

Cost-Effectiveness of Spinal Cord Stimulation versus Coronary Artery Bypass Grafting in Patients with Severe Angina Pectoris – Long-Term Results from the ESBY Study

P. Andréll^a O. Ekre^a T. Eliasson^a C. Blomstrand^b M. Börjesson^a
M. Nilsson^c C. Mannheimer^a

^aMultidisciplinary Pain Centre, Sahlgrenska University Hospital/Östra, ^bInstitute of Clinical Neuroscience, Stroke Research Unit, ^cCardiovascular Centre, Sahlgrenska University Hospital, Göteborg, Sweden

Key Words

Angina · Bypass · Cost-effectiveness · Electrical stimulation

Abstract

The present study is a 2-year follow-up of the 104 patients participating in the ESBY study (Electrical Stimulation versus Coronary Artery Bypass Surgery in Severe Angina Pectoris), a randomised prospective study including patients with increased surgical risk and no prognostic benefit from revascularisation. Hospital care costs, morbidity and causes of death after spinal cord stimulation (SCS) and coronary artery bypass grafting (CABG) were assessed, as well as the complication rate of SCS treatment. SCS proved to be a less expensive symptomatic treatment modality of angina pectoris than CABG ($p < 0.01$). The SCS group had fewer hospitalisation days related to the primary intervention ($p < 0.0001$) and fewer hospitalisation days due to cardiac events ($p < 0.05$). The groups did not differ with regard to causes of death. There were no serious complications related to the SCS treatment.

Copyright © 2003 S. Karger AG, Basel

Introduction

Spinal cord stimulation (SCS) was introduced in the treatment of angina pectoris in patients resistant to conventional treatment modalities in the 1980s [1, 2]. About 80% of the patients subjected to SCS treatment have experienced significant relief of angina, reduced frequency of anginal attacks, reduced need for short-acting nitrates and improved quality of life in several studies; experimental as well as clinical studies have shown the efficacy of SCS in angina treatment [3–9].

Earlier studies have indicated that myocardial ischemia is reduced by SCS, which in turn seems to be due to a reduction in oxygen consumption, and that the treatment does not deprive the patient of a warning signal [1, 3–5, 10–20].

The ESBY (Electrical Stimulation versus Coronary Artery Bypass Surgery in Severe Angina Pectoris) study was a randomised, prospective, open comparison of coronary artery bypass grafting (CABG) and SCS in patients with coronary artery disease, severe angina pectoris, no anticipated prognostic benefit from CABG and increased surgical risk. The patients were all acceptable for CABG on a strict indication of symptom relief. One hundred and four patients were randomised to SCS ($n = 53$) or CABG ($n =$

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 2003 S. Karger AG, Basel
0008-6312/03/0991-0020\$19.50/0

Accessible online at:
www.karger.com/crd

Olof Ekre
Multidisciplinary Pain Centre
Sahlgrenska University Hospital/Östra
S-416 85 Göteborg (Sweden)
Tel. +46 31 3434000, Fax +46 31 3435933, E-Mail olof.ekre@vgregion.se

51). Within 6 months, both groups had adequate symptom relief without any differences between the groups, while the SCS group had lower mortality ($p = 0.02$) and lower cerebrovascular morbidity ($p = 0.03$) than the CABG group [9].

The primary aim of the present study was to compare the cost-effectiveness of SCS and CABG and to analyse morbidity and causes of death during 2 years of follow-up in the ESBY study population. In addition, the complication rate of SCS treatment during the period was assessed.

Methods

Out of the 104 original ESBY study patients, 2 patients from the CABG group declined participation in the follow-up; thus, there were 49 patients in the CABG group and 53 patients in the SCS group. There were no health-related differences between the groups except for current smoking and renal disease (table 1) [9].

Costs of the primary intervention, hospitalisation days and the cost of interventions due to coronary heart disease during the 2-year follow-up period – including angiography, percutaneous coronary intervention (PCI), CABG, SCS implantation, replacement of SCS electrodes and pulse generators – were included in the analysis. All costs are accounted for in Euro in year 2000 prices.

