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RANDOMIZED TRIAL

Cost-Effectiveness of Balloon Kyphoplasty *Versus* Standard Medical Treatment in Patients With Osteoporotic Vertebral Compression Fracture

A Swedish Multicenter Randomized Controlled Trial With 2-Year Follow-up

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Study Design. A multicenter, randomized, controlled, cost-effectiveness analysis.

Objective. To assess the cost-effectiveness of balloon kyphoplasty (BKP) compared with standard medical treatment (control) in patients with acute/subacute (<3 months) vertebral compression fracture (VCF) due to osteoporosis.

Summary of Background Data. Patients with a VCF due to osteoporosis are common and will increase in number in an aging population, putting a substantial strain on health care. Selected patients may benefit from stabilizing the fracture with cement through BKP, a minimally invasive procedure. BKP has been reported to give good short-time clinical results, and economic modeling has suggested that the procedure could be cost-effective after 2 years compared with standard treatment.

Methods. Hospitalized patients with back pain due to VCF were randomized to BKP or to control using a computer-generated random list. All costs associated with VCF and cost-effectiveness were reported primarily from the perspective of society. We used EQ-5D to assess quality of life (QoL). The accumulated quality-adjusted life years (QALYs) gained and costs/QALY gained were assessed using intention to treat.

Results. Between February 2003 and December 2005, a total of 63 out of 67 Swedish patients were analyzed: BKP (n = 32) and control (n = 31). Societal cost per patient for BKP was SEK 160,017 (SD = 151,083) = €16,668 (SD = 15,735), and for control SEK 84,816 (SD = 40,954) = €8835 (SD = 4266), a significant difference of 75,198 (95% confidence intervals [CI] = 16,037–120,104) = €7833 (95% CI = 1671–12,511). The accumulated difference in QALYs was 0.085 (95% CI = −0.132 to 0.306) in favor of BKP. Cost/QALY gained using BKP was SEK 884,682 = €92,154 and US $134,043.

Conclusion. In this randomized controlled trial, it was not possible to demonstrate that BKP was cost-effective compared with standard medical treatment in patients treated for an acute/subacute vertebral fracture due to osteoporosis. However, sensitivity analysis indicated a certain degree of uncertainty, which needs to be considered.

Key words: cost-effectiveness, osteoporosis, vertebral compression fracture, minimally invasive surgery, vertebroplasty, balloon kyphoplasty procedure, spine surgery, randomized controlled trial. **Spine 2011;36:2243–2251**

The prevalence of osteoporosis in the population is high and increases with age, especially among women.[1–3] Osteoporosis is associated with an increased risk of sustaining vertebral compression fracture (VCF),[4–6] and the condition is a common cause for both prophylactic and therapeutic treatment. A VCF may cause severe back pain, functional disability, and a marked decrease in quality of life (QoL),[3] and is also associated with increased mortality.[7,8] Patients sustaining a VCF may suffer from more long-lasting and disabling pain than was previously realized, with associated high societal costs[9] comparable with costs for hip fractures.[10,11] Standard nonsurgical treatment includes bed rest, corseting, pain medication, and functional training.[12]

To facilitate return to prefracture status, including living conditions, selected patients with VCF have in recent years been treated with a mini-invasive "percutaneous vertebroplasty technique" (PVP), where the fractured vertebrae are stabilized using bone cement.[13] One kind of PVP is "balloon kyphoplasty" (BKP) where an inflatable balloon is used aiming at restoring vertebral height before injecting cement in the created cavity.[14] Both techniques have been reported to give rapid pain relief and improved function in 70% to 90% of patients.[15] Theoretical advantages of BKP could

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be realignment of the spinal column, which possibly could prevent future kyphosis.[14]

To evaluate whether BKP should be included in routine clinical practice, the cost-effectiveness of the procedure should be evaluated,[16] with the standard medical treatment as Control. In the recently published FREE trial in the literature[17] clinical results after BKP in osteoporotic patients with back pain less than 3 months due to a VCF, was found to compare favorably with medical treatment within 1 year. One published health-economic modeling evaluation using data from the first year of the FREE trial suggested that BKP may be cost-effective in a UK setting.[18] However, there is still a lack of cost-effectiveness analysis comparing BKP with medical treatment within clinical trials, while such studies have been performed with PVP suggesting cost-effectiveness in a selected patient population in a Danish setting.[19] Should BKP be considered cost-effective, it could be an alternative for physicians to routinely refer selected patients to orthopedic departments for treatment. Our aim was to assess the cost-effectiveness of BKP in a Swedish study population and present results after 2 years both from the societal perspective including all direct and indirect costs, and from the health care perspective including direct costs.[16]

