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Australia and New Zealand Horizon Scanning Network

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AN INITIATIVE OF THE NATIONAL, STATE AND
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AND THE GOVERNMENT OF NEW ZEALAND

Horizon Scanning Technology Prioritising Summary

Spinal cord stimulation treatment of cardiac syndrome X

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PRIORITISING SUMMARY

REGISTER ID: 000352

NAME OF TECHNOLOGY: SPINAL CORD STIMULATION TREATMENT OF CARDIAC SYNDROME X

PURPOSE AND TARGET GROUP: PATIENTS WITH CARDIAC SYNDROME X

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- | | |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- | | |
|---|-------------|
| <input type="checkbox"/> Yes | ARTG number |
| <input checked="" type="checkbox"/> No | |
| <input type="checkbox"/> Not applicable | |

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Italy	✓		

IMPACT SUMMARY:

Spinal cord stimulation (SCS) is an emerging treatment for cardiac syndrome X (CSX). SCS is aimed at treatment of both cardiac symptoms and the pain resulting from episodes of CSX. Modulation of pain and treatment of the symptoms of CSX would improve patient quality of life.

BACKGROUND

Cardiac syndrome X is a subset of angina but occurs in the absence of flow limiting stenoses in cardiac arteries. CSX manifests as normal angina but upon clinical investigation there are no apparent causes of the symptoms, unlike typical angina in which cardiac arteries show signs of reduced blood flow in an angiogram. The diagnosis of CSX is based on the *exclusion* of other causes of non-cardiac chest pain. New research points to the cause of CSX being coronary endothelial dysfunction, which causes ischaemia in the cardiac microvasculature, resulting in angina like symptoms (Hurst et al 2006).

In SCS an electrical pulse is used to stimulate the spinal cord via an implanted electrode. The electrical pulse can be provided by either external generators (for trial application of SCS) or internal generators (for long term treatment after a trial period is completed). The parameters of the stimulation can be fine tuned to the patient's and physician's requirements (Lanza et al 2001).

CLINICAL NEED AND BURDEN OF DISEASE

Limited data exist on the prevalence of CSX in Australia. This is partly due to the lack of a useful clinical definition of CSX. Based on a national survey 355,600 (1.9 %) Australians report that they have coronary heart disease. Of these around three quarters noted that they have angina (AIHW 2004). According to the AIHW National Hospital Morbidity Database approximately 100,000 coronary angiograph procedures occurred in Australia in 2004-05 (AIHW 2005). A United States report showed, of those patients undergoing a coronary angiogram, up to 50 and 17 per cent of women and men respectively show limited signs of coronary artery disease despite recurring symptoms which necessitate subsequent diagnostic tests {Hurst, 2006 #1}. By applying the US rates of limited coronary disease to the 100,000 Australian patients undergoing coronary angiograms, an estimate of the potential Australian CSX population is obtained. Although these patients cannot be formally classified as CSX patients, the high number of subjects with minor coronary artery disease who display symptoms, indicates that there may be a significant number of patients who may be affected by CSX.

Earlier studies indicated that the prognosis for CSX patients was excellent but later studies have identified a subsection of CSX patients in whom endothelial dysfunction is a marker for further coronary events (Hurst et al 2006).

In summary, while there is limited extant evidence it is likely that CSX is a significant problem in the Australian population.

DIFFUSION

No evidence of diffusion of this technology into the Australian health care system was found.

COMPARATORS

High quality therapies for CSX and for management of the pain it causes do not exist. Currently the main therapy for CSX is nitrate treatment, which acts by dilating blood vessels, although this only works in a minority of patients with CSX. Other treatments include lifestyle modifications and newer pharmacological therapies such as beta-blockers and calcium channel blockers. The evidence for the effectiveness of these treatments is currently lacking (Hurst et al 2006).

SAFETY AND EFFECTIVENESS ISSUES

The initial study that indicated that there may be some beneficial effects of electrical nerve stimulation on patients with CSX was performed using transcutaneous electrical nerve stimulation (TENS) rather than SCS. Patients (n=8) included in the study had angina pectoris, normal coronary arteries and heterogeneous myocardial perfusion. The subjects had cardiac parameters measured at baseline and after four weeks of three times daily TENS. The number of angina episodes was reduced during TENS treatment (baseline 20 ± 3 , during TENS 3 ± 1 $p=0.008$). Additionally cardiac perfusion was significantly improved and patient pain indexes also showed significant reductions. It was posited that TENS may influence the cardiac microvasculature improving blood flow and reducing symptomatic pain. This study showed that electrical stimulation may improve both the physiological and pain related aspects of CSX (Jessurun et al 2003) (level IV intervention evidence).

Subsequent studies investigated the use of SCS to improve symptoms of CSX. Patients (n=10) in this study were already on SCS therapy at the time of the initiation of the study (median SCS treatment time = 8 months). SCS therapy was performed via an abdominally implanted electric pulse generating device with an electrode subcutaneously tunnelled to the site of spinal implantation. Patients randomised to the treatment group continued their SCS treatment at the start of the study, whereas patients randomised to the control group had their SCS treatment terminated. After three weeks the groups were crossed over with the patients receiving the alternate treatment. Patients kept records of angina episodes and a variety of other parameters were measured during the trial period. The SCS treatment group showed significant improvements in CSX specific symptoms when compared to the control group. These parameters are detailed in Table 1.