Morbidity was measured as the number of hospital days due to occurrence of heart events and cerebrovascular events. The causes of death were recorded for all the fatalities occurring from the inclusion date up to 2 years thereafter.

Complications after SCS treatment were assessed in the patients who were randomised to SCS according to the study protocol (except 1 patient who had a CABG before the primary intervention and never received SCS), and 5 patients in the CABG group who received SCS during the study period. The SCS-related complications assessed included infections, electrode fractures and electrode displacements. In order to estimate the cost of the SCS treatment, the pulse generator life span was analysed for up to 5 years after intervention.

As statistical methods, the Mann-Whitney U test was used to compare the costs of the treatment groups and the number of hospital days, and Fisher's exact test was used to analyse differences in the number of events and causes of death. The data were analysed on an intention-to-treat basis.

During SCS implantation, the patient is awake and placed in a prone position. An incision is made at the mid-thoracic level after administration of local anaesthesia. The epidural space is identified and punctured using a Touhy needle. A quadripolar electrode is introduced through the needle into the epidural space and is guided to the level of the Th1-Th2 vertebrae during X-ray monitoring. The electrode is placed at the midline, and during the intraoperative test stimulation the patient experiences paraesthesia. It is important to adjust the position of the electrode so that the paraesthesia in the chest covers the area to which the patient localises the anginal pain. This is to ensure that the area of the spinal cord innervating the heart is stimulated. When adequate paraesthesia is obtained, the electrode is fixed to the ligaments and an extension wire is tunnelled subcutaneously to below the left costal arch, where it is connected to a subcu-

Table 1. Patient characteristics in the ESBY study

	CABG (n = 51)	SCS (n = 53)
Gender: male/female	42/9	41/12
Mean age (range), years	68.7 (40–81)	72.2 (42–82)
Angina		
Class 3	48	50
Class 4	3	3
History		
Myocardial infarction	34	36
Cerebrovascular disease	9	11
Carotid artery stenosis	11	12
Peripheral vascular disease	14	13
Renal disease	6	12
Hypertension	19	23
Diabetes	13	14
Current smoking	10	2
Previous CABG	11	14

taneous pulse generator [3, 21]. The CABG operations were performed as open heart surgery with extracorporeal circulation, according to standard clinical practice.

The ethical committee of the University of Göteborg approved the study. Informed consent was obtained from all patients.

Results

Hospital Care Cost

The average total cost of a SCS patient (16,400 Euro) was less than the average total cost of a CABG patient (18,800 Euro; $p < 0.01$; table 2). SCS was also less expensive than CABG ($p < 0.01$) in the group of patients ($n = 87$) for whom hospital care costs were incurred during the whole study period, i.e. excluding patients that died or denied follow-up during the period. The cost of primary intervention is higher in the CABG group, while the interventions during the follow-up (including, for example, replacement of the SCS device, when needed) generate a higher cost in the SCS group.

Morbidity

The CABG group had more hospitalisation days in connection with the intervention to which they were randomised ($p < 0.0001$). The SCS group had fewer hospitalisation days due to cardiac morbidity ($p < 0.05$). There were no differences between the groups with regard to the number of patients with fatal (3 patients in the SCS group and 5 patients in the CABG group) and non-fatal myocardial infarctions (7 patients in the SCS group and 3 patients in the CABG group). The absolute number of

Table 2. Cost per patient in the SCS and CABG groups, respectively, from inclusion to 2 years after intervention (in Euro)

	SCS (Euro)	CABG (Euro)	CABG vs. SCS
Total cost of the primary intervention	8,270	12,070	p < 0.0001
Cost of hospital days during the follow-up	6,730	5,570	NS
Cost of interventions due to coronary heart disease (during the follow-up)	1,420	1,190	p < 0.05
Total cost of the average patient	16,400	18,800	p < 0.01

Table 3. Morbidity (2-year follow-up)

