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Electroacupuncture with Usual Care for Patients with Non-Acute Pain after Back Surgery: Cost-Effectiveness Analysis Alongside a Randomized Controlled Trial

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Abstract: Electroacupuncture (EA) is used to treat pain after back surgery. Although this treatment is covered by national health insurance in Korea, evidence supporting its cost-effectiveness and contribution to the sustainability of the national health care system has yet to be published. Therefore, an economic evaluation, alongside a clinical trial, was conducted to estimate the cost-effectiveness of EA and usual care (UC) versus UC alone to treat non-acute low back pain (LBP). In total, 108 patients were recruited and randomly assigned to treatment groups; 106 were included in the final cost utility analysis. The incremental cost-effectiveness ratio of EA plus UC was estimated as 7,048,602 Korean Rate Won (KRW) per quality-adjusted life years (QALYs) from the societal perspective (SP). If the national threshold was KRW 30 million per QALY, the cost-effectiveness probability of EA plus UC was an estimated 85.9%; and, if the national threshold was over KRW 42,496,372 per QALY, the cost-effectiveness probability would be over 95% percent statistical significance. Based on these results, EA plus UC combination therapy for patients with non-acute LBP may be cost-effective from a societal perspective in Korea.

Keywords: non-acute low back pain; failed back surgery; electroacupuncture; economic evaluation; costs; quality-adjusted life years (QALYs)

1. Introduction

Increasing health care expenditure within the budget constraints caused by an aging population demands the examination of not only the efficacy and effectiveness of treatment, but also the cost-effectiveness of treatment alternatives that support the sustainability of the national health care system [1,2]. This trend impacts the use of therapies in the area of complementary and alternative medicine, which have been commonly employed to treat various diseases, and are already approved for national health insurance reimbursement in Korea [3]. Low back pain (LBP) is a common disease treated by complementary and alternative therapies, and more than 70% of people in industrialized countries experience LBP at some time in life, causing a substantial societal economic burden [4]. The global burden of LBP was ranked as sixth in terms of overall burden measured by disease-adjusted



life years (DALYs) in 2010, and is increasing due to the aging global population [5]. For individual patients, LBP can have profound economic effects, which increase with the addition of comorbidities.

Almost 70% of patients with LBP recover from the condition within 12 weeks, while the remaining 30% do not completely recover and may develop persistent LBP. Recommendations on invasive treatment, including radiofrequency denervation, surgery, and injections, are controversial. According to a recent review, 37% of guidelines recommended radiofrequency denervation for chronic LBP, while 25% recommended it restrictively only if there was no improvement with conservative treatments [6].

The most common reasons for back surgery are intervertebral disk herniation, spinal stenosis, and spondylolisthesis [7], which need appropriate types of surgery according to the diagnosis and symptoms. The most common surgical procedure for intervertebral disk herniation is discectomy, a direct method of removing the herniated disc. Other methods include dissolving the intervertebral disc via injection, laser treatment, heat, microscopic disc aspiration using a specialized instrument that breaks up the intervertebral discs, and percutaneous endoscopic disc removal. For spinal stenosis, the purpose of surgery is decompression through removal of structures (bony and soft tissue) that compress the dura mater or nerve roots. Depending on the range of the affected area, laminotomy, laminectomy, and laminoplasty are available treatment methods. Lumbar infusion may be conducted if there is instability of the spine, e.g., spondylolisthesis, scoliosis, or posterior lumbar lordosis, with careful consideration of patient characteristics, such as degenerative changes according to age, activity status, and bone mineral density [8].

In Korea, the Health Insurance Review and Assessment Service reported that the number of lumbar spinal surgeries increased to 111,672 cases in 2013, which was 36.1% higher than that in 2007 [9]. Moreover, the reoperation rates after back surgery were 13.4% and 14.2% at five years for lumbar disc herniation and spinal stenosis, respectively [10,11]. In the US, the success rate of lumbar disc surgery for the treatment of neuromuscular disease is 60–90% [12]. This suggests that 10–40% of patients may have persistent pain or decreased lumbar motion or function after surgery [13], with estimated health care costs of up to \$20 billion annually [14].

Given that persistent pain is the most common complication of back surgery, pain management is a very important element of patient care [15]. The first-line therapy for pain is conventional medical management using various opioid analgesics, such as morphine, hydromorphone, meperidine, or fentanyl [16]. However, unwanted opioid side effects, such as nausea and vomiting, occur frequently [17]; moreover, opioids are highly addictive [18], thus highlighting the need for safe and effective pain management methods after back surgery.

Acupuncture is commonly used for pain management based on many studies demonstrating that it is safe [19] and cost-effective [20] compared with routine care [21]. Moreover, electroacupuncture (EA), an acupuncture technique with specific electronic stimulation, has already been approved for national health insurance reimbursement in Korea and may be a reasonable approach to pain management for back surgery patients [22]. Given that there have been only a few clinical trials assessing the effectiveness of EA in the treatment of back surgery [23], we have conducted a randomized controlled trial to compare the effectiveness of EA in combination with usual care (UC) with that of UC alone in controlling non-acute pain and improving function at \geq 3 weeks after surgery [24]. Based on that trial, we also analyzed the cost-effectiveness of EA as a complementary method of pain management of back surgery patients. Economic evaluation alongside a clinical trial is one type of economic evaluation that uses a clinical trial as the main source of information through which the cost-effectiveness of a specific intervention is valued [25]. Although several studies have reported the cost-effectiveness of spinal cord stimulation [26–29], none have investigated the cost-effectiveness of EA in post-lumbar surgery patients.

