

Spinal Cord Stimulation for Refractory Angina Pectoris: A Narrative Review

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Summary

Refractory Anginal Pectoris is a condition defined as persistent anginal pain despite best medical treatment. It is a consequence of coronary artery disease which has been treated by revascularization and pharmacological means. Spinal cord stimulation is an established and evidence supported treatment for this condition with significant patient benefits. In this review we present the data available for use of the technique as a palliative tool for refractory angina treatment.

Introduction

Coronary artery disease remains the number one killer in Western world [1]. Each year approximately 73,000 people die due to CAD in UK alone. As the skills and equipment of cardiologists and surgeons has evolved more and more patients are being treated medically, percutaneously and surgically. Although technology has significantly improved the outcomes for patients, it has also led to emergence of a new group of patients in whom all these options get potentially exhausted. Refractory angina pectoris encompasses one such sub-set of coronary artery disease patients.

Refractory angina pectoris (RAP) is conventionally defined as a chronic condition (> 3 month in duration) characterized by angina in setting of coronary artery disease (CAD), which cannot be controlled by a combination of optimal medical therapy, angioplasty or bypass surgery, and where reversible myocardial ischemia has been clinically established to be the cause of the symptoms. In Europe, the annual incidence of RAP is estimated at 30,000-50,000 new cases per year [2].

Commonest reasons, which render these patients unsuitable for revascularization, are unfavorable coronary anatomy, unsuccessful previous CABG or PCI, lack of suitable grafting conduit material, significant comorbidities, advanced age etc. RAP can also include patients with microvascular angina. ESC Joint study group estimated the incidence of refractory angina at between 5-10 % in patients undergoing Cardiac catheterization [1]. Traditional options for this patient group are limited to anti-anginal drug therapy and secondary risk factor modification. Long-term mortality in this patient group was thought to be very high, but recent data contradicts this. The mortality in this subgroup has been found out to be < 4 % annually, which means

almost 70 % of these patients survive for 9 years or more after a confirmed diagnosis of RAP not amenable to revascularization. It thus becomes important to focus on chest pain relief and ways to achieve an improved quality of life in this growing population [3].

Treatment options apart from maximal medical therapy include transmyocardial and percutaneous myocardial revascularization (TMR and PMR), Neuromodulation by Transcutaneous electrical nerve stimulation (TENS) and implantation of patient controlled Spinal Cord stimulators (SCS), Cardiac Sympathectomy (Stellate ganglion blockade), Coronary sinus reducers to optimize endo-epicardial blood flow ratio, gene and cell therapy to promote angiogenesis and neovascularization, use of External enhanced Counterpulsation (EECP), Extracorporeal shock wave therapy (ESWT) and use of rehabilitative measures and patient education [4]. In this review we will focus on the use of Spinal cord stimulation for management of RAP.

Spinal cord stimulation

SCS as a pain control method was a direct derivative of gate control theory of pain transmission (1965) by Melzack and Wall [5]. The first spinal cord stimulator implantation was done in 1967 [6]. This modality was subsequently used in patients with severe arterial circulatory insufficiency of lower extremities, with favorable results in late 70's [7]. TENS was first method of Neuromodulation used patients with RAP in early 80's. TENS provided satisfactory clinical results, but 10-20 % of patients developed discomforting skin irritation with it after a period of use [8, 9]. This led to a trial of use of Spinal cord stimulator in this group of patients with first reported case in 1987 [10].

Mechanism of action for RAP

The mechanism of action of SCS in setting of RAP is complicated and still needs further experimental work, however, following are the proposed/possible mechanisms:

- I. A primarily pain blocking effect due to reduction of nociceptive influx from the heart [11].
- II. Increased Coronary blood flow/redistribution of blood flow (Robinhood effect): There is confirmed evidence that SCS leads to increase in blood flow in ischemia due to PVD,

however experimental data does not show the same for Coronary circulation. However, increase in coronary blood flow and its redistribution is suggested as one possible mechanism through which SCS acts [12].

III. Decreased Cardiomyocyte oxygen demand [13].

IV. Protective changes in myocytes related to ischemic preconditioning [14].

V. Arrhythmia control and resistance due to stabilization of myocardial ganglia [15].

Device overview and stimulation patterns

SCS hardware consists of unipolar, bipolar or tripolar leads, extension wires and a pulse generator. The electrode leads are inserted under local anaesthesia after a puncture through the epidural space at level T4-T8 and are then advanced up to C6-T1 segments under fluoroscopic guidance. Their final location is adjusted up to the level where the activation of the stimulator evokes paraesthesias that cover the area of the anginal pain. The implanted leads are connected directly or through extension cables to the pulse generator. The latter is not yet permanently implanted, and a trial period of some days is exploited in order to evaluate the analgesic effects of neurostimulator to the patient. After this trial period, the pulse generator is permanently implanted subcutaneously, usually below the left coastal arch. The leads are connected to generator through subcutaneously tunneled extension cables [16].

