Radiculopathy and radiating low back pain in general practice

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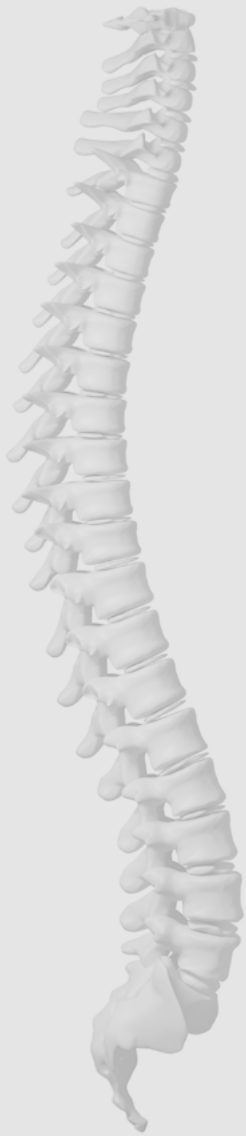
Chapter 5

Epidural steroids for lumbosacral radicular syndrome compared to usual care: Quality of life and cost-utility in general practice



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ABSTRACT

Background

Segmental epidural steroid injections (SESIs) are a widely used additional pain treatment in lumbosacral radicular syndrome (LRS). Little is known about their effects on patients' quality of life (QoL), their cost-effectiveness in terms of utility, and nothing when studied from a societal perspective or compared to other interventions in sciatica. This study aims to investigate the effect of adding SESIs to the usual care compared to usual care alone on quality of life and cost-utility in LRS in general practice.

Method

We performed a pragmatic, randomized, controlled, single-blinded trial in Dutch general practice. Patients with acute LRS were included by GPs. All patients received usual care. Patients in the intervention group received one segmental epidural steroid injection containing 80 mg triamcinolone as well. Follow-up was performed using postal questionnaires at 4, 6, 13, 26 and 52 weeks, that included the SF-36 and a specific cost questionnaire. Statistical analysis for QoL was carried out using mixed models. Economic evaluation was performed from a societal perspective with a time horizon of one year. SF-36 scores were transformed to utility scores by using the SF-6D profiling method described by Brazier *et al.*

Results

Both groups experienced significant increase in quality of life in (especially) the physical domains of the SF-36. The intervention group scored significantly better than the control group at certain time points in the physical domain. The differences were small. The cost-utility analysis showed that with a negligible loss of utility societal costs would be saved, due to more productivity in the intervention group.

Conclusion

Although the beneficial effects of SESIs are small and the natural course of LRS is predominantly favourable, we think decision makers can consider implementing SESIs in daily practice with the purpose of saving resources. Caution must be taken, and further research should be directed at identifying patient subgroups who might benefit from SESIs, with additional focus on (costs of) complications and side effects.

INTRODUCTION

Lumbosacral radicular syndrome (LRS) is pain, radiating from the back to below the knee in one leg ("sciatica"), with a positive straight leg raising test and/or neurological symptoms originating from one nerve root.[1] It is most commonly caused by lumbar disc herniation, resulting in an inflammatory response around the nerve root that causes radicular pain. Sciatica is pain of a burning or shooting nature and has a high impact on patients' general wellbeing due to its intensity.[2] Segmental epidural steroid injections (SESIs), that may inhibit the inflammatory response around the nerve root, are a controversial treatment in LRS.[3,4] They are found to be effective in treating pain on the short term, in the acute phase of well-defined radicular syndrome with sciatica, causing few side-effects.[5,6-15] SESIs are applied in LRS in The Netherlands but they are not advised in the national guideline as a routine treatment.[1] Low back pain and sciatica are expensive as well in terms of health care costs: medical costs of low-back pain amounted to 337,3 million euros in the Netherlands in 2000.[16]

In a pragmatic randomized controlled trial, we compared the effectiveness of adding a segmental epidural steroid injection to the usual care of LRS to usual care alone. We found a small significant difference in favour of the intervention for back pain, impairment, disability and patients' satisfaction with treatment.[17] A cost-effectiveness analysis showed that adding the intervention to the usual care was considerably cheaper than usual care alone, mainly due to more loss of productivity in the control group.[18]

Given an intervention's clinical superiority or equivalence, lower costs are an important economic argument to have it implemented. Its effect on patients' quality of life has to be taken into account. Next, decision makers need to be able to compare different interventions to weigh their costs and benefits. Although SESIs are a widely used additional pain treatment in LRS, little is known about their effects on patients' quality of life, their cost-effectiveness in terms of utility, and nothing when studied from a societal perspective or compared to other interventions in sciatica. We therefore compared health-related quality of life in patients with acute LRS who received usual care with patients who received usual care with an additional SESI. We also carried out a cost-utility analysis assessing the balance between QALYs gained and observed societal costs after one year.

