enhanced external counterpulsation; PCI, percutaneous coronary intervention; SCS, spinal cord stimulation.

Table 2 Pharmacological treatment

Medication	Control (*n* = 30)	SCS (*n* = 44)	EECP (*n* = 79)
β-blockers	70	50	70
Ca^{2+} antagonists	60	51	44
GTN (%)			
0 times/week	7	2	10
1–2 times/week	13	2	9
3–7 times/week	17	4	24
>7 times/week	63	91	57
Anticoagulantia	7	5	8
ACEI or ARB	60	59	47
Diuretics	56	50	35
Insulin	27	11	14
Oral antidiabetics	20	11	11
Statins	77	77	81
Long-acting nitrates	21	34	59

Data are expressed as a percentage of included patients (*n* = number of patients). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin type 1 receptor blocker; EECP, enhanced external counterpulsation; GTN, glyceryl trinitrate; SCS, spinal cord stimulation.

Data collection

Data on demographics, medical history, coronary disease status, and medication were collected from the patients when entering the study. SCS as well as EECP were carried out within 12 weeks from inclusion. One

cardiologist and one specialized nurse performed CCS-classification and regularly followed up the patients and their medication throughout the study. The data were collected from medical records, telephone interviews, and visits to the clinic at baseline with follow-ups at 6 and 12 months after respective therapy. The 12 months follow-up was completed in September 2007. Further follow-up is ongoing. During the study period angina status was estimated using the CCS-classification I–IV for angina pectoris [12]. Class I represents no angina in ordinary physical activity such as walking or climbing stairs and class IV, the most severe with inability to carry on any physical activity without discomfort; angina may be present at rest. The patients assessed the frequency of their sublingual GTN on a scale ranging from none to seven or more times per week. Adverse events were recorded as soon as they were reported.

The primary outcome of the study was the effect on angina expression after 12 months of EECP or SCS treatment. The angina class, as measured by the CCS scale, and GTN usage are comparatively objective methods of measuring angina relief [13]. An improvement of at least one CCS-class was considered clinically significant. Secondary outcomes were the safety profiles of each treatment.

Enhanced external counterpulsation technique

EECP (Vasomedical Inc., Täby, Sweden) operates by applying electrocardiogram-triggered diastolic pressure of approximately 260 mmHg to the vascular bed of the calves, thighs, and buttocks by means of three air-filled cuffs. All pressure is released at the onset of systole. This sequential compression results in increased venous return and augmented diastolic pressure. The diastolic augmentation increases coronary perfusion pressure and provides improved afterload reduction and increased venous return with a subsequent increase in cardiac output. The instantaneous and simultaneous deflation of cuffs during systole enhances systolic unloading and decreases cardiac workload by decreasing peripheral vascular resistance. Finger plethysmography is used to record the response of blood pressure during diastole by adjusting the time delay between the R-wave of the electrocardiogram and the onset of counterpulsation weight. A typical course of EECP therapy consists of 35-h treatment, 1 h per day, 5 days per week, over a 7-week period [7,14].

Spinal cord stimulation treatment

In the SCS (Medtronic AB, Kista, Sweden) a very low dose of electrical current is delivered to the dorsal columns of the high thoracic spinal cord [15]. This results in reduced myocardial oxygen demand and improved myocardial blood flow of the heart; it is today, mainly, considered to block the pain signals, through the gate theory. The surgical procedure is performed under local anesthesia as adequate positioning of the epidural electrode depends on the patient identifying the area of paresthesia during stimulation. The electrode is positioned so that the patient recognizes a prickling sensation in the region of angina pain. The adequate position is when the stimulation produces paresthesia covering the area of radiation of angina pain, that is, confirming that the spinal segments in which the cardiac innervations are located are stimulated. The stimulation sites are at the T1–T2 level of the spinal cord. The patient carries the pulse generator in a subcutaneous pouch below the left costal arch. The system is similar to a pacemaker with the electrode placed in the epidural space instead of the heart. The settings of the neurostimulator are programed to give a strong but acceptable stimulation that could be used for continuous stimulation. The primary setting of a stimulation frequency of 31 Hz and a pulse width of 210 μs is used and could, if needed, be adjusted. The day after the implant the stimulator is programed once more. For each patient, a proper personalized stimulating program is selected to induce a well-localized mild paresthesia. Despite stimulation of depressed angina attacks, instructions to excite parasthesias (stimulation two to three times per day during a 2–3-h period), in agreement with a standard protocol, are given. At the follow-up amplitude, impedance and stimulation are measured and could, if needed, be programed. An ordinary SCS device implantation requires 1–2 days of hospital recreation.