A typical therapeutic regimen of SCS consists of low amplitude stimulation three times a day for 1 hour in addition to strong stimulation during an angina attack. Patients manage stimulation themselves using a simple remote control. Stimulation at a level below the paraesthesia threshold is characterized as subthreshold or subliminal SCS.

Evidence for use of SCS in RAP

- Implementation of SCS for refractory angina is recommended by ESC and the AHA as a Class IIb recommendation, and a level of evidence B and C respectively [17, 18].

- In spite of use of SCS in setting of anginal pain for more than three decades the number of high quality RCT's in this field remains limited. This can be attributed to complicated patient selection, long-term follow up required and difficult blinding/randomization. The potential benefits of SCS as documented by studies to date are summarised below.

- Anginal symptoms: SCS has been consistently shown to decrease the symptoms of angina pectoris. This has been demonstrated by decrease in number of anginal attacks, decrease in consumption of short acting nitrates, improved CCS angina class [19-24].

- Functional status: Improved functional status as demonstrated by increased walk time on 6 MWT or increased working capacity on treadmill.

- Quality of life: Eddicks et al have shown an improvement

of global quality of life as measured by EuroQol visual analogue scale [25].

- Effect on mortality: similar to an external matched control group with angina [29].

The table below (Table 1) has been adapted from a review on spinal cord stimulation by Börjesson et al [30].

Patient selection

British Pain Society in its 2009 guideline for Spinal cord stimulation suggests that a multidisciplinary team should be involved in management of these patients [31]. An interventional cardiologist with experience in managing patients with refractory angina should review the patient and all possibilities of conventional revascularization (PCI, CABG) should be sought for and exhausted. There should be documented evidence of reversible myocardial ischemia.

SCS should be considered when the patient continues to suffer from disabling angina pectoris despite cognitive behavioral intervention and the use of transcutaneous electrical nerve stimulation (TENS).

Contraindications

- Spinal stenosis at the site of lead placement
- Significant psychological or psychiatric disorder
- Evidence of substance abuse
- Pacemakers or defibrillators in situ (relative; contact EP team)
- Requirement of frequent MRI in future (active malignancy)
- Anticoagulation therapy, coagulopathy
- Significant cognitive impairment
- Failed previous trial with SCS

Pre-implantation considerations

I. Stimulation trial: A temporary percutaneous lead can be sited and connected to an external pulse generator. The site of paraesthesias elicited should be confirmed and coverage of anginal pain typical to that patient should be ensured. The adequate length of trial depends on circumstances and there is no consensus on what it should be. After a successful trial a permanent system is implanted. In RAP patients the success rate is high, and therefore the simulation trial is often very short, 10-30 minutes, and the device is implanted immediately[32].

II. IPG type: depends on patient preference and lifestyle

III. Site of IPG implantation: Should discuss with patient. Generally it is anterior abdominal wall in left subcostal area for easy access

IV. Lead type: Cylindrical leads can be placed percutaneously while paddle leads require surgical placement with laminectomy.

V. Co-morbidities like DM, systemic infections,

coagulopathies and low platelets (< 1,00,000/ml) should be identified and optimized.

Table 1: An overview of studies done with use of SCS in RAP and summarized results

Study	Design/inclusion criteria	Number /mean age/males	Intervention	Follow up	Results	Complications
de Jongste et al.[19]	RCT	24	SCS vs placebo	2 months + 1 year	Improved QOL ↓ ischemia	6 electrode dislocations
de Jongste et al.[20]	RCT	17	SCS vs wait list (8 w) and then all SCS	8 weeks + 1 year	Increased working capacity Decreased ischemia Decreased symptoms	2 electrode dislocations
Mannheimer et al[21]	RCT (ESBY)	104	SCS vs CABG	6 months	↓symptoms (same both groups) ↑ working capacity (more in CABG group)	0
Hauvast et al.[22]	RCT	25	SCS + Standard treatment vs standard treatment	6 weeks	SCS + standard treatment ↑ working capacity ↓symptoms ↑ QOL	
Ekre et al.[23]	RCT (ESBY follow up)	104	SCS vs CABG	5 years	6 months -QoL in both groups (n.s) 5years: -QoL in both (n.s) -Mortality 28% (n.s)	SCS: 1 sc infection and 3 electrode dislocations
McNab et al.[24]	RCT	68	SCS vs PMR	12 months	Increased exercise time Symptoms Decreased -Imporved QoL(no difference between groups) -IncreasedTime to angina in SCS	1 electrode dislocation, 2 generator dislocations
Eddicks et al. [25]	RCT (crossover design)	12	SCS at 3 regimes vs placebo	4 months(4 weeks* 4)	Symptoms↓ Walking distance ↑ with all regimes vs placebo stimulation	0