In 2010, the Korean Ministry of Health and Welfare launched several laws regarding medical provider employment and collaboration. Under these laws, doctors and Korean medicine doctors (qualified in acupuncture) can work concurrently to treat the same disease or condition in a single

patient. In addition, disease codes were unified under the Korean classification of disease, which is sourced from the international classification of disease; before this point, Korean medicine doctors had been using different diagnostic systems. Despite these circumstances, many questions remain regarding the clinical effectiveness and cost-effectiveness of combination treatments via collaboration between doctors of various specialties [30]. These unanswered questions are a major barrier to the adjustment and expansion of available treatment options under the national healthcare system. In this context, the economic evaluation of the combination treatment for common diseases involving collaboration between Korean medicine doctors and doctors, as with the use of EA plus UC to treat chronic pain, is a critical issue in Korea. Therefore, we conducted this research to evaluate the cost-effectiveness of concurrent EA and UC treatment compared with that of UC alone for non-acute LBP patients.

The purpose of this study was to examine the cost-utility of using EA with UC versus UC alone for post-back surgery pain by conducting an economic evaluation study alongside a randomized controlled trial. We hypothesized that EA in combination with UC would be cost-effective compared with UC alone.

2. Materials and Methods

This study was a multicenter, randomized, assessor-blinded, active-controlled trial and has been described in detail elsewhere [31]. The study adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (www.CONSORT-statement.org, Supplementary Material 1). We used the economic case report form along with the clinical case report form for capturing the variables of direct medical costs, direct non-medical costs (travel cost, hospital visiting time costs), and indirect costs (productivity losses from absenteeism and presenteeism). The economic evaluation was primarily based on the Korean healthcare perspective, and we conducted a sensitivity analysis using a societal perspective (SP). The analysis was restricted to a 24-week time horizon of a clinical research follow-up period. The economic evaluation was conducted according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS checklist, Supplementary material 2).

2.1. Randomization Design and Participants

Participants with non-acute low back pain after back surgery who had a visual analog scale (VAS) pain intensity score of \geq 50 mm were randomly assigned to either the EA with UC group or the UC alone group at a 1:1 ratio.

2.2. Ethics

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the consolidated institutional review board of Pusan National University Korean Medicine Hospital (approval number: 2016003), Kyung Hee University Oriental Medicine Hospital at Gangdong (approval number: KHNMC OH 2015-10-002), and Jaseng Hospital of Korean Medicine (approval number: KNJSIRB2016-025). All participants participated voluntarily in this study, and written informed consent was obtained from each participant before enrollment.

2.3. Interventions

2.3.1. Usual Care

Participants in both groups received physical therapy and a standardized educational program. Interferential current therapy (ICT; EF-150, OG Giken Co., Okayama, Japan; STI-300, Stratek Co. Ltd., Anyang, South Korea) and superficial heat therapy were applied twice per week during the 4-week treatment period. In addition, participants received a standardized educational program on LBP through a 20-min video and a brochure.

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The patients in the EA with UC group received a total of eight sessions (two sessions/week) of EA treatment and UC for 4 weeks. The treatments were performed at Jia-ji (six acupuncture points, bilateral Ex-B2 at L3, L4, and L5) and a maximum of nine additional acupuncture points using disposable stainless-steel needles (0.25×40 mm, Dongbang Acupuncture Inc., Boryung, Korea). Electrical stimulation (ES-160, ITO Co. Ltd., Tokyo, Japan) was applied to four acupuncture points of Jia-ji (bilateral Ex-B2 at L3 and L5).

2.3.3. Permitted and Prohibited Concomitant Treatments

Conventional pharmaceutical and non-pharmaceutical treatments associated with post-operative LBP were permitted. However, invasive interventions, such as injections and surgery, were prohibited throughout the study period.

2.4. Utility Measure and Valuation

Utilities were measured using the Euroqol five-dimension scale three-level version (EQ-5D-3L). This measures five domains, including mobility, self-care, usual activity, pain, and anxiety/depression (no problem, 1; some/moderate problem, 2; extreme problem, 3). The EQ-5D index is calculated by weighting each level of the five domains (ranging from –1, every domain has extreme problem, to +1, none of the domains has a problem). This measurement was collected at baseline and at 4, 8, 12, and 24 weeks post-randomization. The descriptive categories of the EQ-5D-3L were converted to utilities using the South Korean national tariff [32], and then calculated as quality-adjusted life years (QALYs) using the area under the curve method. These calculated QALYs therefor take into account two factors, the quantity of life and the quality of life, measured during the study follow up. Normally 1 QALY during a year could be derived from 1 life year with the perfect health condition.

2.5. Resource Use and Cost Measures

The resource utilization of both treatment options was assessed from the societal perspective; therefore, the direct medical and non-medical costs, as well as the indirect medical costs, of each treatment were measured. The direct medical costs incurred by the study protocol were determined from the research hospital administrative data. Data on direct medical costs of other hospital visits and purchases of over-the-counter medication, medical devices, and functional foods were collected via an economic case report form developed for this study. Data on time costs for hospital visits and travel costs were also collected using the economic case report form. All medical costs, including EA, were valued using national health insurance reimbursement prices [33]. Productivity losses were calculated based on days of absence and decreased work efficiency due to a disease. As there has been no clear guideline and reasonable friction cost methods for calculating productivity loss in Korea, we used the human capital approach estimation method in this study by simply summing the costs incurred by absenteeism (number of days of absent × cost per day) and presenteeism (number of work days \times cost per day \times percent of decreased efficiency). All cost components in this study were sourced from or transformed to 2017 Korean Rate Won (KRW) monetary values; the details are included in Supplementary File 3. The entire study follow-up period did not exceed 1 year; therefore, the discount rates for reflecting time preferences were not adjusted in costs and utility outcomes.