Pharmacological therapy – control

The standard treatment for symptomatic relief in patients with chronic stable angina includes a long-acting nitrate, β-blockers, or Ca^{2+} antagonists titrated to the lowest heart rate and blood pressure level tolerated. The details of the therapy are given in Table 2.

Statistical analysis

All calculations and statistics were performed using the software program GraphPad Prism 4.0 (GraphPad Software, Inc., La Jolla, California, USA). Statistical significance was accepted when P is lesser than 0.05, using Mann–Whitney test when comparing two groups and Kruskal–Wallis test when comparing more than two groups. A decrease of one CCS-class was considered clinically significant and the difference between SCS and EECP therapy in accomplishing this was evaluated by use of Fischer's exact test. Values are presented as mean ± SEM.

Results

The baseline clinical characteristics are summarized in Table 1. The patients in the three groups had comparable mean age, sex distribution, medical history, and frequency of risk factors for CAD ($P > 0.05$). All the patients had received at least one earlier revascularization procedure

such as coronary bypass graft surgery or percutaneous coronary intervention; some of the patients had both procedures. In addition, CCS classification did not differ. No differences between the groups that might not be expected by chance were present; the slightly higher frequency of diabetes in the control was not significantly different from the other groups ($P > 0.5$). All patients were treated with maximally tolerated antianginal medication at baseline with similar regimens used in the three groups (Table 2) and this did not differ or change during follow-up.

During the follow-up, there were two deaths in the group of patients treated with EECP. In both cases, the cause of death was myocardial infarction. Also, two patients, one in the control group and one in the EECP group, chose to withdraw from the study, resulting in a total dropout of 3% (Fig. 1).

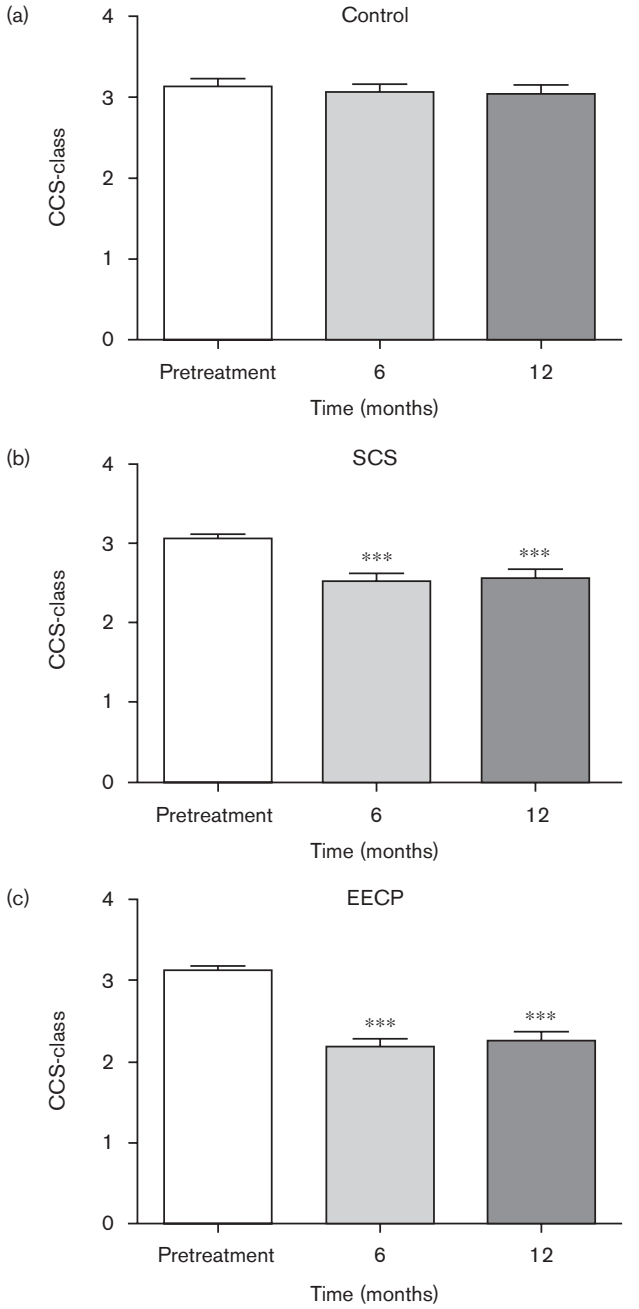
EECP and SCS had significantly reduced the angina pectoris, measured by CCS-class, at 6 and 12 months of follow-up (EECP: $P < 0.001$; SCS: $P < 0.001$, Fig. 2). No relief or change in the angina pectoris frequency or severity in the control group was observed($P =$ NS; Fig. 2). The EECP treatment was significantly more effective in decreasing the angina pectoris by means of CCS-class as compared with SCS therapy during the follow-up (6 months $P < 0.01$; 12 months $P < 0.05$, Fig. 3, Table 3).