METHOD

Overall, 63 patients aged 18-65 years, in the acute phase of LRS, participated in a pragmatic randomized controlled trial comparing usual care to a SESI combined with usual care. Inclusion took place in 2005 to 2007. Patients were followed for one year. Exclusion criteria were a history of spinal surgery or trauma, maintenance therapy with corticosteroids or anticoagulants, bleeding disorder, cauda equina syndrome, a BMI > 35, mental disability, inadequate mastery of the Dutch language, allergy to corticosteroids, pregnancy or an active wish to conceive and breastfeeding. The study was reviewed and approved by the institutional medical-ethical board of the University Medical Centre Groningen.

Patients who contacted their GP for LRS were given written information on the study, a baseline questionnaire and an informed consent form. The forms were completed and sent to the research center. Upon receiving the baseline questionnaire and the informed consent, the primary researcher contacted the subjects to check inclusion and exclusion criteria. Randomization was performed by an otherwise non-involved colleague, using pre-prepared, sequentially numbered, opaque, sealed envelopes containing stickers with either "SESI" or "CAU", balanced after 40 assignments. Upon randomization, the due envelope was opened and the sticker with the allocated treatment was fixed on the completed inclusion form. Inclusion forms were coded and kept separately from coded follow-up questionnaires. Researchers were blinded until after the final analysis of the results.

As demanded by the pragmatic study design, usual daily practice circumstances were closely followed. All patients received care as usual according to the guideline (analgesics, maintaining normal daily activities as much as possible, referral if necessary) from their GPs. Patients in the intervention group received a SESI in addition to usual care. SESIs consisted of 80 mg triamcinolone in normal saline and were administered at the department of anesthesiology pain management center of the university medical hospital Groningen (UMCG). Both groups were followed with questionnaires regarding pain, disability, health-related quality of life and costs. Measuring instruments used were numerical rating scales (NRS) for pain, the Roland-Morris disability questionnaire for disability, the SF-36 questionnaire for quality of life and specifically developed cost questionnaires for costs. The NRS score for back pain at four weeks after the start of the treatment was used as the primary outcome measure for calculating sample size. We needed to include 33 subjects in each group to detect a difference of 1.2 and a common within-group standard deviation of 1.7, as is reported in literature as minimal clinically important difference in back pain ($\beta = 0.80$, $\alpha = 0.05$ two-tailed).[19,20]

Quality of life

Quality of life was measured using the SF-36 health related quality of life questionnaire at baseline and at 4, 13, 26 and 52 weeks after the start of the treatment.[21] Physical and mental component scores were calculated using an uncorrelated (orthogonal) factor solution.[22] Analysis was carried out on an intention to treat basis, using mixed models. In this type of regression analysis, the mean outcomes in our study population (which provide an approximation of the mean values in the general population), were used to estimate the means in the general population. Therefore estimated means, rather than measured values, are presented. Patients were a random factor in the model with variance components as covariance structure, treatment a fixed factor. Time of measurement was as a categorical variable entered in the model. For every outcome variable, treatment and time of measurement as independent variables were tested with sex, age and baseline-values as covariates to account for non-balance in the randomization.

Cost-utility

The aim of cost-utility analyses is to estimate the ratio between the cost (or savings) of an intervention and the benefit it produces in terms of years lived in full health (Quality Adjusted Life Years, QALYs). Cost-utility analyses therefore allow comparison across different health programs and policies by using a common unit of measure (money/QALYs) which is why cost-utility analyses are used to guide procurement decisions. Our cost utility analysis compared societal costs per QALYs at one year between the intervention group and the usual care group. Since the SF-36 is not a preference-based questionnaire, the scores were transformed to utility scores using the SF-6D profiling as described by Brazier *et al.*[23] The SF-6D includes the following health domains: physical functioning, role participation (combined role-physical and role-emotional), social functioning, bodily pain, mental health and vitality. Areas under the curves were calculated for each patient using the standard trapezoidal method which is based on the following formula:

$$AUC_1 = \frac{Y_{i,0} + Y_{i,1}}{2} * (t1\text{-}t0) + \frac{Y_{i,1} + Y_{i,2}}{2} * (t2\text{-}t1) + \frac{Y_{i,2} + Y_{i,3}}{2} * (t3\text{-}t2) + \frac{Y_{i,3} + Y_{i,4}}{2} * (t4\text{-}t3)$$

where Y_x is the utility weight for a given time point and t is the time point expressed in weeks after inclusion.