2.6. Missing Data Analysis

For the intention-to-treat (ITT) analysis, patterns and mechanisms associated with missing data were identified. The total percentage of missing data was 11%, and the mechanism was found to be missing completely at random (MCAR) based on the results of Little's MCAR test (chi-square distance = 32.43, p = 0.985). After identifying the abovementioned value, multiple imputation of incomplete data was conducted using the Stata/MP14 (StataCorp LLC, TX, USA). Five imputed data

sets were created using a multivariate normal model for utility outcomes and predictive mean matching for costs. Baseline covariates, including clinical and economic variables, were used for establishing imputation models.

2.7. Cost-Utility Analyses

The mean incremental cost-effectiveness ratio (ICER) was calculated by dividing the incremental costs by the incremental QALYs [25]. To overcome the sampling uncertainty of the point estimates of ICER, confidence intervals were estimated using the bootstrapping method (1000 times replicate) using Stata/MP 14. The mean values, ICER values and approximate bootstrap confidence intervals were displayed in the cost-effectiveness plane. The net monetary benefit (NMB) results were calculated using the equation below and displayed via a line graph. The probabilities of each alternative being cost-effectiveness acceptability curve.

The NMB equation is as follows: NMB = QALYs differences \times national willingness to pay – cost differences

2.8. Sensitivity Analysis

Some sensitivity analyses of the deterministic ICER results were conducted from a limited societal perspective (LSP) using not only ITT data, but also per protocol (PP) data. By comparing the LSP and SP analysis results, we assessed the impact of productivity loss on the cost components, and by comparing the ITT and PP analysis results, we also confirmed the robustness of the missing data imputation.

3. Results

Between June 2016 and May 2017, 108 patients with non-acute low back pain who were eligible for participation were enrolled. Among the 108 participants, 106 were included in the cost-utility analysis and randomized equally to the two treatment groups (EA with UC in combination [n = 53] or UC alone [n = 53]); two participants (1 participant in each group) withdrew their consent before enrolling on the economic evaluation study. One participant in the EA with UC group withdrew from the study, and 12 were lost to follow-up. Three participants in the UC group withdrew from the study, and seven were lost to follow-up (Figure 1). The total percentage of missing data at the patient level was 22.6%, and that at the value level was 15.3%. Table 1 shows the demographic and prognostic characteristics of the participants. There were no significant differences between the groups at baseline for any of the variables except direct medical cost (Table 1).

3.1. Costs

Detailed unit costs, sources of direct medical and direct non-medical costs, and productivity losses from presenteeism and absenteeism are shown in Supplementary File 4. The frequency of treatment with each alternative during the trial and throughout the follow-up period was recorded, and these data are listed in Supplementary File 3. From the SP, the total cost of EA in combination with UC based on data from participants who completed the trial was estimated as KRW 3,085,423 (SD 1,338,813), while the total cost of UC alone was KRW 3,043,643 (SD 1,098,816). From the LSP, the total costs of EA plus UC and UC alone were estimated as KRW 812,438 (SD 382,578) and KRW 682,409 (SD 274,958), respectively.

3.2. Utilities

Table 2 shows Quality of Life (QoL) scores of both treatment groups at each follow-up time point, and Table 3 shows the QALYs gained during the clinical trial and follow-up period. Although patients receiving EA plus UC showed a larger QALYs value than those receiving UC alone, the difference did not reach statistical significance (p = 0.358). The QALYs for 6 months for both treatment groups

were estimated using the area under the curve method. The advantage of this approach was that the differences in the baseline utility values (whether statistically significant or not) could be considered for calculating the QALYs for the entire follow-up period [34].

3.3. Sensitivity Analyses

Sensitivity analyses were performed using the imputation data from a different perspective, which excluded the productivity losses associated with both treatment alternatives from the cost components. Even the differences in total costs increased from this LSP, with the mean ICER estimated to have a lower value (KRW 17,716,572 cost per QALY) than that of the Korean national threshold (Table 4).

In addition, we examined the mean ICERs from the SP and LSP using complete case data. Based on the PP analyses, the estimated mean ICER from the LSP was KRW 14,549,698.4 cost per QALY and that from the SP was KRW 4,674,999 cost per QALY, which was similar to the results of the main analyses using the value of the Korean national threshold.



Figure 1. Flow diagram of participant screening, treatment allocation, and follow-up.

Variables		Usual Ca	re (N = 53)	Electroacupu		
		Mean, SD or N, Percent		Mean, SD	<i>p</i> -Value	
Sex	Male (N, %)	26	49.06	27	50.94	0.846
	Female (N, %)	27	50.94	26	49.06	
	Age	46.08	14.56	45.91	13.09	0.950
	Less than 10 million	8	15.09	6	11.32	0.445
Income	10–50 million	25	47.17	23	43.40	
(KRW)	50–100 million	19	35.85	19	35.85	
. ,	More than 100 million	1	1.89	5	9.43	
OP	BMI	23.9	3.89	23.9	3.06	0.996
	Clinic	22	41.51	16	30.19	0.340
	Hospital	23	43.40	24	45.28	
nospitai	General hospital	8	15.09	13	24.53	
	None	5	9.43	5	9.43	0.631
Caror	Family	37	69.81	41	77.36	
Carer	Family and carer	4	7.55	1	1.89	
	Carer	7	13.21	6	11.32	
А	dmission day	20.43	19.71	34.35	68.08	0.156
С	Deration cost	4,403,529	3,183,233.00	7,941,085	21,800,000.00	0.253
Dire	Direct medical cost		1,965,332.00	3,798,113	5,806,710.00	0.016
	Care time		526.10	262	333.90	0.502
W	Week work time		23.83	50.06	24.62	0.747
Absenteeism (day)		32.26	86.25	27.55	71.10	0.774
Presenteeism (percent)		6.151	2.38	6.039	2.58	0.819
EQ	2-5D (baseline)	0.72	0.13	0.74	0.15	0.296
EQ-VAS		62.15	11.31	60.58	14.26	0.532

Table 1. Baseline characteristics of participants.