	SCS	CABG	CABG vs. SCS
Days of hospitalisation due to primary intervention (mean)	5.0	11.1	p < 0.0001
Total number of hospital admissions (mean)	3.7	4.2	NS
Total number of days of hospitalisation (mean)	23.0	26.0	NS (p = 0.055)
Hospital admissions due to heart event (mean)	2.5	2.9	NS
Days of hospitalisation due to heart event (mean)	11.7	15.5	p < 0.01
Hospital admissions due to other causes (mean)	1.2	1.1	NS
Days of hospitalisation due to other causes (mean)	9.5	9.6	NS
Number of patients hospitalised due to cerebrovascular event	1	6	NS (p = 0.053)

Table 4. Causes of death (2-year follow-up)

Causes of death	SCS	CABG	CABG vs. SCS
Heart disease	3	5	NS
Cerebrovascular disease	1	1	NS
Cerebrovascular and heart disease	0	2	NS
Other causes	1	2	NS
Total deaths	5	10	NS

patients who had a cerebrovascular event was smaller in the SCS group than in the CABG group. However, the difference was not statistically significant (p = 0.053; table 3). Neither did the groups differ with regard to all-cause hospital admissions or hospitalisation days due to other causes, which were defined as all other events that were not related to heart disease or cerebrovascular disease (table 3).

Causes of Death

The long-term mortality data for the ESBY patients have been presented elsewhere, and there were no differences between the groups [8]. The groups did not differ with regard to mortality from heart disease or cerebrovas-

cular disease, respectively (table 4). The 2-year mortality was 14.7% in the ESBY patients, i.e. an approximate annual mortality of 7.4%. Seven of the CABG patients died before, in relation to, or shortly after the primary intervention.

Crossovers

There were 10 crossovers during the study period, 5 from the SCS group (1 patient before the primary intervention and 4 patients thereafter) and 5 from the CABG group (2 patients before the primary intervention and 3 patients thereafter) [9].

Complications and Efficacy of SCS

During the study period, an SCS system was implanted in 57 patients. No intraspinal infection occurred. One patient had a subcutaneous infection in the pulse generator pocket, and the system was extirpated. Three electrodes were surgically replaced due to electrode fractures during the study period. All minor electrode displacements could be corrected by re-programming the stimulator. There were three pulse generator replacements due to battery depletion during the 2-year study period. From intervention up to 5 years thereafter, the average life span of the pulse generator was 3.3 years – there were 17 pulse generator replacements within 5 years from intervention.

Forty-eight of the 57 patients (84%) had symptomatic improvement from the treatment in terms of reduced frequency and severity of angina attacks.

Discussion

In this study, SCS turned out to be less expensive than CABG not only with respect to the primary intervention costs but also the total costs during a 2-year follow-up. So far, no other randomised study has compared the cost of CABG versus SCS, although the costs of treatment modalities have been analysed separately [22–25]. Concerning SCS, earlier studies have found that SCS in patients with angina pectoris is more cost-effective than pharmacological treatment, in terms of the number of hospital days and/or hospital admissions [22, 23, 26].

SCS treatment is capital-intensive (approximately 90% of the operation cost is material cost). CABG, on the other hand, is personnel-intensive as it includes extracorporeal circulation and intensive care, for example, which is not needed for the SCS implantation.

Compared to the SCS group, the CABG group needed more than twice as many days of hospital care in connection with the primary intervention. In the ESBY study, implantation of a stimulator required, on average, 5 days of hospital stay but no intensive care – at present, the average hospital stay in connection with SCS implantation has decreased to 2.5 days. After a CABG operation, the patients stayed 11.1 days in hospital, on average, which included intensive care during at least 1 day (the present average hospital stay is 9 days). Furthermore, the CABG patients with complicating diseases often require 2–4 weeks of additional rehabilitation. This cost is not included in the present calculation.

During the follow-up period, the only significant difference between the groups is the number of days of hospitalisation due to heart events, which is higher in the CABG group.

The ESBY patients have a mortality rate similar to that of a pharmacologically treated angina pectoris population with a similar extent of coronary artery disease and comorbidity [8]. A considerable number of the CABG patients died in relation to or shortly after the primary intervention, which may be an indication of the hazard of major surgery in patients with increased surgical risk. Extracorporeal circulation during surgery is considered to be a risk factor for cerebrovascular events. However, this is not reflected by any difference in cerebrovascularly caused deaths between the groups. No increase in the

number of cardiac deaths was seen in the SCS group compared to the revascularised group.