MATERIALS AND METHODS

The patients included in this cost-effectiveness study were the Swedish participants in the previously published FREE trial. Details about the inclusion and exclusion criteria together with details about the interventions in this multicenter randomized study together with clinical results after 1 year have previously been described.[17] Eligible patients were above 21 years and suffering from severe thoracic and/or low back pain due to an acute or subacute (<3 months) VCF, confirmed on magnetic resonance imaging. One to 3 fractured vertebrae (Th5–L5), adjacent or separate levels, were accepted. No malignancy, neurological impairment, relevant comorbidity, or previous spinal surgery due to vertebral fractures was allowed. Pretreatment questionnaires and protocols were completed before randomization, if necessary with the help of a study nurse. At follow-up, all measurements were repeated using the same questionnaires and routines. Four Swedish Orthopedic Departments participated, 2 University hospitals (Malmö, Uppsala) and 2 county hospitals (Danderyd, Falun). Patients provided written informed consent and approval was obtained from the ethics committees of participating hospitals.

Patients were randomized during the "Index episode," defined as the initial admission to hospital due to the fracture(s)-randomization-treatment-discharge. Permuted block randomization stratified by etiology, sex, bisphosphonate use, and steroid use was used.[17] Masking was considered not possible for the patients and involved therapists. All patients received the same medical and functional treatment at the discretion of the participating departments (treatment as usual), with the exception of a BKP in the experimental group. Experienced spine surgeons using radiographic assistance performed all procedures. All fractured vertebrae were stabilized during the same procedure.[17]

Costs were estimated beginning with the Index episode, which was costed according to the hospital's billing systems, mostly on the basis of the costing guidelines (diagnose-related groups) issued by the Swedish National Board of Health and Welfare. The costs for other health care utilities were mainly derived from interregional county hospital price lists. Resource utilization related to hospital services after the Index episode were recorded at each follow-up at 1, 3, 6, 12, and 24 months by a study nurse interviewing the patient, and by studying medical records. In addition, costs were captured by patients reporting resource utilization in a "cost diary"[20] covering the following time periods: 1, 1–3, 3–6, 6–12, 12–18, and 18–24 months. The cost diary was distributed to the patients at the beginning of each period and included information on hospital visits plus rehabilitation, primary care visits, pharmaceuticals, support from family or relatives, the use of services from the community including transportation, and work absenteeism. One study secretary reminded those who did not return the diary, by means of personal phone calls. Care provided by relatives was costed assuming that the opportunity cost was lost working time. Costs are presented as SEK, €, and US $ (Table 1). Exchange rates of 2008: 1 € = 9.6 SEK and 1 US $ = 6.6 SEK.

Clinical Effects and Estimation of the Quality-adjusted Life Years

Primary clinical outcome was QoL using the preference-based generic five-dimensional EQ-5D instrument,[21] at baseline and after 1, 3, 6, 12, and 24 months. To aggregate the dimensions and levels to a common QoL score between 0 (equal to death) to 1 (perfect health), we used the algorithm created by Dolan *et al*.[22] Quality-adjusted life years (QALYs) gained over the 2 years were estimated by area under the curve.[16] Baseline differences in the QoL between the groups were adjusted by the multiple regression model suggested by Manca *et al*.[23] The incremental cost-effectiveness ratio (ICER) was estimated as the ratio between the differences in costs, and QALYs gained between BKP and Control, that is, the cost/QALY-gained. The uncertainty in the ICER estimate was assessed through bootstrapping[24] and presented in a cost-effectiveness plane[25] and an acceptability curve.[26]

Statistical Considerations

Power with regard to costs was chosen using information from the existing literature in 2003,[9] indicating that costs to society were substantial after osteoporotic VCF. We estimated that BKP would be half as costly compared with standard treatment (control) after 2 years, or SEK 75,000 *versus* SEK 150,000 (€7800 *vs*. €15,600 and US $11,400 *vs*. 22,800), with a standard deviation (SD) of SEK 75,000. To be able to detect differences as significant (5% risk level and 80% power), we decided to include approximately 35 patients in each group. For differences within groups, we used Wilcoxon sign test, and for differences among groups the Mann-Whitney *U* test. Two-tailed tests were used. Confidence intervals for cost and effect differences and uncertainty of the ICER ratios were assessed using bootstrapping (resampling