BMI, body mass index; EQ-5D, Euroqol five-dimension scale; EQ-VAS, Euroqol-Visual Analogue Scale; KRW, Korean Rate Won; OP, operation; SD, standard deviation. EQ-5D ranges from 0 to 1. EQ-VAS ranges from 0 (the worst health you can imagine) to 100 (the best health you can imagine). Direct medical cost refers to the costs incurred after operation (surgery) before being enrolled in our study (excluding the cost of surgery). Continuous variables analyzed using an independent t test, and categorical variables analyzed using a chi-square test, except income and career variables (Fisher's exact test).

Variables	Follow-Up Time	Usual Car	re (n = 43)	Electroacupuncture (n = 40)		
variables	ronow-op mile	Mean	SD	Mean	SD	
	Baseline	0.741	0.11	0.755	0.155	
	4 weeks	0.771	0.105	0.797	0.095	
EQ-5D	8 weeks	0.782	0.108	0.810	0.097	
	12 weeks	0.791	0.105	0.820	0.117	
	24 weeks	0.804	0.101	0.803	0.15	
	1–4 weeks	119,355	24,013	230,085	50,409	
Direct medical	5–8 weeks	2474	8552	11,320	69,990	
costs (KRW)	9–12 weeks	1228	6937	6285	34,834	
	13–24 weeks	37,660	162,502	83,875	351,700	
Direct	1–4 weeks	143,365	63,631	130,000	6236	
non medical	5–8 weeks	125,780	56,194	116,210	6230	
costs (KRW)	9–12 weeks	125,909	56,212	116,796	8160	
	13–24 weeks	126,637	56,265	117,868	9596	
	1–4 weeks	610,361	130,076	600,011	142,028	
Productivity	5–8 weeks	330,598	191,156	338,616	215,182	
costs (KRW)	9–12 weeks	313,959	173,367	313,205	225,202	
	13–24 weeks	1,106,316	742,713	1,021,153	693,301	

Table 2. Quality of life (QoL) outcomes and costs during follow-up (per protocol, 2017 KRW).

KRW, Korean Rate Won; SD, standard deviation. EQ-5D ranges from 0 to 1.

Usual Care (n = 43)		Electroacupuncture (n = 40)		Mean Difference	
Mean	SD	Mean	SD	Mean	95% CI
0.361	0.041	0.370	0.047	0.009	(-0.010, 0.028)
160,718	159,735	331,565	374,476	170,847	(46,645, 295,049)
521 <i>,</i> 691	231,482	480,873	26,190	-40,818	(-114,105, 32,468)
2,361,235	1,044,315	2,272,985	1,142,409	-88249.4	(-565,821, 389,322)
682,409	274,958	812,438	382,578	130,029	(-14,718, 274,776)
3,043,643	1,098,816	3,085,423	1,338,813	41,780	(-491,576, 575,136)
	Usual Can Mean 0.361 160,718 521,691 2,361,235 682,409 3,043,643	Usual Care (n = 43) Mean SD 0.361 0.041 160,718 159,735 521,691 231,482 2,361,235 1,044,315 682,409 274,958 3,043,643 1,098,816	Usual Care (n = 43) Electroacuput Mean SD Mean 0.361 0.041 0.370 160,718 159,735 331,565 521,691 231,482 480,873 2,361,235 1,044,315 2,272,985 682,409 274,958 812,438 3,043,643 1,098,816 3,085,423	Usual Care (n = 43)Electroacupuncture (n = 40)MeanSDMeanSD0.3610.0410.3700.047160,718159,735331,565374,476521,691231,482480,87326,1902,361,2351,044,3152,272,9851,142,409682,409274,958812,438382,5783,043,6431,098,8163,085,4231,338,813	Usual Care (n = 43) Electroacupuncture (n = 40) Me Mean SD Mean SD Mean 0.361 0.041 0.370 0.047 0.009 160,718 159,735 331,565 374,476 170,847 521,691 231,482 480,873 26,190 -40,818 2,361,235 1,044,315 2,272,985 1,142,409 -88249.4 682,409 274,958 812,438 382,578 130,029 3,043,643 1,098,816 3,085,423 1,338,813 41,780

Table 3. Total costs and quality-adjusted life years (QALYs) of usual care and electroacupuncture (Per protocol, 2017 KRW).

KRW, Korean Rate Won; LSP, limited societal perspective; QALY, quality-adjusted life year (6 months with perfect health is 0.5 QALY); SD, standard deviation; SP, societal perspective.