The economic evaluation was performed with a time horizon of one year from a societal perspective, which means that all direct medical, and all direct and indirect non-medical costs including loss of productivity, were taken into account regardless of who pays for them. Unit prices were drawn from the guidelines for cost-studies (methods and unit-prices for economic evaluations in health care) and online information on medication costs by the Dutch health insurance board.[24,25] The cost utility analysis was performed with as main outcome the Incremental Cost Utility Ratio (ICUR). Differences between groups over the entire study period were calculated with 95% confidence intervals based on bootstrap resampling with 5000 replications. The bootstrapped confidence interval was calculated by taking the 2.5th and 97.5th percentile of the rank ordered scores. The simulated values of the cost and QALY estimates were plotted in a cost effectiveness plane. Finally, a cost effectiveness acceptability curve was generated, depicting the probability that adding SESIs to usual care is cost-effective over a range of thresholds.

RESULTS

Population

Our patients were recruited from the urbanized countryside in the northern part of the Netherlands. A flow schedule is presented in figure 5.1. Of 84 patients presented to us by 24 GPs, 73 were randomized and 50 subjects included in the final analysis for quality of life. Of six people only the direct medical costs were known, and since we needed a complete 'cost-effect pair' to calculate societal costs per QALY, these had to be excluded, resulting in 22 subjects per group. The mean age of the study participants at the time of the inclusion was 44,3 years (SD 9,5).

Quality of life

In table 5.1, all measured baseline values of both groups for all domains of the SF-36 are presented. In table 5.2, we present all estimated group means stratified by study arm, and the estimated differences between group means for every measuring moment, including 95% confidence intervals. The group means were significantly different (i.e. the confidence interval did not include zero) in favor of the intervention at some time points for the domains of physical functioning, physical role limitations, general health perceptions and the physical component summary. The largest differences between group means were found in the domain of physical role limitations: -33.7 [95% CI -54.8, -12.7] and -29.1 [95% CI -50.9, -7.4] after a follow-up time of half a year and a year respectively.

