



Effect of spinal cord stimulation on myocardial perfusion reserve in patients with refractory angina pectoris

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Aims

Epidural spinal cord stimulation (SCS) provides symptom relief in refractory angina pectoris, but its mechanism of action remains incompletely understood. We studied effects of short-term SCS therapy on myocardial ischaemia tolerance, myocardial perfusion reserve (MPR), and endothelium-mediated vasodilatation induced by cold pressor test (CPT) in patients with refractory angina pectoris.

Methods and results

We prospectively recruited 18 patients with refractory angina pectoris and studied them after implantation of SCS device at baseline before starting the therapy and after 3 weeks of continuous SCS therapy. Myocardial ischaemia was evaluated by dobutamine stress echocardiography. Global and regional myocardial blood flow (MBF) were measured using positron emission tomography and ¹⁵O-water at rest, during adenosine stress, and in response to CPT. Systemic haemodynamics were comparable before and after 3 weeks of SCS at rest, during adenosine stress and during CPT. Appearance of angina pectoris induced by dobutamine stress was delayed after SCS therapy. Global MPR increased ($P = 0.02$) from 1.7 ± 0.6 at baseline to 2.0 ± 0.6 after 3-week SCS therapy. This was associated with a significant reduction in global MBF at rest and increase in MBF induced by adenosine in the ischaemic regions. Global MBF response to CPT was improved after SCS (0.27 ± 0.20 vs. 0.40 ± 0.15 , $P = 0.03$).

Conclusion

Short-term SCS therapy improved myocardial ischaemia tolerance, absolute MPR, and endothelium-mediated vasomotor function in refractory angina pectoris, indicating that this therapy can alleviate myocardial perfusion abnormalities in advanced CAD.

Keywords

Spinal cord stimulation • Angina pectoris • Positron emission tomography • Coronary flow reserve • Myocardial blood flow

Introduction

Refractory angina pectoris is defined as 'a chronic condition caused by clinically established reversible myocardial ischemia in the presence of coronary artery disease (CAD), which cannot be adequately controlled by a combination of medical therapy, angioplasty or coronary artery bypass graft'.¹ Epidural spinal cord stimulation (SCS) is a treatment option for this patient group. It is based on stimulation

of the dorsal column fibres of the spinal cord, which in turn activate the inhibitory interneurons, by means of an electrode positioned in the epidural space under local anaesthesia. Randomized trials and registry data have demonstrated the clinical efficacy of SCS in providing symptom relief when compared with 'no-stimulation' in refractory angina.^{2–4} Current European and American guidelines on the treatment of stable angina pectoris give class IIb (evidence level B or C) recommendation for the use of SCS therapy in refractory

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angina.⁵ However, the evidence regarding reduction in mortality and ischaemia burden by SCS therapy is currently lacking.

The mechanism of action of SCS in refractory angina is still incompletely understood.^{6,7} In contrast to the improved tissue perfusion observed in peripheral artery disease, there are no studies supporting the hypothesis that SCS increased global myocardial blood flow (MBF).^{8–10} However, clinical studies have suggested that SCS can cause redistribution of MBF^{11–14} and decrease myocardial oxygen consumption^{12,15} correcting the imbalance between myocardial oxygen demand and supply in the ischaemic regions. These effects are related to reduced sympathetic tone and normalization of the intrinsic cardiac sympathetic nervous function by SCS.^{16–19} Since sympathetic nervous system plays an important role in the regulation of MBF, we hypothesized that SCS could alleviate perfusion abnormalities and impaired coronary vasoreactivity in advanced CAD.²⁰

Positron emission tomography (PET) can provide quantitative, non-invasive measurements of MBF that enable detailed physiological assessment of CAD.²¹ It is possible to measure absolute myocardial perfusion reserve (MPR), that is, the ratio of MBF during maximal adenosine-induced vasodilatation to MBF at rest. Assessment of MPR using PET provides a combined measure of coronary flow through the epicardial arteries and microcirculation. Thus, MPR can be reduced by either functionally significant epicardial coronary stenosis or microvascular dysfunction caused by vascular smooth muscle cell and endothelium-dependent mechanisms.^{21,22} Response of MBF to cold pressor test (CPT) measures primarily endothelium-dependent regulation of MBF in response to sympathetic stimulation caused by immersion of hand or foot in cold water.²³ Both MPR and MBF response to CPT are validated surrogate markers of the effects of therapies on coronary vasomotor function in patients with risk factors for or established CAD.^{22–24}