TABLE 1. Baseline Demographics

	BKP, n = 35* (%)	Control, n = 32* (%)	*P*	FREE†* BKP, n = 149 (%)	FREE† Control, n = 151 (%)
Female (n)	25 (71)	25 (78)	ns	115 (77)	117 (77)
Age (SD)	72 (10,1)	75 (9,7)	ns	72 (9,3)	74 (9,4)
Index fractures, n	48	42	ns	213	195
Fractures treated, n	43	42		188	195
Fractures levels, n					
1	26 (74)	22 (69)	ns	100 (67)	115 (76)
2	7 (20)	10 (31)	ns	34 (23)	28 (19)
3	2 (6)	0		15 (10)	8 (5)
Thoracic (T5–T9), n	5 (10)	10 (24)	ns	49 (23)	41 (21)
Thoraco-Lumbar (T10–L2), n	33 (69)	23 (55)	ns	127 (59)	130 (67)
Lumbar (L3–L5), n	10 (21)	9 (21)	ns	38 (18)	24 (12)
Fracture age (months, SD)	1.2 (0,8)	1.2 (0,8)	ns	<3	<3

**Only patients reporting EQ-5D values at all FU were included in the analyses (n = 63/67, BKP = 32, control = 31).*

†As a comparison, the corresponding base line figures from the total population in the FREE trial (300 pat, dropout 22% after 1 year) is presented. The Swedish subpopulation, 70 of 300 patients (23% of the patients included in the FREE trial), is included in the entire FREE trial figures presented in the Table. In all, 67 of 70 (35+32) Swedish patients participated in the current cost-utility trial, and the dropout rate in this population was 6% after 2 years (4 patients died).

10,000 times).[24] Intention to treat was the main principle,[16] and equaled treatment per protocol as there was no cross-over. Sensitivity analysis was performed on the basis of the following scenarios:

1. BKP procedure was decreased with SEK 25,000 (€2600 and US $3790) per patient to be comparable to the approximate costs of other vertebroplasty techniques.
2. All hospital costs after the Index episode exceeding SEK 60,000 (€6250 and US $9090) were excluded to adjust for outliers.
3. Cost/QALY-gained was analyzed also using the EQ-5D difference between the study groups in the entire FREE trial.

The FREE trial is registered with ClinicalTrials.gov, number NCT00211211. In the current trial, all costs attributed to the Swedish patients in that study were included.

The sponsor of the study had no role in study design, data collection, analyses, interpretation, writing, or the decision to submit for publication. The corresponding authors had full access to data and the final manuscript prior to submit for publication.

RESULTS

During February 2003 to December 2005, 70 Swedish patients were randomized either to BKP or to nonsurgical control treatment and 67 patients agreed to participate in a health-economic evaluation (BKP = 35 and control = 32). Patients who died, none of the reasons associated with treatment, 4 in the BKP group and 3 in the control group, were included in the analyses in that costs and EQ-5D value were recorded as 0 at every follow-up (FU) occasion after death. Patients alive but not reporting data at all FU were excluded from the analyses (BKP = 3 and control = 1), leaving 63 patients in the final analyses. Flow chart is shown in Figure 1.

The mean age and female distribution in the BKP group was 72 years and 71%, and in the control group 75 years and 78%. Baseline demographics were similar (Table 1). Almost no patient was due to age reasons working in either group, why cost due to work absenteeism was not a relevant issue. Also almost no patient in either group reported they were using help from the community.

During the study period, 5 patients in the BKP and 4 patients in the control group had new painful VCF in 1 or 2 adjacent levels and were treated according to protocol either with a new BKP in the experimental group or with continuous standard treatment (control group). In 1 of the patients in the BKP group, the cement in the Index vertebra migrated toward the aorta in the thoracic region, however, without obvious clinical consequences. Another patient in the BKP group suffered an infection in the Index-cemented vertebra and was treated in hospital for several weeks. These 2 patients were regarded as serious adverse events, and they were also associated with high costs.

Costs

Costs associated with the different services offered are presented in Table 2. The response rates with respect to the cost diaries after 1, 3, 6, 12, 18, and 24 months in the BKP group were 97%, 97%, 97%, 88%, 79%, and 79%, and in the control group 100%, 94%, 97%, 84%, 84%, and 81%,