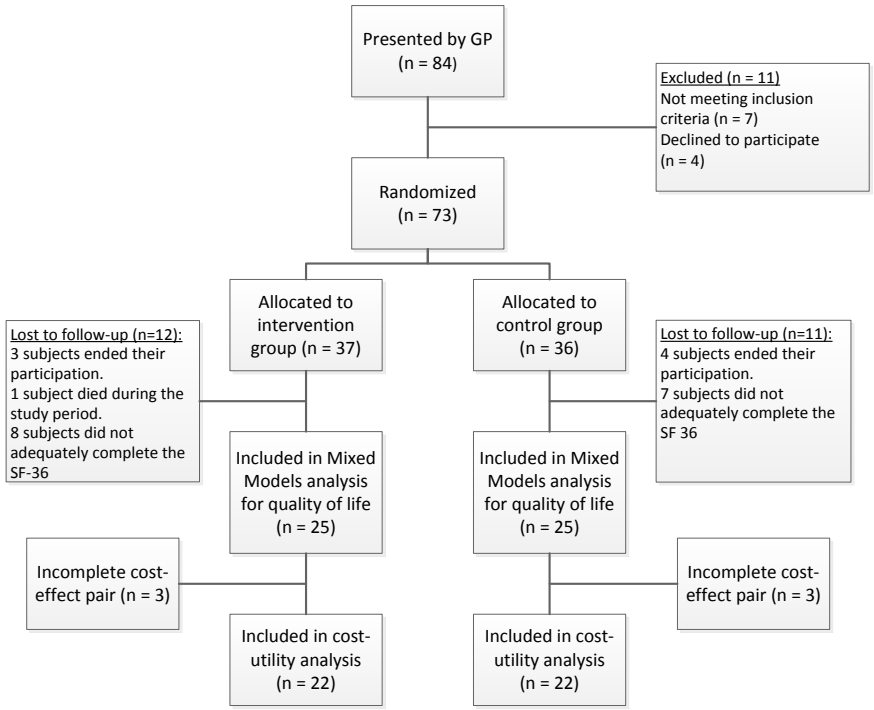

Figure 5.1: Population flow schedule

Table 5.1: Baseline participant characteristics for quality of life

Group	Intervention group (n = 25)	Control group (n = 25)
Physical functioning	53 (17)	61 (22)
Social functioning	48 (15)	44 (19)
Role limitations, physical	14 (29)	23 (38)
Role limitations, emotional	70 (43)	70 (43)
Emotional wellbeing	65 (27)	66 (20)
Energy/fatigue	52 (24)	51 (17)
Pain	45 (17)	45 (16)
General health perception	70 (18)	67 (16)
Change in perceived health	40 (21)	40 (21)
Physical component score	45 (11)	49 (15)
Mental component score	58 (20)	58 (17)

Table 5.2: Estimated mean SF-36 scores

Variable		Week 4	Week 12	Week 26	Week 52
Physical functioning	*SESI*	74.8 (69.2, 80.5)	87.7 (82.1, 93.4)	91.9 (86.2, 97.6)	94.5 (88.7, 100.3)
	UC	73.9 (68.4, 79.3)	79.0 (73.2, 84.7)	82.5 (76.7, 88.3)	87.0 (81.1, 93.0)
	Difference	-0.97 (-8.9, 6.9)	-8.8 (-16.9, -0.7)	-9.4 (-17.6, -1.2)	-7.5 (-15.9, 0.9)
Social functioning	*SESI*	48.1 (42.4, 53.8)	48.9 (43.1, 54.6)	53.4 (47.7, 59.1)	51.7 (45.9, 57.6)
	UC	45.4 (39.8, 50.9)	44.5 (38.8, 50.2)	50.0 (44.1, 55.7)	47.1 (41.2, 53.0)
	Difference	-2.7 (-10.7, 5.2)	-4.3 (-12.5, 3.8)	-3.5 (-11.6, 4.7)	-4.6 (-13.0, 3.7)
Physical role limitations	*SESI*	29.0 (14.4, 43.6)	59.7 (45.3, 74.1)	87.2 (72.6, 102.0)	92.3 (77.4, 107.2)
	UC	26.2 (12.3, 40.2)	45.7 (30.8, 60.6)	53.3 (38.6, 68.5)	63.2 (47.5, 79.0)
	Difference	-2.8 (-23.0, 17.5)	-14.0 (-34.8, 6.8)	-33.7 (-54.8, -12.7)	-29.1 (-50.9, -7.4)
Emotional role limitations	*SESI*	78.5 (66.7, 90.4)	87.5 (75.7, 99.4)	93.5 (81.5, 105.6)	94.3 (82.1, 106.6)
	UC	66.8 (55.3, 78.2)	74.0 (61.7, 86.2)	79.5 (67.0, 92.0)	85.2 (72.6, 98.0)
	Difference	-11.7 (-28.3, 4.8)	-13.6 (-30.7, 3.5)	-14.0 (-31.4, 3.3)	-9.1 (-26.7, 8.6)
Emotional wellbeing	*SESI*	69.8 (63.7, 75.9)	69.8 (63.8, 75.8)	67.6 (61.6, 73.6)	67.4 (61.3, 73.6)
	UC	64.9 (59.1, 70.7)	71.0 (64.9, 77.1)	67.2 (61.0, 73.4)	72.2 (65.9, 78.5)
	Difference	-4.9 (-13.4, 3.5)	1.2 (-7.3, 9.8)	0.4 (-9.0, 8.2)	4.7 (-4.1, 13.5)
Energy/ fatigue	*SESI*	49.0 (43.3, 55.3)	54.3 (50.5, 62.9)	56.9 (53.2, 65.9)	55.6 (50.5, 63.4)
	UC	49.3 (43.8, 56.1)	56.7 (48.2, 60.5)	59.6 (50.7, 63.1)	57.0 (49.3, 62.0)
	Difference	-0.6 (-9.2, 7.9)	2.4 (-6.4, 11.1)	2.7 (-6.1, 11.5)	1.4 (-7.7, 10.4)
Pain	*SESI*	52.4 (48.5, 56.3)	51.5 (47.6, 55.3)	49.6 (45.8, 53.4)	49.7 (45.8, 53.6)
	UC	47.6 (43.9, 51.3)	48.4 (44.5, 52.2)	48.8 (44.9, 52.7)	51.2 (47.2, 55.2)
	Difference	-4.8 (-10.1, 0.60)	-3.1 (-8.5, 2.3)	-0.82 (-6.3, 4.7)	1.5 (-4.1, 7.1)
General health perceptions	*SESI*	74.0 (68.6, 79.6)	73.5 (67.9, 79.0)	77.1 (71.5, 82.6)	78.2 (72.4, 83.9)
	UC	66.0 (60.6, 71.4)	66.7 (61.1, 72.4)	70.2 (64.5, 76.0)	73.5 (67.6, 79.3)
	Difference	-8.0 (-15.8, -0,26)	-6.8 (-14.7, 1.2)	-6.8 (-14.8, 1.2)	-4.7 (-12.9, 3.52)
Change in perceived health	*SESI*	45.2 (35.2, 55.2)	57.9 (47.9, 67.9)	68.6 (58.6, 78.6)	87.8 (77.5, 98.1)
	UC	45.5 (35.8, 55.2)	55.3 (45.1, 65.4)	64.0 (53.6, 74.3)	73.3 (62.8, 83.8)
	Difference	0.3 (-13.6, 14.3)	-2.6 (-16.9, 11.7)	-4.6 (-19, 9.8)	-14.5 (-29.3, 0.2)
Physical component summary	*SESI*	58.2 (52.8, 63.5)	68.9 (63.6, 74.2)	77.7 (72.3, 83.0)	79.5 (74.4, 85.0)
	UC	53.3 (48.1, 58.4)	59.4 (54.0, 64.9)	63.1 (57.6, 68.5)	67.6 (61.9, 73.4)
	Difference	-4.9 (-12.3, 2.5)	-9.5 (-17.1, -1.8)	-14.6 (-22.3, -6.9)	-11.9 (-19.8, -3.9)
Mental component summary	*SESI*	61.8 (57.0, 66.6)	65.0 (60.3, 70.0)	67.3 (62.4, 72.1)	67.0 (62.1, 71.9)
	UC	56.4 (51.8, 61.0)	61.2 (56.3, 66.2)	64.1 (59.1, 69.1)	65.2 (60.1, 70.3)
	Difference	-5.4 (-12.0, 1.2)	-3.8 (-10.6, 3.1)	-3.2 (-10.1, 3.8)	-1.9 (-8.9, 5.2)