The aim of this study was to assess whether short-term SCS improves myocardial ischaemia tolerance, MPR, and coronary vasoreactivity in patients with refractory angina pectoris. We evaluated myocardial ischaemia by dobutamine stress echocardiography and measured MBF using PET at rest, during adenosine stress as well as in response to CPT at baseline with SCS turned off and after 3 weeks of continuous SCS therapy.

Methods

Patients

We prospectively recruited 21 consecutive patients referred for SCS therapy due to refractory angina pectoris in the Turku University Hospital from January 2007 to February 2012. Inclusion criterion was chronic refractory angina pectoris defined according to the European Society of Cardiology (ESC) as angiographically documented CAD, evidence of myocardial ischaemia, angina pectoris of Canadian Cardiovascular Society (CCS) class ≥ 3 for at least 3 months despite optimal antianginal medication and no benefit from revascularization.¹ Exclusion criteria were contraindication for implantation of SCS device; age over 80 years; left ventricular ejection fraction $\leq 40\%$; acute coronary syndrome, decompensated heart failure, ventricular fibrillation, or sustained ventricular tachycardia within 3 months; severe asthma; second- or third-degree atrioventricular block or pregnancy. One patient refused to participate, one patient had accidental non-cardiac death after inclusion, and one patient was excluded due to SCS lead failure detected at follow-up. Thus, the final study

Table 1 Patient characteristics

Gender (male/female)	16/2
Age (years)	69 \pm 7
Weight (kg)	86 \pm 14
BMI (kg/m ²)	29 \pm 4
Risk factors	
Diabetes mellitus	10 (56)
Hypertension	15 (83)
Hypercholesterolaemia	16 (89)
Current smoker	4 (22)
Medication	
Statins	18 (100)
Beta-blocker	17 (94)
Calcium-channel blocker	10 (56)
Long-acting nitrates	18 (100)
ACE-inhibitor or ARB	18 (100)
Diuretics	8 (44)
Aspirin	18 (100)

Values are mean \pm SD or number (%) $n = 18$.
BMI, body mass index; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker.

population consisted of 18 patients whose clinical characteristics are shown in Table 1. The study was conducted according to the declaration of Helsinki, the study protocol was approved by the ethics committee of Hospital district of Southwest Finland, and all study patients gave their written informed consent.

Device implantation

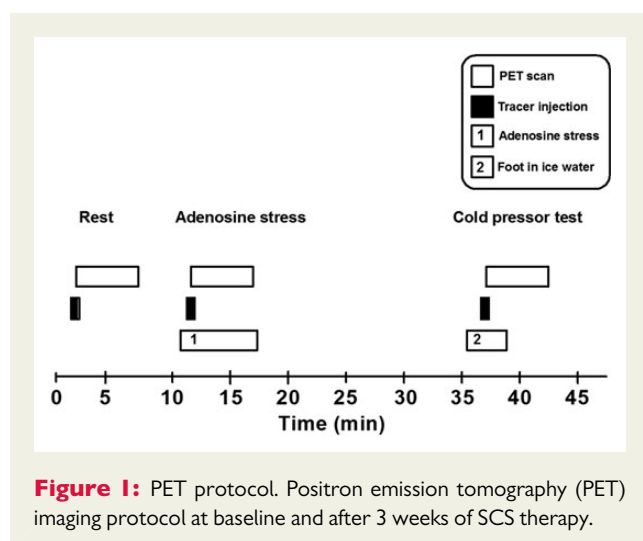
After a screening visit, commercially available implantable SCS devices (St. Jude Medical) were implanted. Implantation was performed by experienced anaesthesiologists at the Turku University Hospital. The lead was advanced under radiographic screening to the epidural space at the level of mid-thoracic spinal cord. Leads were positioned under fluoroscopy guidance with the tip of the electrode at the level of C7 or Th1. Upon obtaining adequate paresthesia, the pulse generator was implanted.