3.4. Incremental Cost-Effectiveness Ratio (ICER)

The ICER results are provided in Table 4. Treatment with EA plus UC resulted in a greater mean health benefit (0.009 QALYs) achieved at a higher mean total cost (KRW 64,603) than that with UC alone based on ITT analysis from the SP. The dominance of EA treatment (more benefit at a lower cost) was shown in 18.4% of the replications, and all other bootstrapped likelihood replications (81.6%) were located in the northeast quadrant, indicating that EA was more expensive but also more effective in the cost-effectiveness plane (Figure 2). Figure 3A presents the NMB and confidence intervals of EA plus UC compared to UC alone according to changes in the national threshold. At the point of the Korean national threshold (KRW 20,000,000), mean NMB was estimated to be KRW 115,182, and the upper and lower confidence intervals around this value did not exclude zero, which indicated no statistical confirmation of the cost-effectiveness of EA plus UC treatment compared to UC alone in Korea. These results are also displayed as cost-effectiveness acceptability curve in Figure 3B, which show the cost-effectiveness probability of EA plus UC compared with that of UC alone at the points of national thresholds. At the point of the Korean national threshold, the percentage of cost-effectiveness was estimated as 87.1%, and if the national threshold was >KRW 42,591,316, EA plus UC may be confidently defined as a cost-effective alternative for treating non-acute LBP patients compared with UC alone.



Figure 2. Incremental cost-effectiveness ratio (ICER) and 95% confidence interval (CI) based on 1000 bootstrap replicates (intention-to-treat analysis).



Figure 3. (**A**) The 95% confidence interval of net monetary benefit (NMB) calculated from the Korean national threshold (KRW 20,000,000 per QALY). KRW, Korean Rate Won; QALY, quality adjusted life year. (**B**) Cost-effectiveness acceptability curve (CEAC) of electroacupuncture in combination with usual care according to the changes in the national threshold. CI, confidence interval; wtp, willingness to pay.

Analyses	Perspectives	Treatments	Cost	Delta Cost	QALYs	Delta QALYs	ICER
ITT	SP	UC (N = 53)	3,052,480		0.35836		
		EA (N = 53)	3,117,082.6	64,602.56	0.367526	0.009	7,048,602.88
	LSP	UC (N = 53)	683,687		0.358677		
		EA (N = 53)	827,131	143,444	0.366774	0.008	17,716,572.4
PP	SP	UC (N = 43)	3,043,643		0.361		
		EA(N = 40)	3,085,423	41,780	0.37	0.009	4,674,999.16
	LSP	UC (N = 43)	682,409		0.361		
		EA (N = 40)	812,438	130,029	0.37	0.009	14,549,698.4

Table 4. Incremental cost-effectiveness ratio (deterministic analysis).

ICER, incremental cost-effectiveness ratio; ITT, intention to treat; LSP, limited societal perspective; PP, per protocol; QALY, quality-adjusted life year; SP, societal perspective.

4. Discussion

As sustainability is a critical issue in the establishment of healthcare polices, "smart spending" that expands investments in essential factors and reduces unnecessary costs is pursued [35]. Health sustainability can be divided into economic sustainability and fiscal sustainability. Fiscal sustainability considers only the balance of government spending and budget related to healthcare, and an increasing healthcare costs are interpreted as a threat to sustainability. However, if the benefits produced by healthcare are greater than the total cost, and healthcare costs do not threaten other economic activities, these benefits contribute to economic sustainability [36]. In this study, the overall benefits and total costs related to non-acute pain after back surgery were considered.

EA in combination with UC is a commonly used therapy for patients with LBP after back surgery or for those who experience side effects from the opioids prescribed to treat their pain. In previous research, the effectiveness of EA was shown to alleviate the sensory symptoms and regulate components of pain through specific neuroscientific mechanisms, and is therefore thought to contribute to the reduction of pain medication dosages [37]. Additional research has reported the use of EA for managing postoperative pain from various procedures other than back surgery, such as cardiopulmonary bypass, mixed hemorrhoid surgery, and gynecological laparoscopic surgery [24].

To our knowledge, this is the first study in Korea using economic evaluation alongside a clinical trial to compare EA plus UC with UC alone in the treatment of patients with non-acute pain after back surgery. Prior research in the UK demonstrated that additional acupuncture treatment was cost-effective compared with UC alone for treating chronic LBP [38]. Moreover, in Germany, acupuncture was shown to be relatively cost-effective [39]. Our research results showed similar trends and indicated the cost-effectiveness of EA plus UC compared with that of UC alone via the deterministic ICER. Although

there are uncertainties surrounding the dominance of the EA plus UC combination using mean values, if the national threshold was >KRW 20,000,000 per QALY, the probability for cost-effectiveness of EA plus UC would exceed 59.2%. The CEAC also showed favorable results, with a 59.2% probability of willingness to pay with the threshold at KRW 20,000,000 per QALY and 85.9% probability at a threshold of KRW 30,000,000 per QALY. Overall, in Korea, the collaboration of specialists using EA plus UC in combination shows the possibility for increased cost-effectiveness, from the LSP (healthcare perspective) in treating LBP patients after back surgery. In addition to examining the parameter uncertainties, we explored other factors that might affect the conclusions of the study, such as different perspectives (whether to consider productivity cost) and missing data imputation. Table 4 shows the combined results accounting for the different perspectives and after addressing missing data.

The findings of our study are consistent with those of previous studies that have reported acupuncture treatment as being cost-effective for chronic LBP [40]. According to a clinical trial conducted in United Kingdom [41] and a Korean study using a Markov model decision analysis, acupuncture collaborative therapy has been regarded as a cost-effective treatment compared to usual care only for LBP. In the same context, a meta-analysis revealed that acupuncture as a complementary treatment is highly cost-effective for chronic LBP [42]. However, substitutional use of acupuncture was only cost-effective when the condition was accompanied by depression [42]; and an economic evaluation conducted in Iran showed that EA was less cost-effective than non-steroidal anti-inflammatory drugs, but this study did not report the ICER [43]. Further studies are needed to draw a definitive conclusion.