In this table, all mean scores with standard deviations of the intervention group and the control group for all domains of the SF-36 questionnaire at all measuring moments including the difference between groups with 95% confidence intervals are presented. The score range of the SF-36 is 0-100, with higher scores indicating better quality of life. The measured values of our study population were used to estimate the values in the general population.

Over time, when calculated for the entire follow-up period as a whole, both groups experienced a significant decline of symptoms for physical functioning ($p < 0.0001$ in both groups), physical role limitations ($p = 0.0001$ in the intervention group, $p < 0.0001$ in the control group), emotional role limitations ($p = 0.03$ in the intervention group, $p = 0.01$ in the control group), change in perceived health ($p < 0.0001$ in both groups) and the physical component score ($p < 0.0001$ in both groups). The control group experienced a significant decline of symptoms for emotional wellbeing ($p = 0.03$), energy/fatigue ($p = 0.04$), general health perception ($p = 0.03$) and the mental component score ($p = 0.003$) but the intervention group did not. For social functioning, neither group experienced a significant decline of symptoms.

When groups were compared, the intervention group experienced significantly less symptoms for physical functioning ($p = 0.03$), physical role limitations ($p = 0.006$), emotional role limitations ($p = 0.04$), general health perceptions ($p = 0.02$) and the physical component score ($p = 0.0002$) than the control group. Interactions between groups were not significant for any of the SF-36 domains when calculated over the follow-up period as a whole.