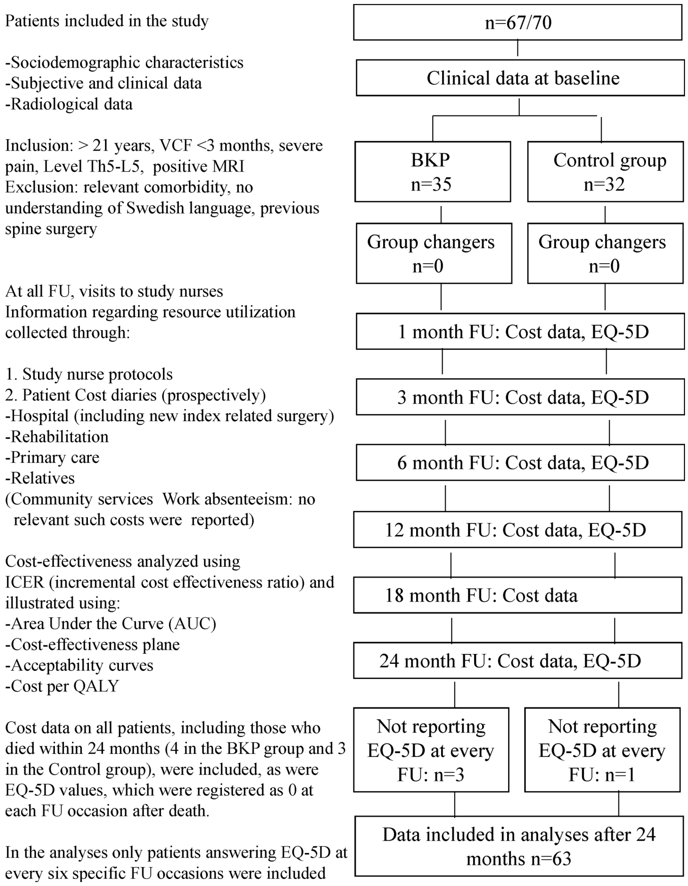

Figure 1. Flow chart. Algorithm for patients included in the study.

TABLE 2. Cost Per Item

Hospital Costs Index Episode*	SEK	€	US $
Control group (standard treatment), DRG†	30,326	3,159	4,609
Balloon kyphoplasty procedure, DRG†	80,558	8,391	12,243
Implant cost (included in the DRG procedure)	31,718	3,304	4,820
Hospital costs after the Index episode			
Physician per visit	2,168	226	330
Other actions by physician	542	56	82
X-ray	794	83	121
CT (used rarely on specific indications)	2,731	284	415
MRI	5,217	543	793
Diagnostic test, facet injections and others	2,372	247	360
Corset	2,075	216	315
Indoor treatment per day	5,119	533	778
Minute cost operation theater	159	17	24
Minute cost anesthesia	64	7	10
Intensive care/h (in case of reoperation)	1,400	146	213
"Wake up ward"/h	610	64	93
Reoperation associated with BKP‡	96,796	10,083	14,711
Indoor rehabilitation per day	3,876	404	589
Outdoor rehabilitation per day	2,252	235	342
Primary care			
Physician visit	1,447	151	220
Physiotherapist visit	723	75	110
Chiropractors and naprapats	724	75	110
Pharmaceuticals according to FASS§			
Relatives, cost/hr			
Travels, shopping, house cleaning	280	29	43
Community care	"Not utilized"		
Indirect costs (work absenteeism)	All patient on pension		

Swedish Kronor (SEK) 2008 years currency (2008 years currency: 1€ = SEK 9.6 and 1 US $ = SEK 6.6).

**Index episode: initial hospital admission-treatment-discharge.*

†Costs according to diagnose-related groups (DRG) were used to estimate costs associated with the "Index episode".

‡Five patients with new painful VCF in the BKP group, according to protocol. Four patients in the control group with new painful VCF received control treatment.

§FASS information on drug prizes.

BKP indicates balloon kyphoplasty; CT, computed tomography; DRG, diagnosis-related group; FASS (Information about Farmaceutical Specialities in Sweden); MRI, magnetic resonance imaging.

respectively. The societal mean costs per patient in the BKP group was SEK 160,017 (SD = 151,082), and in the control group SEK 84,818 (40,953). The difference was significant, SEK 75,198 (95% CI = 16,037–120,104, Table 3).

Clinical Outcome

Follow-up rates regarding EQ-5D after 1, 3, 6, 12, and 24 months in the BKP group were 100%, 97%, 100%, 94%, and 88% and in the control group 100%, 97%, 97%, 94%, and 91%. QoL improved significantly within both groups, with most significant improvement occurring within the first 3 months (Figure 2). After adjusting for random differences in EQ-5D values at baseline, and using multiple regression, the difference in QALYs gained over 24 months was 0.085 (95% CI = −0.132 to 0.306) in favor of BKP.