Study procedures and follow-up

After successful device implantation and testing, the device was turned off for 2 weeks. Thereafter, the baseline assessments were performed including both evaluation of MBF by PET at rest, during adenosine stress and during CPT; and evaluation of myocardial ischaemia tolerance by dobutamine stress echocardiography. Patients also filled in the 15D-form measuring quality of life. Then, SCS was turned on and, after 3 weeks of follow-up with continuous SCS therapy, the same assessments were repeated.

All patients underwent PET perfusion studies at rest and during adenosine stress at both time points according to the protocol. However, two patients refused from repeated CPT at follow-up due to procedural discomfort. Owing to logistic reasons or patient discomfort, dobutamine echocardiography could not be performed in four patients at both time points.

Clinical follow-up and care of the patients was done according to standard treatment protocol. The medications were continued unchanged throughout the study and patients were advised to use sublingual



nitrates for angina episodes as required. No adverse cardiac events occurred during the three week follow-up period.

Positron emission tomography

Myocardial perfusion was evaluated using PET scanner (GE Advance, General Electric Medical Systems, Waukesha, WI, USA) and ^{15}O -labelled water as previously described.²⁵ The PET imaging protocol is demonstrated in Figure 1. Patients were instructed to avoid any caffeine containing substances for 24 h before the scan. First, a dynamic PET scan of the heart was performed after injection of ^{15}O -labelled water (900–1100 MBq) as an intravenous bolus over 15 s at rest. After decay of radioactivity, a second scan was performed during adenosine-induced stress. Adenosine infusion was started 2 min before the start of the scan at a rate of 140 $\mu\text{g}/\text{kg}$ of body weight/min and continued until the end of the scan. After a minimum of 10 min, a third scan was performed during CPT that was performed by immersing the patient's foot in ice water for 3 min starting 90 s before start of the scan. Heart rate, blood pressure and a 12-lead electrocardiogram were recorded at rest and every 3 min during adenosine stress and CPT.

The perfusion studies were analysed using validated software (Carimas version 2.5, www.turkupetcentre.net/carimasturku) as previously described blinded to the clinical data, time point, and physiologic state.²⁶ Global left ventricle MBF and regional MBF were calculated as an average of three repeated analyses to minimize operator-dependent variability using a standard anatomic template and Carimas software. MPR was calculated as the ratio of MBF during adenosine stress and at rest. Flow response to CPT was calculated as the difference in absolute MBF during CPT and at rest. Segmental flow values were analysed separately in the ischaemic and non-ischaemic myocardial regions. Ischaemic myocardium was defined as a regional perfusion defect during adenosine stress before therapy.²⁷ In order to assess redistribution or homogenization of MBF, coefficient of variation of perfusion was calculated.

Dobutamine echocardiography

Dobutamine echocardiography was performed using Acuson Sequoia 520 (Acuson Siemens, Mountain view, CA, USA) within a maximum of 6 days from the corresponding PET study. A standard protocol with graded dobutamine infusions of 5, 10, 20, 30, 40 μg per kg of body weight per minute with increments every 2 min was used. Infusion was continued until the appearance of severe angina pectoris or until the protocol was completed. Images were stored for off-line analysis.

Time to the appearance of severe angina pectoris after starting dobutamine infusion was recorded. Standard parasternal and apical views (long axis-, two-chamber-, four-chamber-, and short-axis views from the apical, papillary muscle, and basal levels) were recorded at rest, during dobutamine infusion and at recovery immediately after stress. Images were analysed off-line blinded to time point. Ejection fraction (EF) was measured using Simpsons's biplane method and regional wall motion abnormalities were evaluated in all views to calculate average wall motion score (WMS). In order to quantitatively assess ischaemic wall motion abnormalities, average longitudinal myocardial strain was measured using the vector velocity imaging technique in the apical four-chamber view before and after SCS therapy. Myocardial strain was repeatedly measured at baseline and at follow-up at the time of appearance of angina pectoris on the first (baseline) echocardiography and at termination of dobutamine infusion (peak stress).