Cost-utility

The difference in utility between the intervention group and the control group was 0.0084 QALYs in favor of the control group. This equals a loss of three days in perfect health in the intervention group. Societal costs were higher in the control group than the intervention group, which resulted in a mean cost difference of €1,626 [-€2,133 to €5,384 95% CI] between groups over the course of one year, mainly due to loss of productivity. The ICUR, (point estimate for costs saved per QALY lost) was €193,354 [-€859,133 to €2,352,223 95% CI]. Figure 5.2 shows the results of the bootstrap simulations of cost-QALY pairs. The majority of estimates were located in the south-western quadrant (78%) indicating less QALYs at lower costs (costs saved per QALY lost). Figure 5.3 shows the cost-effectiveness acceptability curve (CEAC). The probability that adding SESIs to standard care is cost-effective starts at 80% with a threshold of €0. This implies that, (compared to usual care), the chance that adding SESIs to the protocol is cost-effective in terms of utility, is 80% at no extra costs.

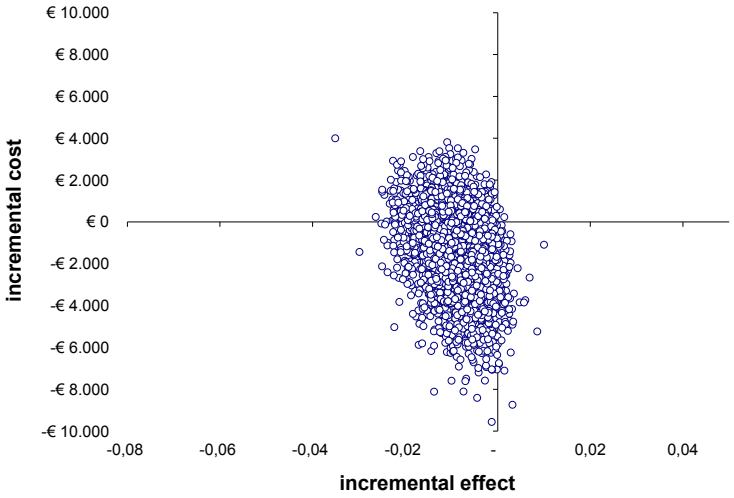

Figure 5.2: Bootstrapped costs and utility.

The majority of estimates (78%) were located in the south-western quadrant indicating less QALYs at lower costs (costs saved per QALY lost). Another 19% of cost-utility pairs were in the north-western quadrant (less utility at higher costs) and a negligible amount of estimates were in the eastern part (more utility) of the plot.

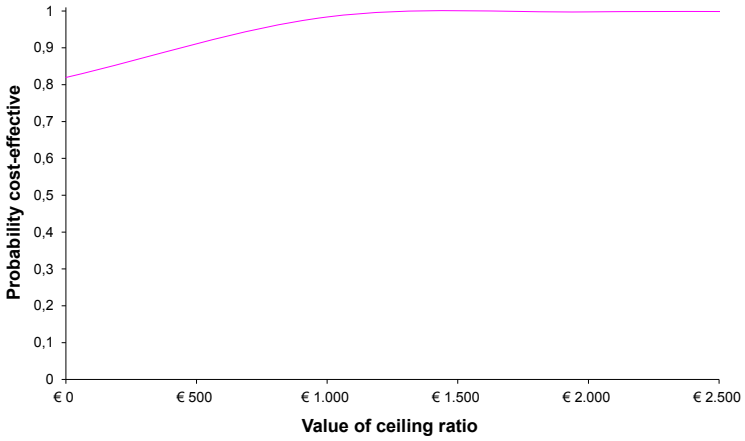

Figure 5.3: Cost-effectiveness acceptability curve

The CEAC graphically shows the probability of whether it would be cost-effective in terms of utility to add SESIs to care as usual, compared to care as usual alone, at a specific ceiling ratio. This means that the probability that a certain intervention is considered cost-effective rises with the willingness of decision makers to invest in this intervention. In the current situation, without additional investment, the probability that SESIs as an additional treatment are cost-effective is already 80% (the starting point of the curve).

DISCUSSION

Principal findings

Both our study groups experienced significant increase in quality of life, in (especially) the physical domains of the SF-36, with the intervention group scoring significantly better than the control group at certain time points. In terms of utility, implementing SESIs as an additional pain treatment for LRS in general practice would lead to a negligible loss of QALYs. These seemingly paradoxical outcomes are probably explained by the manners in which they are generated: quality of life, derived from the SF-36 questionnaire, is a patient-based outcome whereas utility, derived from the SF-6D, is a preference-based outcome.[23] The cost-utility analysis showed that with a minimal loss of utility, societal costs would be saved, due to more productivity in the intervention group.