There are several limitations that should be considered when interpreting the study results. First, similar to other economic evaluation alongside clinical trials, the main purpose of this research was to examine the effectiveness of both treatments and, as such, the predefined sample size was not large enough to address the research question of cost-effectiveness with adequate statistical power. Second, the patients included according to predefined criteria do not represent the general population in a real-world context, which is common for economic evaluations alongside randomized controlled trials. Third, records of medical utilization outside research hospitals during follow-up periods was gathered using self-report forms, introducing the potential for recall bias in estimating cost values. Fourth, although all costs incurred after randomization were captured by identification, measurement, and valuation using the economic case report form, costs incurred before entering this research could not wholly be identified due to the memory loss of the participants, and so we excluded the costs identified at baseline from the cost estimation analysis. Finally, even though this study was a multi-center trial, concerns about the generalizability of the results from a single randomized controlled trial remain. Despite these limitations, this study is the first report of an economic evaluation alongside a clinical trial, highlighting the issue of collaboration between Korean medicine doctors and medical doctors for concurrent treatment of LBP in Korea. Moreover, patient utilities and cost components, including productivity losses, may be captured directly from trial participants and could reflect real-world economic and clinical situations. The steps for conducting an economic evaluation within an RCT are defined as follows: the quantification of the cost and effect of care, assessment of the difference in the cost and effect between the treatment groups, comparison of the magnitudes of differences in cost and effect, and reporting of the ICER, NMB, and CEAC [25]. We followed this whole process and reported the results according to both the trial (CONSORT) and economic evaluation (CHEERS) reporting guidelines.

In sum, the EA and UC combination therapy resulted in better clinical outcomes and higher total costs relative to UC alone from the LSP, with a 59.2% cost-effectiveness probability at the national threshold of KRW 20,000,000 per QALY and an 85.9% probability at the threshold of KRW 30,000,000 per QALY in Korea.

5. Conclusions

The deterministic and sensitivity analyses of different perspectives using PP and ITT data showed that the EA and UC combination was more effective and costlier than UC alone. The bootstrapping

analysis results displayed in the CE plane showed the mean values (KRW 704,861 per QALY) and 95% CI (KRW –6,957,703 and KRW 42,496,372) of the ICER, and NMB and CEAC estimate results also showed the mean values, 95% CI, and cost effective probabilities according to changes in the national threshold. These results show that the ICER of EA plus UC was estimated as KRW 7,048,602 per QALY from the societal perspective, and, if the national threshold was KRW 30,000,000 per QALY, the cost-effectiveness probability of EA plus UC was an estimated 85.9%. Moreover, if the national threshold exceeds KRW 42,496,372 per QALY, the EA combination treatment will be cost-effective with statistical significance. To confirm our study results, future economic evaluation research in conjunction with clinical trials or modeling analyses may be needed to compare multiple treatment options or estimate longer term cost-effectiveness.

Supplementary Materials: Materials available online at http://www.mdpi.com/2071-1050/12/12/5033/s1: Table S1: CONSORT 2010 checklist of information to include when reporting a randomized trial'; Table S2: CHEERS Checklist; Table S3: Unit prices (2017 KRW) and treatment frequencies; Table S4: Summary of censored data about outcome variables.

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References

- Ogura, S.; Jakovljevic, M. Health Financing Constrained by Population Aging-An Opportunity to Learn from Japanese Experience/Finansiranje Zdravstvene Zaštite U Uslovima Starenja Popualcije-Prilika Da Učimo Na Japanskom Iskustvu. J. Exp. Clin. Res. 2014, 15, 175–181. [CrossRef]
- 2. Lee, S.; Moon, Y. A Study of the Financial Projection of Health Expenditures of The Aged of National Health Insurance Focused on the Healthy Ageing of EU -. *J. Crit. Soc. Policy* **2018**, *58*, 53–93.
- 3. Health Insurance Review & Assessment Service. Available online: https://www.hira.or.kr/rd/insuadtcrtr/ bbsView.do?pgmid=HIRAA030069000400&brdScnBltNo=4&brdBltNo=51540&isPopupYn=Y#none (accessed on 1 May 2020).
- 4. Andersson, G.B. Epidemiological features of chronic low-back pain. *Lancet* **1999**, 354, 581–585. [CrossRef]
- Hoy, D.; March, L.; Woolf, A.; Blyth, F.; Brooks, P.; Smith, E.; Vos, T.; Barendregt, J.; Blore, J.; Murray, C. The global burden of neck pain: Estimates from the global burden of disease 2010 study. *Ann. Rheum. Dis.* 2014, 73, 1309–1315. [CrossRef]
- Oliveira, C.B.; Maher, C.G.; Pinto, R.Z.; Traeger, A.C.; Lin, C.-W.C.; Chenot, J.-F.; van Tulder, M.; Koes, B.W. Clinical practice guidelines for the management of non-specific low back pain in primary care: An updated overview. *Eur. Spine J.* 2018, 27, 2791–2803. [CrossRef] [PubMed]
- 7. Cummins, J.; Lurie, J.D.; Tosteson, T.; Hanscom, B.; Abdu, W.A.; Birkmeyer, N.J.; Herkowitz, H.; Weinstein, J. Descriptive epidemiology and prior healthcare utilization of patients in the spine patient outcomes research trial's (sport) three observational cohorts: Disc herniation, spinal stenosis and degenerative spondylolisthesis. *Spine* 2006, *31*, 806. [CrossRef]
- 8. Korea Institute of Oriental medicine. *Lumbar Herniated Intervertebral Disc Korean Medicine Clinical Practice Guideline;* Elsevier Korea: Seoul, Korea, 2015.
- 9. Sin, S.; Kim, M.; Kim, C.; Jung, C. *A study on medicinal Service Use of spinal Surgery Patients*; Health Insurance Review & Assessment Service Seoul: Seoul, Korea, 2015; p. 124.
- 10. Kim, C.H.; Chung, C.K.; Park, C.S.; Choi, B.; Kim, M.J.; Park, B.J. Reoperation rate after surgery for lumbar herniated intervertebral disc disease: Nationwide cohort study. *Spine* **2013**, *38*, 581–590. [CrossRef]
- 11. Kim, C.H.; Chung, C.K.; Park, C.S.; Choi, B.; Hahn, S.; Kim, M.J.; Lee, K.S.; Park, B.J. Reoperation rate after surgery for lumbar spinal stenosis without spondylolisthesis: A nationwide cohort study. *Spine J.* **2013**, *13*, 1230–1237. [CrossRef]