15D health-related quality-of-life instrument

The health-related subjective quality of life of the patients was measured with 15D instrument that is a validated measure of health-related quality-of-life in patients with chronic pain.²⁸

Statistical methods

Data are shown as mean \pm standard deviation, unless otherwise stated. Normalcy of data was tested using the Kolmogorov–Smirnov test. Paired samples *t*-test was used to evaluate differences between baseline and follow-up. Associations between improved MPR and other variables were assessed by Fisher's exact test. A value of $P < 0.05$ was considered statistically significant. Statistical tests were performed with IBM® SPSS® Statistics 20.0.0 software.

Results

Patient characteristics

The basic clinical characteristics of the study patients are shown in Table 1. All patients had stable CCS 3 or 4 angina pectoris, previous evidence of myocardial ischaemia (either stress-induced myocardial perfusion abnormality in nine or reversible ST-depression in ECG during angina in nine patients) despite optimal medication and no option for revascularization. All patients had three-vessel CAD and had undergone coronary artery bypass surgery. In nine patients, percutaneous coronary interventions had also been performed in addition to CABG. There were seven patients who had a history of myocardial infarction and three patients had Q-waves in the ECG, but echocardiography showed ejection fraction of $\geq 40\%$ in all patients. All patients were using statin, long-acting nitrate and either beta-blocker or calcium-channel antagonist on stable dose throughout the study.

Clinical follow-up and quality of life

One patient was excluded at follow-up due to malposition of the SCS lead in the epidural space requiring correction. There were no adverse events in the other 18 study patients. Based on the 15D questionnaire, 82% of the study patients reported improvement in health-related quality of life after 3-week continuous SCS therapy when compared with before therapy. Compared with baseline, SCS therapy improved mean 15D score from 0.77 ± 0.07 to 0.80 ± 0.06 ($P = 0.02$).

Table 2 Systemic haemodynamics at rest, during adenosine stress, and in response to CPT at baseline and after SCS

	Baseline SCS OFF	3 weeks SCS ON	P-value
Rest			
Systolic blood pressure (mmHg)	131 ± 18	134 ± 23	0.66
Diastolic blood pressure (mmHg)	65 ± 8	68 ± 8	0.33
RPP (mmHg/min)	8072 ± 1834	8255 ± 2280	0.80
Adenosine stress			
Systolic blood pressure (mmHg)	130 ± 21	133 ± 28	0.69
Diastolic blood pressure (mmHg)	68 ± 14	67 ± 10	0.98
RPP (mmHg/min)	10094 ± 2897	10189 ± 2439	0.92
Cold pressor test			
Systolic blood pressure (mmHg)	155 ± 22	155 ± 21	0.97
Diastolic blood pressure (mmHg)	78 ± 12	75 ± 6	0.52
RPP (mmHg/min)	11167 ± 3017	11107 ± 2191	0.96

RPP, rate pressure product; min, minute.

Systemic haemodynamics

Systemic hemodynamic measurements of the study patients are shown in Table 2. After 3 weeks of SCS therapy, there was no change in blood pressure or rate pressure product at rest, during adenosine stress or in response to CPT compared with baseline. All patients were in sinus rhythm and there were no arrhythmias during imaging.

Dobutamine echocardiography

Dobutamine stress caused angina in all patients at baseline. Compared with baseline, there was an increase in time to the onset of angina in 10 out of 14 patients after SCS therapy. The average time to the onset of angina increased from 366 ± 118 s at baseline to 468 ± 122 s after SCS ($P = 0.005$).

Average EF and WMSs of patients are shown in Table 3. In all patients, dobutamine-induced worsening of regional wall motion abnormalities. However, EF and WMS were comparable at baseline and after SCS therapy. In addition to these, average myocardial longitudinal peak systolic strain was measured in patients with the same or prolonged time to the onset of angina after SCS therapy ($n = 10$). At the time of onset of angina at baseline (i.e. on average 366 s of dobutamine infusion), there was a significant improvement in systolic strain from $-11.2 \pm 3.4\%$ at baseline to $-13.4 \pm 4.6\%$ ($P = 0.002$) after SCS therapy.