Cost-Effectiveness

The cost/QALY gained using BKP instead of standard medical treatment was SEK 884,682 (€92,154 and US $134,043). The uncertainty is represented in the cost-effectiveness plane and the acceptability curve (Figure 3). Assuming that the Swedish society is willing to pay maximum SEK 600,000 (€62,500 and US $90,910) for a QALY gained, this should mean that there is less than 40% chance that BKP is cost-effective in this population.

TABLE 3. Mean Cost/Patient in the BKP Group and the Control Group After 24 Months (SEK)*

BKP *vs.* Control Treatment	BKP		Control		Difference in SEK	
Costs†	N = 32	SD	N = 31	SD		(95% CI)‡
1. Index episode (DRG)	70,381	17,062	27,972	851	42,406	(36,120–47,982)§
2. Indoor Stay Index episode—24 months	53,527	134,004	24,274	40,089	29,253	(−25,502–68,473)
3. Costs radiography	2,828	1,848	3,036	1,189	−207	(−1116–678)
4. Hospital perspective (1 + 2 + 3)	126,736	138,198	55,282	40,370	71,429	(15,909–112,068)§
5. Primary/Private care	2,556	6,349	2,989	5,556	−432	−3,402–2372
6. Back-related drugs	11,571	298,784	11,627	327	−56	(−208–98)
7. Health care perspective (4 + 5 + 6)	140,864	138,351	69,898	39,863	70,966	(14,894–111,627)§
8. Family support, house keeping	19,154	32,254	14,921	20,086	4232	(−9779–16,734)
9. Societal perspective (7 + 8)	160,017	151,083	84,819	40,954	75,198	(16,037–120,104)§

In this study there was due to old age no cost associated with early retirement and productivity losses, and only a small cost with no difference between the groups associated with work loss for family/caregivers

**1 € = 9,6 SEK, and 1 US $ = 6.6 SEK (2008 years currency).*

†Mean of observed cost in SEK, with standard deviation (SD).

‡95% CI calculated using bootstrapping technique.

§Meaning difference was significant.

Sensitivity Analyses

(1) When cost in the BKP group was decreased with SEK 25,000 per patient to be more comparable to other cementing techniques, the incremental cost fell to SEK 52,938 (95% CI = 1261–104,615), resulting in a cost/QALY gained of SEK 622,800 (€64,875 and US $94,364). (2) When all patients with a hospital cost of more than SEK 60,000 after the Index episode were excluded in both groups (5 patients in the BKP group with a mean cost of SEK 237,304 per patient, and 7 patients in the control group with a mean cost of SEK 88,486 per patient), the incremental cost decreased somewhat (SEK 63,394; 95% CI = 44,538–82,250) providing a cost/QALY gained of SEK 745,812 (€77,689 and US $113,002). (3) The QALY gained with BKP compared with the control treatment for the whole FREE trial was estimated to 0.21 QALY ($P = 0.002$),[17] and using this result instead of 0.085 as in the current Swedish study resulted in a cost/QALY gained of SEK 359,146 (€37,411 and US $54,416).

DISCUSSION

Patient Population

Patients suffering from painful VCF due to osteoporosis are numerous, and the numbers will increase as the population grows older.[1] It should be important to investigate possible cost-effective treatment strategies so that these patients as

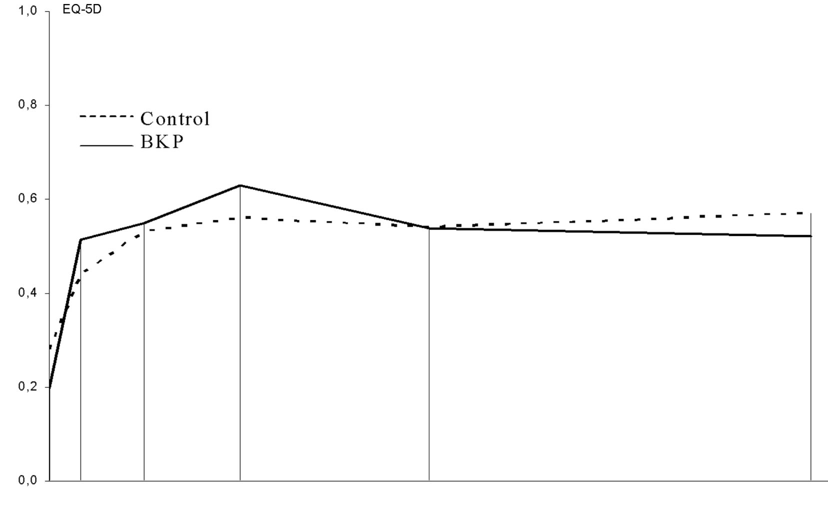

Figure 2. Area under the curve. Estimated QALYs gained for patients in the BKP group (n = 32) and the control group (n = 31). EQ-5D: 1 = perfect QoL, 0 = "death." The difference after 24 months is illustrated as the areas under the 2 "curves" from the horizontal *x*-axis (area under the curve). The difference was 0.085 QALY to the advantage of BKP (ns).