A clinically improved angina pectoris status, a reduction by at least one CCS-class, was more pronounced, at 6 as well as at 12 months follow-up, in the EECP-treated patients ($P < 0.05$, Fig. 3, Table 3). In the EECP group 23% of the patients improved by two CCS-classes. Such improvement was not seen in patients treated with SCS.

No significant decrease in the angina pectoris status in the control group during the 12 months follow-up was observed. None of the patients receiving EECP or SCS were seen to have any worsening in their angina pectoris status after treatment. In the control group two patients showed an increased degree of angina pectoris during the study period.

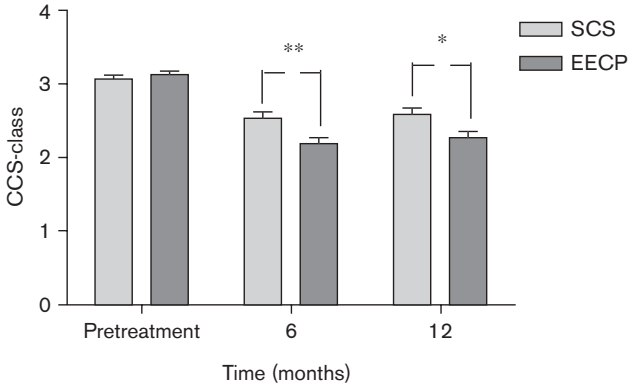
A total of 7% of the study patients did not use GTN during the study period. Patients who used GTN, and were treated with EECP or SCS, demonstrated a reduction in their weekly use of GTN. After 6 months the reduction was significant for both EECP-treated (77%, $P < 0.001$, Fig. 4a) and SCS-treated (74%, $P < 0.001$, Fig. 4b) patients. The decrease in weekly use of GTN was maintained in 67 and 76% at 12 months after completing the EECP ($P < 0.001$) and the SCS ($P < 0.001$), respectively. None of the patients had increased their use of GTN after EECP or SCS treatment. The reduction in GTN administration by patients who needed it more than seven times a week was prominent for both EECP (86%) and SCS (79%). The reduction in GTN was

Fig. 2



Changes in Canadian Cardiovascular Society classification (CCS-class) means over time; before, 6 and 12 months after (a) control, (b) spinal cord stimulation (SCS), and (c) enhanced external counterpulsation (EECP) therapy. CCS-class I: ordinary physical activity does not cause angina. CCS-class II: there is a slight limitation of ordinary activity. Angina may occur on walking more than two blocks, in the wind, or under emotional stress. CCS-class III: there is a marked limitation of ordinary physical activity. Angina may occur after walking one block. CCS-class IV: there is inability to carry on any physical activity without discomfort; angina may be present at rest. All values were compared with pretreatment in each group and presented as mean ± SEM. ***$P < 0.001$.