MBF and MPR

Absolute MBF and MPR were measured by ^{15}O -labelled water PET before and after 3 weeks of SCS therapy. Myocardial perfusion was homogeneously distributed at rest. As expected, there were widespread perfusion abnormalities during adenosine stress. Before therapy, all patients had an ischaemic area of $>10\%$ of the LV.

The average global MBF and MPR values of the study patients are shown in Table 4. Global MPR was higher ($P = 0.02$) after 3-week SCS therapy than before therapy (Table 4 and Figure 2). This was associated with lower global MBF at rest ($P = 0.02$), whereas peak

Table 3 Ejection fraction (EF) and average regional wall motion score (WMS) during dobutamine stress echocardiography

	Baseline SCS OFF	3 weeks SCS ON	P-value
EF (%)	52 ± 12	52 ± 11	0.61
WMS rest	1.4 ± 0.3	1.4 ± 0.3	0.20
WMS stress	1.6 ± 0.3	1.4 ± 0.3	0.74

Table 4 Global MBF at rest and during adenosine stress, myocardial perfusion reserve (MPR) and MBF response to CPT at baseline and after spinal cord stimulation (SCS) therapy

	Baseline SCS OFF	3 weeks SCS ON	P-value
MBF Rest (mL/g/min)	0.91 ± 0.22	0.78 ± 0.10	0.02
MBF Adenosine (mL/g/min)	1.49 ± 0.51	1.61 ± 0.57	0.14
MPR	1.69 ± 0.61	2.04 ± 0.63	0.02
CPT ΔMBF (mL/g/min)	0.27 ± 0.20	0.40 ± 0.15	0.03

ΔMBF, absolute change of MBF from baseline to CPT.

absolute global MBF during adenosine stress was comparable after 3-week SCS therapy and at baseline before therapy. Coefficient of variation of regional MBF within the left ventricular myocardium was comparable before and after 3 weeks on SCS therapy both at rest ($15 \pm 9\%$ vs. $10 \pm 5\%$, $P = 0.055$) and during adenosine stress ($31 \pm 15\%$ vs. $33 \pm 13\%$, $P = 0.65$).

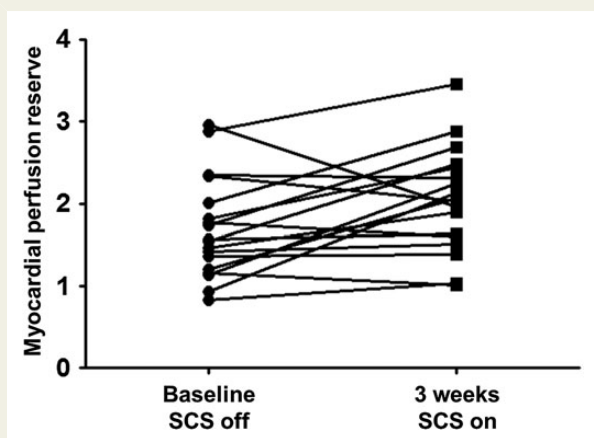


Figure 2: MPR. Individual global myocardial perfusion reserve (MPR) values in response to adenosine stress at baseline with epidural SCS turned off and after 3 weeks of continuous SCS therapy (SCS on). Average MPR increased significantly after SCS therapy ($P = 0.02$ between time points).

Table 5 MBF at rest and during adenosine stress, myocardial perfusion reserve (MPR) and MBF response to CPT in the ischaemic or non-ischaemic segments at baseline

	Baseline SCS OFF	3 weeks SCS ON	P-value
Ischaemic (n = 18)			
MBF rest (mL/g/min)	0.85 ± 0.21	0.75 ± 0.12	0.07
MBF adenosine (mL/g/min)	1.24 ± 0.42	1.39 ± 0.52	0.046
MPR	1.53 ± 0.54	1.89 ± 0.62	0.02
CPT Δ MBF (mL/g/min)	0.21 ± 0.26	0.25 ± 0.15	0.03
Non-ischaemic (n = 18)			
MBF rest (mL/g/min)	1.02 ± 0.27	0.86 ± 0.14	0.02
MBF Adenosine (mL/g/min)	1.83 ± 0.68	1.75 ± 0.59	0.57
MPR	1.89 ± 0.62	2.10 ± 0.65	0.23
CPT Δ MBF (mL/g/min)	0.32 ± 0.34	0.43 ± 0.26	0.09

n, number of patients; Δ MBF, absolute change of MBF from baseline to CPT.