Zipes et al.[26]	RCT	68	SCS low vs high stimulation	6 months	No difference	65 device related events
Lanza et al.[27]	RCT(3 arm)	25	Paraesthetic vs Subliminal vs sham SCS	3 months	Paraesthetic SCS better than Subliminal and control	0
Bondesson et al.[28]	Observational trial	153(44 SCS, 79 EECp, and 30 controls)	SCS and EECp vs control	12 months	Both SCS and EECp decreased angina and nitrate consumption. Angina control better in EECp	
Jessurun et al[29]	CT (retrospective)	57	SCS vs external control group		SCS mortality (6.5%) similar to control group	

Procedure

All patients should have a MRSA screen within a month of proposed implantation date. MRSA carriers should undergo eradication therapy before the procedure.

Patients should receive appropriate counselling and information regarding prone position and use of local anaesthetics for the procedure. Procedure can take as long as 2 hours so patients should be forewarned about lying relatively still in prone position for that duration. They should be provided with adequate cushioning and made as comfortable as possible on the operating table. As a clinician it is especially important to establish good rapport with the patient who is in pain, likely to lie in uncomfortable position for prolonged duration and is at risk of getting an anginal attack during the procedure.

Intreavenous antibiotic prophylaxis as per the local guidelines should be given 30 minutes before the procedure.

Position and ease of using C-ARM should be kept in mind while adjusting the height, position of the operating table.

The post procedural observation regimen should take account of potential complications such as spinal cord compression, neurological injury, bleeding, and infection. Ideally patients should be monitored for paraplegia overnight after implant. This would lead to early diagnosis of epidural hematoma, if any and surgical decompression when required. This policy would lead to prevention of permanent neurological damage.

SCS is a long-term treatment for a chronic condition. Patients with non-rechargeable systems could need IPG replacement at some stage. Mechanisms should be in place to predict when this is likely to occur, so that with planning, SCS function can be restored promptly.

If patients move beyond a reasonable travelling distance from the implanting centre, systems must be in place to transfer their care appropriately to other services.

Special considerations

MRI compatibility

There are no clear-cut guidelines for use of MRI in patients with SCS. MRI incompatible epidural leads may lead to heating, unintended stimulation and damage to SCS system. Newer SCS systems are MRI conditional and have specific lead shielding, which avoids significant heating and tissue damage. A review of MRI conditionality of SCS devices is available, which suggests a MRI can be undertaken in most of the patients provided adequate precautions are taken [33]. This is going to improve further as technology evolves and better MRI compatible leads and devices become available.

Diathermy

Should be used prudently if at all in patients with SCS in place. Bipolar diathermy is preferred and if unipolar is used reference plate should be as far away from the SCS system as possible.

Pacemakers and ICD's

Demand mode is affected as pacemaker may perceive SCS stimulation as electrical activity and may not pace. Cardiac electrophysiology team should reprogram pacemaker to reduce its sensitivity to extra-cardiac activity. It is a good practice that same person/team who programs SCS IPG also evaluates and changes pacemaker/ICD settings as required [34].

Complications

Complications from spinal cord stimulators have been reviewed by Eldabe et al. [35]. Complications can be divided into hardware related problems which include lead migration (up to 20 % in some studies), lead failure and IPG battery failure (depends on use pattern, initial battery life and recharge ability of battery). One risk factor for lead migration and failure is mobility of spine at the site of implantation. Since thoracic spine is quite

immobile, lead migration rate is relatively lower for refractory angina patients as compared to other indications of SCS.

Other complications are biological like pain at the site of leads or IPG (0.9-10%), wound infection (commonest cause of explantation of device; 4-10%, most common organism is *S. aureus*), skin erosion (infrequent) and dural puncture while implantation.

The most dreaded complication is of course possibility of permanent neurological injury due to direct trauma by needle or during surgery, epidural hematoma and lead displacement. In a review done by Cameron et al. risk of epidural hematoma was estimated at 0.3 % while risk of paralysis was 0.03% [36].

Conclusion

Spinal cord stimulation is an effective therapy for patients with refractory angina pectoris and is backed by evidence. It has potential to improve anginal pain as well as quality of life for these patients. Careful patient selection and involvement of a multidisciplinary team is the key to success of this therapy.

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