Fig. 3



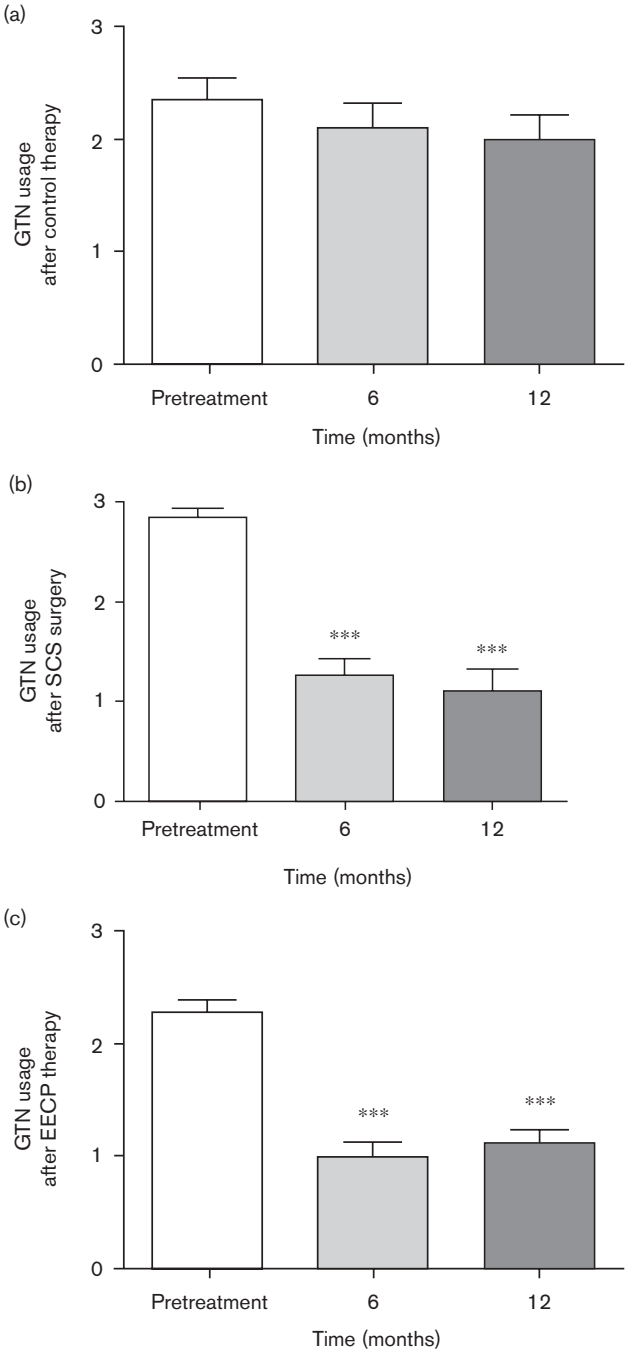
Comparison of the mean difference in angina measured by Canadian Cardiovascular Society (CCS) angina class after enhanced external counterpulsation (EECP) therapy, respectively, spinal cord stimulation (SCS), before, and after 6 and 12 months of treatment. CCS-class I: ordinary physical activity does not cause angina. CCS-class II: there is a slight limitation of ordinary activity. Angina may occur on walking more than two blocks, in the wind, or under emotional stress. CCS-class III: there is a marked limitation of ordinary physical activity. Angina may occur after walking one block. CCS-class IV: there is inability to carry on any physical activity without discomfort; angina may be present at rest. All values are presented as mean ± SEM. *$P<0.05$, **$P<0.01$.

Table 3 Comparisons of CCS-class between EECP and SCS at 6 and 12 months

	EECP	SCS	*P* value
CCS-class at 6 months	*n*=78	*n*=43	
I	10 (13%)	1 (2%)	0.0071**
II	46 (59%)	18 (42%)	
III	19 (24%)	24 (56%)	
IV	3 (4%)	0	
Changes in CCS-class, ≥ 1 class			
Yes	57 (73%)	23 (53%)	0.0441*
No	21 (27%)	20 (47%)	
CCS-class at 12 months	*n*=76	*n*=44	
I	9 (12%)	0	0.0250*
II	39 (51%)	19 (43%)	
III	26 (34%)	24 (55%)	
IV	2 (3%)	1 (2%)	
Changes in CCS-class, ≥ 1 class			
Yes	50 (66%)	20 (45%)	0.0355*
No	26 (34%)	24 (55%)	

CCS-class, Canadian Cardiovascular Society classification; EECP, enhanced external counterpulsation; SCS, spinal cord stimulation.
*$P<0.05$; **$P<0.01$.

Fig. 4



Changes in glyceryl trinitrate (GTN) at baseline, 6 months, and at 12-months follow-up after (a) enhanced external counterpulsation (EECP) treatment, (b) spinal cord stimulation (SCS) surgery, and (c) control. GTN was divided into four groups. 0=no short-acting GTN/week; 1=1–2/week; 2=3–7/week, and 3=7 or more/week. All values were compared with pretreatment values in each group and are presented as mean ± SEM. *$P<0.05$, **$P<0.01$, ***$P<0.001$.

maintained at 12 months follow-up for both treated groups, EECP versus SCS. The GTN consumption remained unchanged in the control group during the 12 months follow-up as compared with baseline (Fig. 4c).

Discussion

The majority of patients with angina pectoris secondary to coronary artery ischemia can be adequately controlled by medication and revascularization procedures. A subset of patients has chronic angina pectoris that is refractory to the above treatments and neuromodulation (SCS) or EECP has been implemented with some success. In this study we have, in one center, directly compared the

responses to EECP, SCS, and a matched control group. The results demonstrate that EECP and SCS are more effective in decreasing angina measured by CCS-class as compared with patients only receiving optimal tolerable antiangina pharmacological treatment. The direct comparison of SCS and EECP in two groups showed that EECP treatment appeared more effective in decreasing the angina pectoris measure as reduction in CCS-class. A direct comparison in a double-blinded, randomized manner is, however, required to verify this suggestion.