The MBF and MPR values were separately compared in the ischaemic and non-ischaemic regions of the LV (Table 5). In the ischaemic segments, MPR was higher ($P = 0.02$), resting MBF was slightly lower ($P = 0.07$), and peak MBF during adenosine stress was higher ($P = 0.046$) after SCS therapy than before therapy. In the non-ischaemic segments, MPR and peak MBF during adenosine stress were comparable before and after SCS therapy ($P = 0.23$ and $P = 0.57$), whereas resting MBF was lower after therapy ($P = 0.02$).

There was $\geq 20\%$ improvement in global MPR after SCS therapy in 56% of patients that was associated with improvements in MBF response to CPT ($\geq 20\%$ improvement, $P = 0.01$), quality of life ($P = 0.02$) and ischaemia tolerance on dobutamine stress echocardiography ($P = 0.01$) after SCS therapy. The presence of diabetes or

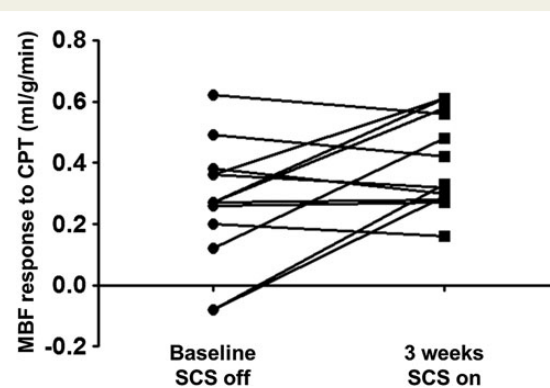


Figure 3: CPT response. Global MBF response to CPT was calculated as the absolute difference in MBF during CPT and at rest at baseline and after 3 weeks of continuous SCS therapy. Average MBF response to CPT increased significantly after SCS therapy ($P = 0.03$ between time points).

other risk factors of CAD, EF before therapy or extents of perfusion abnormalities before therapy were not predictive of MPR response.

Effect of SCS on MBF response to CPT

Absolute global MBF during CPT was comparable after 3-week SCS therapy and at baseline before therapy. However, average global MBF response to CPT (defined as the absolute difference between MBF during CPT and at rest) was 51% higher ($P = 0.03$) after 3-week SCS therapy than at rest (Table 4 and Figure 3). The CPT-induced MBF responses were comparable in the ischaemic and non-ischaemic segments.

Discussion

Our results provide evidence that short-term SCS therapy is associated with improvement in ischaemia tolerance, MPR, and endothelium-mediated vasodilatation in patients with refractory angina pectoris. This supports the view that alleviation of abnormal myocardial perfusion and vasomotor function contributes to the relief of chest pain provided by SCS in patients with severe CAD.

SCS and ischaemia tolerance

The study patients had documented ischaemia, wide-spread myocardial perfusion abnormalities during vasodilator stress, and dobutamine-induced chest pain consistent with severe CAD. As in previous clinical trials,^{2–4} SCS provided symptom relief as shown by improved quality of life and delayed appearance of chest pain during dobutamine stress. However, the number of patients is small and our study was not blinded and therefore, the effect of SCS on quality of life and symptoms during dobutamine stress can be confounded by patients' subjective expectations for the therapy. Although the extent of ischaemic wall motion abnormalities was comparable at peak dobutamine stress before and after SCS therapy, there was an improvement in peak longitudinal systolic strain at the time of symptom onset before SCS therapy also suggesting improved tolerance or threshold to dobutamine-induced

myocardial ischaemia. This is consistent with a reduction in ischaemic ST changes during exercise ECG by SCS therapy in some previous studies.³ The SCS therapy was well tolerated and safe, but the displacement of SCS lead in the epidural space in one patient highlights the need for procedural expertise.