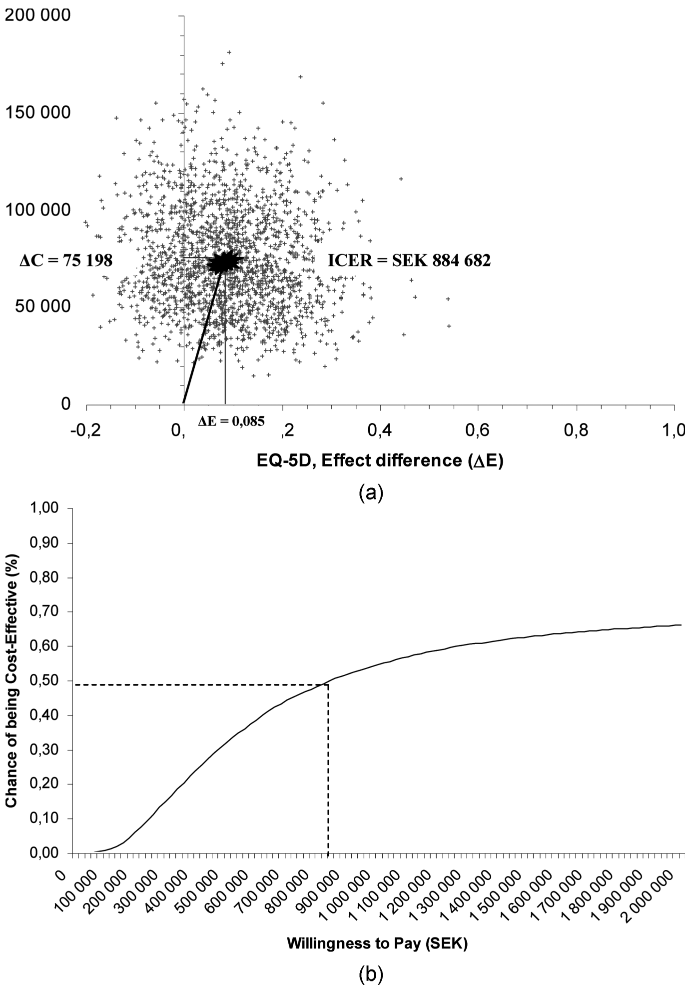

Figure 3. (**A**) Cost-effectiveness plane. On the vertical axis the difference between BKP and control in societal costs, ΔC = SEK 75,198, is illustrated, and on the horizontal axis the difference in treatment effects, ΔE = 0.085 EQ-5D units. The ICER illustrates the cost/QALY gained using BKP instead of control treatment. The uncertainty is analyzed using bootstrapping technique and illustrated by the "uncertainty cloud" indicating different possible ICERs. (**B**) Acceptability curve. The acceptability curve illustrates the probability of BKP being cost-effective for different values of λ = willingness to pay (WTP – horizontal axis) attributed to a QALY. P = 0.50 illustrates the value of λ, where the chance of BKP being cost-effective is 50%, here SEK 884,682 (€92,154, US $134,042).

soon as possible can return to prefracture functional status, including living conditions.

It seems as if most researchers agree that stabilizing a painful fractured vertebra, whether using PVP or BKP, may result in rapid pain relief but that conservatively treated patients will "catch up" with time.[27] The question of cost-effectiveness that includes the time variable therefore becomes crucial; that is, what is the society willing to pay for a more rapid pain relief and increase in QoL. Late complications could also be an issue.

Patients in this Swedish health-economic randomized study were all hospitalized because of severe disabling back pain due to an acute or subacute (mean approximately 1.2 months) VCF. Treatment was executed in line with contemporary routines at each hospital (treatment as usual) and differed only with regard to BKP in the experimental group. It should, therefore, be possible to generalize results to other similar patient populations.