Strengths and limitations

To our knowledge, this study is the first to evaluate the influence of adding SESIs to the treatment of acute LRS on quality of life and cost-utility from a societal perspective. Furthermore, our study was undertaken entirely in general practice, where the majority of patients with LRS are cared for, unlike most other research which is performed in a hospital setting. This study also has some possible limitations. The SF-36 cannot be used directly to measure utility since it is not preference based. A meaningful health state classification (the SF-6D) can be created from the SF-36 by applying the score transformation as described in the method section.[23] Direct measures of utility, for example the EuroQoL questionnaire, may have more construct responsiveness and validity in chronic pain.[28] However, to our knowledge, no comparison between the two questionnaires in acute pain is made as yet, and in some other disease areas the SF-6D was found superior.[29] Moreover, the SF-6D is also used by other authors performing cost-utility analyses in patients with sciatica.[6,26,30]. We therefore feel that the use of an indirect measure of utility was justified. Another limitation is the relatively large number of dropouts due to unsatisfactorily completion of the SF-36 questionnaires. We probably overloaded our study subjects. Our selections of 50 and 44 subjects did not differ in age or distribution among the sexes and the research groups from each other, nor from our randomized population.

Differences in utility between all kinds of interventions for sciatica are small. Differences in societal costs vary. From our study results, we learned that a societal costs can be saved against a negligible loss of utility by implementing SESIs as an additional pain treatment in LRS. It seems a logical choice for decision makers to implement an intervention that is not inferior to the usual treatment and less expensive to society. However, SESIs are invasive procedures with risks of both local complications and systemic side-effects.[5,31,32] The beneficial effects of SESIs in terms of pain, disability and quality of life are small and the natural course of LRS is predominantly favourable. We therefore conclude that decision makers can consider implementing SESIs in daily practice with the purpose of saving resources, provided that caution is taken. Further research should be aimed at identifying patient subgroups that might benefit the most from SESIs, with additional focus on (costs of) complications and side effects.

Other research

The WEST-study is a hospital-situated, multi-centre, pragmatic RCT in which quality of life and utilities were measured using the SF-36 and SF-6D. The researchers found a significant improvement in quality of life in both the SESI and the placebo group over time ($p<0.001$ after both 13 and 52 weeks).[6] They did not, however, find any significant difference in quality of life between groups. The incremental QALY gained provided by their cost-utility analysis was 0.0059 which is equivalent to an additional 2.2 days of full health. The incremental costs were £152 from a provider perspective (costs to the provider based on real resource use) and £992 from a purchaser perspective (prices charged to purchasers based on total costs of service including overheads). The costs found per QALY gained were therefore £25,746 from a provider perspective and £167,145 from a purchaser perspective. The results of the cost-utility analyses are in this case difficult to compare to ours since we have used a societal perspective (all costs are measured regardless of who pays for them). In our study, the majority of costs are saved in the field of productivity loss, which is not taken into account using a purchaser's or provider's perspective.

As stated in the introduction section, cost-utility analyses enable comparison between different health care interventions by using a single unit of measure (QALYs). In sciatica, the cost-effectiveness in terms of utility of other interventions has been studied. In a cost-utility analysis alongside a randomized controlled trial comparing prolonged conservative care with early surgery in patients with sciatica, researchers found incremental QALYs in favour of early surgery of 0.044 (0.005 –

0.83) using the UK EQ-5D, 0.032 (0.005 – 0.059) using the US EQ-5D and 0.024 (0.003 – 0.046) using the SF-6D.[24] They found a negligible difference in total societal costs of €12 (-€4,029 - €4,006) in favour of early surgery. In this case, the higher healthcare costs of early surgery balanced out against its lower costs in productivity loss. This amounts to costs per QALY gained of €273, €375 and €500 respectively. Another cost-utility analysis alongside a randomized controlled trial compared the differences between tubular discectomy and conventional microdiscectomy in the treatment of sciatica.[25] They found non-significant incremental QALYs in favour of conventional microdiscectomy of -0.012 (-0.046 – 0.021), -0.014 (-0.056 – 0.029) and -0.11 (-0.037 – 0.014) with the US EQ-5D, the UK EQ-5D and the SF-6D respectively. The difference in incremental societal costs was $1032 (-$1,494 - $3,557), also in favour of conventional microdiscectomy (€826 (-€1,196 - €2,847)). This amounts to savings per QALY of $86,000, $73,714 and $9,382 respectively (€68,844, €59,015 and €7,511) for not implementing tubular discectomy.

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