SCS and MBF

In order to study mechanisms underlying improved ischaemia tolerance associated with SCS therapy, we evaluated maximal MBF and MPR in response to vasodilator stress that are important determinants of myocardial ischaemia in CAD.²¹ In our previous studies using [¹⁵O]-labelled water PET either MPR <2.5 or adenosine-stimulated MBF <2.4 mL/g/min identified haemodynamically significant epicardial coronary artery stenosis.^{25,29} In addition to epicardial stenosis, abnormal coronary vasomotor function or microvascular dysfunction can also contribute to reduced MBF or MPR in extensive CAD.^{21,22,24} The important novel finding in this study is that MPR was improved during SCS therapy. This was not only associated with globally reduced resting MBF, but also improved adenosine-stimulated MBF in the ischaemic regions consistent with improved vasomotor function and perfusion reserve in these areas. Relatively modest improvements in maximal absolute MBF during adenosine stress is conceivable, because maximal perfusion during adenosine stress in patients with advanced CAD is largely determined by the presence of fixed epicardial coronary artery stenosis that cannot be corrected by vasomotor function alone. Another novel finding in our study is that SCS improved blood flow response to CPT, which is consistent with improved vasomotor function. While adenosine stimulates flow via both endothelium and smooth muscle-mediated effects, blood flow response to CPT is considered as a more specific measure of endothelium-mediated vasodilatation.^{16–19}

Reduced resting MBF and increased MPR in the ischaemic myocardial areas are consistent with previous observations that SCS can correct abnormal sympathetic nervous activation^{16–19} and reduce myocardial oxygen consumption.^{12,15,30} It has also been proposed that SCS can cause redistribution of MBF into the ischaemic regions,^{11–14} but we did not find a significant change in coefficient of variation of MBF. Notably, PET with [¹⁵O] measures MBF in the perfuseable tissue fraction excluding scar in the areas of subendocardial infarction that can partly explain the lack of regional perfusion defects at rest. Since CPT measures endothelium-mediated vasodilatation in response to a sympathetic stimulus, improved CPT response provides additional evidence of normalization of the cardiac sympathetic nervous activity by SCS.^{16–19} The effects on myocardial perfusion were caused by local myocardial effects, because no changes were observed in systemic haemodynamics during the intervention. Recruitment of new collaterals is possible within 3 weeks, but this time frame is not likely long enough for formation of new capillaries via angiogenesis.

Study limitations

Blinded, cross-over study protocol would have been difficult or impossible to achieve, because of the sensation of paresthesia induced by effective SCS. Because of the demanding study protocol and relatively low number of candidates for SCS therapy with the

current indications, the number of patients is limited and notably, only two female patients were included. Absolute changes in MBF after SCS therapy were relatively small. However, reproducibility of quantitative MBF measurements at rest, during adenosine stress, or in response CPT have been reported to be good (coefficients of variation 15%) and therefore, statistical power was calculated to be sufficient for the detection of significant changes.^{31,32} We did not include direct measures of sympathetic neuronal function by specific tracers, such as metaiodobenzylguanidine or hydroxyephedrine that could provide further information on the role of sympathetic nervous system and the possible direct inhibitory effects of SCS on intrinsic cardiac neurons in the cardiac effects of SCS. It is notable that left ventricular dysfunction, ischaemia, and beta-blocker therapy may result in compensatory changes in the cardiac sympathetic nervous activity and increase beta-receptor density and sensitivity. Therefore, our findings may not apply to patients with heart failure who were not included in the study. Furthermore, it remains to be studied whether the beneficial effects on myocardial perfusion continue beyond 3 weeks³³ and whether positive effects can be achieved by the patient-controlled, intermittent use of SCS therapy in clinical practice.

Conclusions

The results from our study provide evidence that in patients with severe CAD and chronic refractory angina pectoris, short-term epidural SCS can correct abnormal vasomotor function and MPR that are associated with improved ischaemia tolerance. Larger clinical studies with longer follow-up would be needed to confirm the beneficial effects on myocardial ischaemia as well as to study the potential long-term consequences of SCS therapy. Demonstration of anti-ischaemic action supports the use of SCS therapy as an effective symptomatic therapy in refractory angina pectoris.

Conflict of interest: An unrestricted grant from St Jude Medical.

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