Patients were defined by specific inclusion and exclusion criteria, and they were therefore possibly healthier than the average patient admitted with a VCF. This could be 1 explanation for the surprisingly low utilization of resources, including health care, after the Index episode, and almost all patients were discharged directly to their own previous living. Possibly the relatively short period between the fracture and the admission to hospital played a role (relatively good natural course), and also a substantial decrease in the number of hospital beds in Sweden during the study period may have had an influence. Today, Sweden has 1 of the lowest number of hospital beds per citizen in Europe, or 3.7/1000, compared with, for example, Switzerland with 18.3/1000 citizens (www.oecd.org). However, according to the cost diaries, patients did not need much assistance from the community after the Index episode in any group, giving an impression of patients being reasonably able to return to prefracture conditions once the acute/subacute "fracture phase" was over. The response rate with regard to the cost diary was good, which could be seen as a result of the careful information before study inclusion, the tradition in Sweden to answer queries and the reminders together with personal phone calls from the study secretary in case of missing answers.

Costs Differences, Effect Gains, and Cost-Effectiveness

This study was powered to detect a cost difference where BKP was half as costly as standard medical treatment for society after 2 years, and it turned out to be approximately the other way round, mainly depending on surgical costs during the Index episode. There was no difference between the groups with regard to any indirect costs as virtually no patients were working, but were on pension due to old age. The comparably low societal cost of SEK 84,818 (€8835 and US $12,851) after standard medical treatment in the Control group is in contrast to what have been reported by others,[18] and our findings should be evaluated further, also using information from national registers such as Swespine (www.4s.nu).

We did not include inflation as in Sweden the health care is covered by social insurance; that is, health care is being paid by allocating tax revenue. The problem with inflated prices in such a context is of less concern than in a country where most of the health care may be covered by private insurance where there is a different incentive from the health care providers to inflate the prices. Thus, we do not perceive that there is an issue of inflated costs in our study that will have an impact on the results.

The cost/QALY gained for society using BKP compared with control treatment was SEK 884,682 in this study (€92,154 and US $134,043). There is generally no established threshold for the willingness to pay for a QALY in Sweden (or indeed in most other countries), but it has been calculated to approximately SEK 600,000 (LFN http://www.tlv.se, Ekman *et al*) (€62,500 and US $90,910). Given these reference values for a QALY, it was not possible to conclude that BKP would be cost-effective compared with standard medical treatment in this Swedish population.

This conclusion in the perspective of the society was not altered by reducing costs for the BKP procedure or by removing the patients with highest hospital costs in both groups. When using the difference in QoL units gained by using BKP instead of medical treatment in the full FREE study population (0.21 after 1 year), compared with the gain in the Swedish study (0.085 after 2 years), the cost/QALY gained decreased to a level that can be considered cost-effective. One explanation for the difference in the QALY gained between the Swedish population within the FREE trial (n = 67) and the full study population (n = 300) could be that the FREE trial was powered to detect differences in the 36-Item Short Form Health Survey PCS on the basis of the full sample; therefore, a degree of randomness is expected. However, the use of the whole FREE sample in analyzing cost-effectiveness should be regarded as hypothetical, as costs were uniquely collected only for the Swedish patients, and also QoL measured with EQ-5D has been shown to differ in the same diagnostic entities between countries, possibly because of sociocultural circumstances.

As the Swedish population was defined using the same specific inclusion and exclusion criteria as was the total FREE study population (composed of 6 different national subpopulations), the difference in the Swedish compared with the total FREE trial with regard to QALYs gained could be of random reasons. But it could possibly also reflect a true picture accurately describing the Swedish comparative results in our specific population defined as a specific socio-cultural-economic society, and possibly differing from other societies in these respects.

There was a power analysis performed on costs in the Swedish substudy (accounted for in the manuscript) but not on QALYs. From the available literature we assumed that the costs in the control group would be approximately twice as high as in the BKP group. The opposite was true in the end. Why is that? It could be that the Swedish patient population was a nongeneralizable subgroup of healthier patients, but it could also be that previous cost estimations based on osteoporotic vertebral fractures in elderly are partly erroneous. There are certainly many patients suffering from osteoporotic vertebral fractures who will be institutionalized and very costly after the Index episode, but there could also be many patients who return to previous status after a fracture, without subsequent heavy cost burden to the society.

In hindsight, a power analysis also based on the QALYs or on the cost-effectiveness ratio would have improved the study design and the interpretation of the results. However, the decision of looking at the necessary sample for costs was taken on the basis of the literature available at that point in time.

The alternative to using the QALY on the basis of the Swedish patients is to apply the QALY gained estimated on the overall FREE population. This was done in a sensitivity analysis (see this section). However, this also provides some additional uncertainty since we cannot control for possible differences between countries in terms of demographics and different sociocultural perceptions of QoL.