Table 1 Improvements in patient condition in the SCS treatment group compared to the SCS terminated group (n=10)

CSX Parameters while undergoing SCS (versus SCS withdrawal)	SCS	SCS withdrawal	p value
Reduction in angina occurrence (episodes/ week)	10±7 (11, 0-20)	38±27 (33, 2-78)	0.01
Reduction in angina severity	2.0±1 (2.2, 0-3.5)	4±1 (3.7, 2.0-4.5)	0.011
Reduction in angina duration	12+15(7, 0–48)	22+18 (16, 3–56)	0.022
Improved Seattle angina questionnaire score ¹			≤0.013
Improved EuroQOL visual analogue scale ²	75+9 (80, 60–85)	35+8 (30, 20–50)	0.001
Reduced occurrence of ST-segment depression ³	0.6+1.3 (0)	2.5+2.2 (3.5)	0.014
Prolonged time to angina (min) ⁴	8+5	13+3	0.045
Prolonged time to ST-segment depression (min) ⁵	15+2	11+3	0.04

¹ This questionnaire has 5 sections. Hence results are not displayed in the table. The p value reported is for the section with the least significant improvement ² Quality of life scale, ³ As determined by 24 hour Holter monitoring; ST-segment depression is a marker of ischaemia, ^{4,5} Determined during an echocardiographic dobutamine stress test (source: Lanza et al 2005)

SCS had a beneficial effect on the patients compared to withdrawal of SCS in the control group. Importantly there were improvements in both cardiac performance markers and quality of life parameters, indicating that SCS is treating underlying causes and not just the symptoms of CSX (Lanza et al 2005) (level II intervention evidence).

In a subsequent, prospective study the long term effectiveness of SCS was investigated. Treatment refractory patients who underwent SCS (n=19) or refused SCS (n=9) were assessed at baseline and over long term follow-up (median 36, range 15-82 months). Patients were consecutively recruited. At baseline the two study populations did not show any significantly different clinical characteristics. As in the previous study there were significant improvements in patients in the treatment group which were not observed in the untreated control group. In the SCS treatment group a significant reduction in the number of angina episodes, as well as the duration and severity of these episodes was observed. The use of medication was also significantly reduced. Importantly, all controls reported angina episodes at rest while only 21 per cent of treated patients reported angina episodes at rest. Additionally there were improvements in clinical parameters such as performance in exercise stress testing and reduced ischaemia. No adverse effects were reported in the treatment group (Sgueglia et al 2007) (level III-2 intervention evidence).

No study reported adverse safety events in patients treated with SCS therapy.

All the evidence presented was derived from studies involving small patient populations and hence must be interpreted with care. However, the results all show a similar trend which indicates SCS as being a new and effective treatment for previously untreatable CSX. No negative effects were seen in treated patients.

COST IMPACT

No cost information was found for the cost of CSX.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

SCS improved several CSX patient clinical and quality of life markers, namely reductions in the number, severity and duration of angina episodes and concurrently improving stress test values and quality of life scores and reducing pain. These findings must be tempered by the small study sizes and the lack of cost effectiveness data. However, SCS appears to be a promising treatment for a previously untreatable ailment.

HEALTHPACT ACTION:

There is a lack of effectiveness data supporting CSX therapy. Therefore HealthPACT has recommended that further assessment of this technology is no longer warranted.

NUMBER OF INCLUDED STUDIES

Total number of studies

Level II intervention evidence	1
Level III-2 intervention evidence	1
Level IV intervention evidence	1

REFERENCES:

AIHW (2004). *Heart, stroke and vascular diseases*, Australian Institute of Health and Welfare. <http://www.aihw.gov.au/publications/cvd/hsvd04/hsvd04.pdf>

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Hurst, T., Olson, T. H. et al (2006). 'Cardiac syndrome X and endothelial dysfunction: new concepts in prognosis and treatment', *Am J Med*, 119 (7), 560-566.

Jessurun, G. A., Hautvast, R. W. et al (2003). 'Electrical neuromodulation improves myocardial perfusion and ameliorates refractory angina pectoris in patients with syndrome X: fad or future?' *Eur J Pain*, 7 (6), 507-512.

Lanza, G. A., Sestito, A. et al (2001). 'Spinal cord stimulation in patients with refractory anginal pain and normal coronary arteries', *Ital Heart J*, 2 (1), 25-30.

Lanza, G. A., Sestito, A. et al (2005). 'Effect of spinal cord stimulation on spontaneous and stress-induced angina and 'ischemia-like' ST-segment depression in patients with cardiac syndrome X', *Eur Heart J*, 26 (10), 983-989.

Sgueglia, G. A., Sestito, A. et al (2007). 'Long-term follow-up of patients with cardiac syndrome X treated by spinal cord stimulation', *Heart*, 93 (5), 591-597.

SEARCH CRITERIA TO BE USED:

Electric Stimulation Therapy/adverse effects/ methods

Microvascular Angina/physiopathology/ therapy

Pain/etiology

Spinal Cord/ physiology

Angina Pectoris/etiology/physiopathology/ therapy

Electric Stimulation Therapy/ methods

Electrocardiography, Ambulatory