One of the most feared complications in connection to SCS is epidural infection, as this may spread to the central nervous system and cause serious neurological sequelae. In the ESBY study, there has been no epidural infection. In addition, no SCS-related epidural infection has occurred in Göteborg in any of the more than 600 angina patients treated with SCS since 1985, when SCS for angina was introduced. This is in accordance with results from other centres [27].

Postoperative subcutaneous infection in the pulse generator skin pocket developed in 1 patient in the ESBY study. As the SCS system is fully implanted, without percutaneous connections, the risk of late-occurring infections is minimal [21].

Study Limitations

The ESBY study investigators were not blinded as the two procedures differ significantly and it was not possible to blind the treatment to either patient or surgeon. The study included a limited number of patients.

Conclusions

Previous studies have shown that SCS is effective at relieving myocardial ischemia and severe angina pectoris. The present study suggests that SCS is a more cost-effective symptomatic treatment method in angina pectoris than CABG in a selected patient group, i.e. patients with coronary artery disease, severe angina pectoris, no anticipated prognostic benefit from CABG and at increased surgical risk.

Taking into account that previously presented data from the ESBY study have found SCS and CABG to be comparable in terms of symptom relief, quality of life and survival, this study further supports the results from the ESBY study showing that SCS may be a therapeutic alternative for these patients.

Acknowledgements

The Faculty of Medicine, University of Göteborg, Sweden, the Swedish Heart Lung Foundation and the Swedish Society of Medicine supported the study.