For the hospital and the health care sectors, the mean cost in the BKP group was comparably higher after 2 years (Table 3), and a few outliers especially in the BKP group were very costly. Approximately as many patients in both groups (BKP = 5, control = 4) were diagnosed with a clinically relevant new VCF during the FU period, and these patients received treatment according to the study protocol. In the control group, it meant nonsurgical treatment, and in the experimental group it meant a new BKP procedure. Adjusting for these additional comparative costs did not alter results and the conclusions. It should be noted that one patient in the BKP group experienced a forward cement migration in the Index vertebra, and in addition suffered VCF in adjacent levels both above and below with subsequent reoperations with BKP. One other patient suffered a hematogenous infection in the cemented vertebra. In both patients, these serious adverse events resulted in comparably long total hospital stay with subsequent high costs.

Comparisons With Other Studies

The improvement in QoL after the BKP procedure in this study is comparable with other studies, and also comparable with results reported after PVP.[27] Recently 2 randomized controlled trials (RCTs) questioned the efficacy of PVP compared with a placebo sham procedure in patients with a VCF due to osteoporosis with equally positive short-time effects on pain, function, and QoL.[28,29] Using modeling on 1-year data from the patients in the FREE trial, Ström *et al*, however, suggested that BKP could be cost-effective in a UK setting.[18] Because that study was based on a UK population and it was extrapolating the 1-year results from the FREE trial[17] over a longer time horizon it is not directly comparable to our results that uses actual patient-reported EQ-5D values after 2 years.

Problems With the Study

(1) Treatment could not be masked, which may have affected the patient's response. (2) We relied mostly on the "cost diary"[20] to measure costs after the Index episode. This diary was meticulously supervised during the study period, but we cannot exclude the possibility that some costs were missed. (3) Patients in this study setting were due to specific inclusion and exclusion criteria possibly not representative for the average patient admitted to a hospital with a VCF, making external validity an issue. (4) It is rather established knowledge that the cost-effectiveness may differ between countries, which might lead to different inference whether an intervention is cost-effective or not due to different health care systems, sociocultural perceptions regarding QoL, mortality, *etc*. In fact, most national health-economic guidelines strongly recommend that cost-effectiveness analysis/cost utility analysis should use as much country-specific data as possible, especially for costs. This means that the results and conclusion reached in the current study should be interpreted with some care, and seen partly as hypothesis generating and not without careful consideration be used as guidelines for other health care systems.

Future Research and Reflections

It is probable that specific patient populations will benefit more from 1 of the 2 treatments used in this study, and the matter of patient selection should be addressed in future studies, as should the preventive perspectives and the risk factors of sustaining a VCF.[30] Future research should also focus on long-time follow-up, both in clinical studies but even more so using increasingly available data from national registers like Swespine (www.4s.nu), and modeling.

We could not document that BKP was cost-effective, but it should be remembered that the current study to a certain extent is hypothesis generating. However, in a time when cementing osteoporotic vertebral fractures in the elderly on an almost routine basis is advocated by some, our results should certainly be a mind raiser.

One should not forget that we are implanting foreign material in a vertebral body, and that we as a profession must be held responsible for long-term as well as short-term effects. To stabilize a fractured vertebra with cement in a very old person suffering from intense pain is one thing—to do the same in a rather young person should be more questionable. As biological age is changing, an old person with respect to remaining life-time yesterday may not be regarded an old person today or indeed tomorrow. In this light, and from what we know from the current literature, cementing also nonfractured vertebrae prophylactically outside scientific studies should today, if there are no evidence-based arguments for doing so, be discussed from an ethical perspective.

CONCLUSION

In this health-economic evaluation conducted as an RCT including patients with an acute/subacute (<3 months) vertebral compression fracture due to osteoporosis, it was not possible to demonstrate that BKP was cost-effective compared with standard medical treatment in Sweden. Sensitivity analysis indicated a certain degree of uncertainty that needs to be considered.

➢ Key Points

- ❑ VCF due to osteoporosis are common and will increase in number in an aging population, putting a substantial strain on health care.
- ❑ Selected patients with a VCF may benefit from stabilizing the fracture with bone cement through a minimally invasive procedure, BKP.
- ❑ Between February 2003 and December 2005, using a randomized controlled setting, a total of 63 of 67 Swedish patients were analyzed with respect to cost-effectiveness, comparing BKP (n = 32) with standard medical treatment in a control group (n = 31).
- ❑ After 2 years societal costs for BKP were significantly higher. The difference in QALYs gained was higher for BKP but the statistical significance of this finding for the Swedish subpopulation could not be verified.
- ❑ The cost/QALY gained using BKP was SEK 884,682 (€92,154 and US $134,042), which was not considered cost-effective in this patient population. Uncertainty is an issue.

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