- 12. Ostelo, R.W.; Costa, L.O.P.; Maher, C.G.; de Vet, H.C.; van Tulder, M.W. Rehabilitation after lumbar disc surgery. *Cochrane Database Syst. Rev.* **2008**, *14*, CD003007.
- Ostelo, R.W.; De Vet, H.C.; Vlaeyen, J.W.; Kerckhoffs, M.R.; Berfelo, W.M.; Wolters, P.M.; Van den Brandt, P.A. Behavioral graded activity following first-time lumbar disc surgery: 1-year results of a randomized clinical trial. *Spine* 2003, *28*, 1757–1765. [CrossRef]
- 14. Taylor, R.S.; Taylor, R.J. The economic impact of failed back surgery syndrome. *Br. J. Pain* **2012**, *6*, 174–181. [CrossRef] [PubMed]
- 15. Skolasky, R.L.; Wegener, S.T.; Maggard, A.M.; Riley III, L.H. The impact of reduction of pain after lumbar spine surgery: The relationship between changes in pain and physical function and disability. *Spine* **2014**, *39*, 1426–1432. [CrossRef] [PubMed]
- Hutchison, R.W.; Chon, E.H.; Tucker Jr, W.F.; Gilder, R.; Moss, J.; Daniel, P. A comparison of a fentanyl, morphine, and hydromorphone patient-controlled intravenous delivery for acute postoperative analgesia: A multicenter study of opioid-induced adverse reactions. *Hosp. Pharmacy* 2006, *41*, 659–663. [CrossRef]
- 17. Ricardo Buenaventura, M.; Rajive Adlaka, M.; Nalini Sehgal, M. Opioid complications and side effects. *Pain Physician* **2008**, *11*, S105–S120.
- Ballantyne, J.C.; LaForge, S.K.J.P. Opioid dependence and addiction during opioid treatment of chronic pain. *Pain* 2007, 129, 235–255. [CrossRef]
- 19. Wheway, J.; Agbabiaka, T.B.; Ernst, E. Patient safety incidents from acupuncture treatments: A review of reports to the National Patient Safety Agency. *Int. J. Risk Saf. Med.* **2012**, 24, 163–169. [CrossRef]
- 20. Lin, C.-W.C.; Haas, M.; Maher, C.G.; Machado, L.A.; van Tulder, M.W. Cost-effectiveness of guideline-endorsed treatments for low back pain: A systematic review. *Eur. Spine J.* **2011**, *20*, 1024–1038. [CrossRef]
- 21. Lee, J.-H.; Choi, T.-Y.; Lee, M.S.; Lee, H.; Shin, B.-C.; Lee, H. Acupuncture for acute low back pain: A systematic review. *Clin. J. Pain* **2013**, *29*, 172–185. [CrossRef]
- 22. Casimiro, L.; Barnsley, L.; Brosseau, L.; Milne, S.; Welch, V.; Tugwell, P.; Wells, G.A. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. *Cochrane Database Syst. Rev.* **2005**, *19*, CD003788. [CrossRef]
- 23. Huang, H.; Zheng, S.; Feng, J. Thin's abdominal acupuncture for treatment of failed back surgery syndrome in 20 cases of clinical observation. *Guid. J. Trad. Chin. Med. Pharm.* **2012**, *18*, 63–65.
- 24. Heo, I.; Hwang, M.-S.; Hwang, E.-H.; Cho, J.-H.; Ha, I.-H.; Shin, K.-M.; Lee, J.-H.; Kim, N.-K.; Son, D.-W.; Shin, B.-C. Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: A pilot randomised controlled trial. *BMJ Open* **2018**, *8*, e018464. [CrossRef] [PubMed]
- 25. Glick, H.A.; Doshi, J.A.; Sonnad, S.S.; Polsky, D. *Economic Evaluation in Clinical Trials*; OUP Oxford: Oxford, UK, 2014.
- 26. Annemans, L.; Van Buyten, J.P.; Smith, T.; Al-Kaisy, A. Cost effectiveness of a novel 10 kHz high-frequency spinal cord stimulation system in patients with failed back surgery syndrome (FBSS). *J. Long-Term Eff. Med Implant* **2014**, *24*, 173–183. [CrossRef] [PubMed]
- 27. Roulaud, M.; Durand-Zaleski, I.; Ingrand, P.; Serrie, A.; Diallo, B.; Peruzzi, P.; Hieu, P.D.; Voirin, J.; Raoul, S.; Page, P.; et al. Multicolumn spinal cord stimulation for significant low back pain in failed back surgery syndrome: Design of a national, multicentre, randomized, controlled health economics trial (ESTIMET Study). *Neuro-Chir.* **2015**, *61*, S109–S116. [CrossRef]
- Zucco, F.; Ciampichini, R.; Lavano, A.; Costantini, A.; De Rose, M.; Poli, P.; Fortini, G.; Demartini, L.; De Simone, E.; Menardo, V.; et al. Cost-Effectiveness and Cost-Utility Analysis of Spinal Cord Stimulation in Patients With Failed Back Surgery Syndrome: Results From the PRECISE Study. *Neuromodulation J. Int. Neuromodulation Soc.* 2015, 18, 266–276. [CrossRef]
- 29. Farber, S.H.; Han, J.L.; Elsamadicy, A.A.; Hussaini, Q.; Yang, S.; Pagadala, P.; Parente, B.; Xie, J.; Lad, S.P. Long-term Cost Utility of Spinal Cord Stimulation in Patients with Failed Back Surgery Syndrome. *Pain Physician* **2017**, *20*, E797–E805.
- Kim, N.; Yang, B.; Lee, T.; Kwon, S. An economic analysis of usual care and acupuncture collaborative treatment on chronic low back pain: A Markov model decision analysis. *BMC Complement. Altern. Med.* 2010, *10*, 74. [CrossRef]