References

- 1 Mannheim C, Augustinsson LE, Carlsson CA, Manhem K, Wilhelmsson C: Epidural spinal electrical stimulation in severe angina pectoris. *Br Heart J* 1988;59:56-61.
- 2 Murphy DF, Giles KE: Dorsal column stimulation for pain relief from intractable angina pectoris. *Pain* 1987;28:365-368.
- 3 Eliasson T, Augustinsson LE, Mannheim C: Spinal cord stimulation in severe angina pectoris - Presentation of current studies, indications and clinical experience. *Pain* 1996;65:169-179.
- 4 Hautvast RW, Blanksma PK, DeJongste MJ, Pruim J, van der Wall EE, Vaalburg W, Lie KI: Effect of spinal cord stimulation on myocardial blood flow assessed by positron emission tomography in patients with refractory angina pectoris. *Am J Cardiol* 1996;77:462-467.
- 5 Greco S, Auriti A, Fiume D, Gazzeri G, Gentilucci G, Antonini L, Santini M: Spinal cord stimulation for the treatment of refractory angina pectoris: A two-year follow-up. *Pace* 1999;22:26-32.
- 6 Meyerson B, Linderth B: Spinal cord stimulation; in Loeser J (ed): *Bonica's Management of Pain*. Philadelphia, Lippincott Williams & Wilkins, 2001, pp 1857-1876.
- 7 DeJongste MJ: Spinal cord stimulation for ischemic heart disease. *Neurol Res* 2000;22:293-298.
- 8 Ekre O, Eliasson T, Norrsell H, Währborg P, Mannheim C: Long-term effects of spinal cord stimulation and coronary artery bypass grafting on quality of life and survival in the ESBY study. *Eur Heart J* 2002;23/24:1937-1944.
- 9 Mannheim C, Eliasson T, Augustinsson LE, Blomstrand C, Emanuelsson H, Larsson S, Norrsell H, Hjalmarsson A: Electrical stimulation versus coronary artery bypass surgery in severe angina pectoris: The ESBY study. *Circulation* 1998;97:1157-1163.
- 10 Mannheim C, Eliasson T, Andersson B, Bergh CH, Augustinsson LE, Emanuelsson H, Waagstein F: Effects of spinal cord stimulation in angina pectoris induced by pacing and possible mechanisms of action. *BMJ* 1993;307:477-480.
- 11 Andersen C, Hole P, Oxhøj H: Does pain relief with spinal cord stimulation for angina conceal myocardial infarction? *Br Heart J* 1994;71:419-421.
- 12 TenVaarwerk IA, Jessurun GA, DeJongste MJ, Andersen C, Mannheim C, Eliasson T, Tadmaw W, Staal MJ: Clinical outcome of patients treated with spinal cord stimulation for therapeutically refractory angina pectoris. *Heart* 1999;82:82-88.
- 13 Sanderson JE, Ibrahim B, Waterhouse D, Palmer RB: Spinal electrical stimulation for intractable angina - Long-term clinical outcome and safety. *Eur Heart J* 1994;15:810-814.
- 14 Linderth B, Foreman RD: Physiology of spinal cord stimulation: Review and update. *Neuromodulation* 1999;2:150-164.
- 15 Norrsell H, Eliasson T, Albertsson P, Augustinsson LE, Emanuelsson H, Eriksson P, Mannheim C: Effects of spinal cord stimulation on coronary blood flow velocity. *Coron Artery Dis* 1998;9:273-278.
- 16 Norrsell H, Eliasson T, Mannheim C, Augustinsson LE, Bergh CH, Andersson B, Waagstein F, Friberg P: Effects of pacing-induced myocardial stress and spinal cord stimulation on whole body and cardiac norepinephrine spillover. *Eur Heart J* 1997;18:1890-1896.
- 17 Eliasson T, Mannheim C, Waagstein F, Andersson B, Bergh CH, Augustinsson LE, Hedner T, Larson G: Myocardial turnover of endogenous opioids and calcitonin-gene-related peptide in the human heart and the effects of spinal cord stimulation on pacing-induced angina pectoris. *Cardiology* 1998;89:170-177.
- 18 Hautvast RW, Ter Horst GJ, DeJong BM, DeJongste MJ, Blanksma PK, Paans AM, Korf J: Relative changes in regional cerebral blood flow during spinal cord stimulation in patients with refractory angina pectoris. *Eur J Neurosci* 1997;9:1178-1183.
- 19 Foreman RD, Linderth B, Ardell JL, Barron KW, Chandler MJ, Hull SS Jr, TerHorst GJ, DeJongste MJ, Armour JA: Modulation of intrinsic cardiac neurons by spinal cord stimulation: Implications for its therapeutic use in angina pectoris. *Cardiovasc Res* 2000;47:367-375.
- 20 Latif OA, Nedeljkovic SS, Stevenson LW: Spinal cord stimulation for chronic intractable angina pectoris: A unified theory on its mechanism. *Clin Cardiol* 2001;24:533-541.
- 21 Eliasson T: Spinal cord stimulation in angina pectoris and ischemic heart disease - A topical overview. *Acta Chir Austriaca* 2000;32:61-65.
- 22 Merry AF, Smith WM, Anderson DJ, Emmens DJ, Choong CK: Cost-effectiveness of spinal cord stimulation in patients with intractable angina. *NZ Med J* 2001;114:179-181.
- 23 Bladt Rasmussen M, Andersen C, Andersen P, Frandsen F: Cost-utility analyse af elektrisk rygmærksstimulation til behandling af angina pectoris. *Ugeskr Laeger* 1992;154:1180-1184.
- 24 Kumar K, Malik S, Demeria D: Treatment of chronic pain with spinal cord stimulation versus alternative therapies: Cost-effectiveness analysis. *Neurosurgery* 2002;51:106-115; discussion 115-106.
- 25 Henderson RA, Pocock SJ, Sharp SJ, Nanchahal K, Sculpher MJ, Buxton MJ, Hampton JR: Long-term results of RITA-1 trial: Clinical and cost comparisons of coronary angioplasty and coronary-artery bypass grafting. *Lancet* 1998;352:1419-1425.
- 26 Murray S, Carson KG, Ewings PD, Collins PD, James MA: Spinal cord stimulation significantly decreases the need for acute hospital admission for chest pain in patients with refractory angina pectoris. *Heart* 1999;82:89-92.
- 27 Andersen C: Complications in spinal cord stimulation for treatment of angina pectoris. Differences in unipolar and multipolar percutaneous inserted electrodes. *Acta Cardiol* 1997;52:325-333.