Earlier studies have shown that EECP therapy and SCS treatment result in symptomatic relief among patients with refractory angina pectoris [7,8,16–18]. These results are confirmed in this study; however, here we add the dimension that in our center EECP appears slightly better. The underlying mechanisms by which these two treatments work are poorly understood [3].

SCS has been used for treating patients with angina intractable to conventional medical and surgical treatment strategies. SCS has been found to be an effective treatment, although the mechanism of action is complex and not fully elucidated [3,6,19,20]. It is proposed that SCS affects the balance between myocardial oxygen supply and demand by recruitment of collaterals and increases angiogenesis. Beneficial effect on pain relief and on sympathetic tone is observed; this yields reduction in pain and oxygen consumption in the heart [20]. The final pathways for the effects of SCS are the intracardiac neurons [6]. Results from an earlier study have shown that even during coronary occlusion, SCS therapy continues to suppress the activity of intracardiac neurons [19]. However, the international working group of neuromodulation performed a study on dog hearts at rest and during acute myocardial ischemia [3]. They concluded that SCS does not influence the distribution of blood flow within the nonischemic or ischemic myocardium. In addition, they found no proof of modification of left ventricular pressure–volume dynamics in the anesthetized dog [3]. They suggest that SCS modifies through a spinal-brain stem modulating of afferent signaling.

The hemodynamics of EECP mimics that of an intraaortic balloon counterpulsation by augmenting diastolic blood flow in multiple vascular beds, including the coronary arteries, and by reducing afterload [21]. The mechanisms thought to be responsible for the improvement of the angina status include promotion of collateral circulation, enhancement of the endothelial function, and improved ventricular function [22]. The consequences of these mechanisms are a reduction in ischemia, which subsequently yields pain relief. EECP causes shear stress in the coronary circulation by diastolic augmentation. This is thought to activate factors that modify endothelial functions, which may be potent activators of angiogenesis, such as fibroblast growth factors [23]. In addition to the central effects, EECP has proven to exert peripheral effects similar to physical exercise [22].

The majority of the patients in the control group of refractory patients were treated adequately with antiangina medication and showed no improved effect in their angina status over time. In the study by Rana *et al.*, 2005 [24], a late effect of placebo has been observed at 2 years post treatment with fibroblast growth factors or laser myocardial revascularization. However, we did not see such an effect. The control group remained unattended as did EECP and SCS. Overall, using traditional therapies in the management of pain in patients with refractory angina pectoris is commonly associated with inadequate symptom control. Many patients require numerous drugs to control their angina. The potential for adverse drug interaction and side effects may limit the ability of this group of patients to tolerate their medication and also limits the compliance. These patients represent an end-stage in refractory angina characterized by severe myocardial insufficiency episodes [21]. The shortcomings of pharmacological therapy for patients suffering from refractory angina pectoris have resulted in the development of new therapies such as SCS and EECP that are now being studied.

EECP is a single treatment period whereas SCS prolongs. This may have an impact on patients' reporting of symptoms of this chronic condition in that SCS patients may increase their patient control to the SCS system. The long-term compared efficacy of angina status, of these patients treated with EECP versus SCS, has not been evaluated.

It is fair to discuss if the beneficial results of EECP therapy and SCS treatments may to some extent be caused by a placebo effect, although, according to Lasagna [25], the placebo effect is almost negligible after 2–3 months of treatment. As the patients in this study were followed up over a period of 12 months and the reduction in angina was sustained, the results cannot be explained only as placebo. Furthermore, the presence of a nonresponding third group of patients, the medically treated control, stabilizes the findings. Earlier studies suggest that refractory angina is indeed a chronic condition with little change over time. The impact of the placebo effect as in each of the two therapy regimes at the level of patient's perception could not be measured and limits the study.

Patients with refractory angina, as might be expected, have according to Loh [26] a relatively high rate of events over a 12 months follow-up period. In this study

two patients (1%) died of cardiac events and were lost to follow-up. One percent of the total cohort of cardiac events was lost to follow-up; this is not infrequent and might be expected as this group of patients lives at the end-stage of their refractory angina. Two patients chose to withdraw from the study during the follow-up. The total dropout during the follow-up was 3%, which is a small amount according to earlier studies [18,27].

EECP as well as SCS are effective treatment strategies for patients with severe angina. Both therapies are superior to pharmacological treatment only. Preexisting comorbid conditions, which preclude the use of one or another treatment option, and patient preference should guide clinicians when choosing between treatments. These two available treatments, EECP and SCS, should be considered as additions to the modern medical and revascularization therapy in this patient group that has significant disability and limiting symptoms interfering with activities of daily life.

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