- 31. Shin, B.-C.; Cho, J.-H.; Ha, I.-H.; Heo, I.; Lee, J.-H.; Kim, K.-W.; Kim, M.-R.; Jung, S.-Y.; Kwon, O.; Kim, N.-K. A multi-center, randomized controlled clinical trial, cost-effectiveness and qualitative research of electroacupuncture with usual care for patients with non-acute pain after back surgery: Study protocol for a randomized controlled trial. *Trials* **2018**, *19*, 65. [CrossRef]
- 32. Lee, Y.-K.; Nam, H.-S.; Chuang, L.-H.; Kim, K.-Y.; Yang, H.-K.; Kwon, I.-S.; Kind, P.; Kweon, S.-S.; Kim, Y.-T. South Korean time trade-off values for EQ-5D health states: Modeling with observed values for 101 health states. *Value Health* **2009**, *12*, 1187–1193. [CrossRef]
- 33. Ministry of Health and Welfare. Designating 65 Hospitals as the Pilot Project Participating Hospitals and Clinics for Chuna of Korean Medicine. Available online: http://www.mohw.go.kr/react/al/sal0301vw.jsp? PAR_MENU_ID=0403&page=1&CONT_SEQ=338360 (accessed on 1 May 2020).
- 34. Richardson, G.; Manca, A.J.H.E. Calculation of quality adjusted life years in the published literature: A review of methodology and transparency. *Health Econ.* **2004**, *13*, 1203–1210. [CrossRef]
- 35. Shin, H. Current Issues and Tasks in Health Policy. *Health Welf. Policy Forum* 2020, 1, 9–22.
- 36. Thomson, S.; Foubister, T.; Mossialos, E. *Financing Health Care in the European Union: Challenges and Policy Responses*; World Health Organization. Regional Office for Europe: Copenhagen, Denmark, 2009.
- 37. Zhang, R.; Lao, L.; Ren, K.; Berman, B.M. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology* **2014**, *120*, 482–503. [CrossRef] [PubMed]
- Ratcliffe, J.; Thomas, K.J.; MacPherson, H.; Brazier, J. A randomised controlled trial of acupuncture care for persistent low back pain: Cost effectiveness analysis. *BMJ (Clin. Res. Ed.)* 2006, 333, 626. [CrossRef] [PubMed]
- Witt, C.M.; Jena, S.; Selim, D.; Brinkhaus, B.; Reinhold, T.; Wruck, K.; Liecker, B.; Linde, K.; Wegscheider, K.; Willich, S.N. Pragmatic randomized trial evaluating the clinical and economic effectiveness of acupuncture for chronic low back pain. *Am. J. Epidemiol.* 2006, *164*, 487–496. [CrossRef] [PubMed]
- 40. Andronis, L.; Kinghorn, P.; Qiao, S.; Whitehurst, D.G.; Durrell, S.; McLeod, H.J. Cost-effectiveness of non-invasive and non-pharmacological interventions for low back pain: A systematic literature review. *Appl. Health Econ. Health Policy* **2017**, *15*, 173–201. [CrossRef] [PubMed]
- 41. Willich, S.N.; Reinhold, T.; Selim, D.; Jena, S.; Brinkhaus, B.; Witt, C.M.J.P. Cost-effectiveness of acupuncture treatment in patients with chronic neck pain. *Pain* **2006**, *125*, 107–113. [CrossRef] [PubMed]
- 42. Taylor, P.; Pezzullo, L.; Grant, S.J.; Bensoussan, A.J.P.P. Cost-effectiveness of Acupuncture for Chronic Nonspecific Low Back Pain. *Pain Pract.* **2014**, *14*, 599–606. [CrossRef]
- 43. Toroski, M.; Nikfar, S.; Mojahedian, M.M.; Ayati, M.H. Comparison of the Cost-utility Analysis of Electroacupuncture and Nonsteroidal Antiinflammatory Drugs in the Treatment of Chronic Low Back Pain. *J. Acupunct. Meridian Stud.* **2018**, *11*, 62–66. [CrossRef]



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