Cost-effectiveness analysis for trigeminal neuralgia: Cyberknife vs microvascular decompression

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Background/Aims: We present the preliminary results of a cost-effectiveness analysis of cyberknife radiosurgery (CKR) versus microvascular decompression (MVD) for patients with medically unresponsive trigeminal neuralgia.

Methods: Direct healthcare costs from hospital's perspective attributable to CKR and MVD were collected. Pain level caused by trigeminal neuralgia was measured through the Barrow Neurological Institute pain intensity scoring criteria, at admission and after an average of 6 months follow-up.

Results: 20 patients for both arms were enrolled, for a total of 40 patients. The two procedures resulted equally effective at 6 month follow-up, with different resources consumption: CKR reducing hospital costs by an average of 34% per patient. The robustness of these results was confirmed in appropriate sensitivity analyses.

Conclusion: CKR resulted to be a cost-saving alternative compared with the surgical intervention.

Keywords: decision-making, cost-effectiveness analysis, Cyberknife, microvascular decompression, trigeminal neuralgia

Introduction

Technological innovation is considered as one of the principal factors of costs escalation in healthcare (Oh 2005). A field in which lot of technological progress has been registered in the last decades is radiotherapy. Radiotherapy began almost a hundred years ago with the discovery of X-rays and the first use of the natural radioactivity. The greatest challenge for radiation therapy is to cure the disease while controlling for side-effects. Theoretically, the simplest way to achieve this with radiation is to encompass all target cells with sufficient doses of radiation, while sparing surrounding normal tissues (Bucci et al 2005).

Nowadays the new frontier is represented by stereotactic cyberknife radio surgery (CKR) that has been proven to be an effective treatment strategy for trigeminal neuralgia (TN) or "tic douloureux" (Lim et al 2005, 2006). Using noninvasive head immobilization and advanced image-guidance technology, the robotic arm of CKR dynamically tracks skull position and orientation during treatment, thereby ensuring targeting accuracy throughout the entire procedure (Romanelli et al 2005).

TN is the most common facial pain syndrome. Incidence is approximately 4.3 per 100,000 population per year, women are more frequently affected than men: 2.5 and 5.7 per 100,000 per year, respectively, while prevalence is approximately 15.5 per 100,000 population per year (Wilkins 2002; Edlich et al 2006). Pain onset is usually in the fifth through seventh decades of life. The disorder is characterized by unilateral,

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episodic, shock-like or stabbing pain involving one or more divisions of the trigeminal nerve. Patient activities of daily living are often impaired by fear of experiencing chronic episodes; something as simple and routine as brushing the teeth, putting on make-up or even a slight breeze can trigger an attack, resulting in sheer agony for the patient (Pollok et al 2005).

Medical therapy (anticonvulsant medications, such as carbamazepine, phenytoin or baclofen, clonazepam, gabapentin, etc.) eliminates or significantly reduces the pain in approximately 75% of patients, and is considered the treatment of choice for incident cases of TN (Fields 1996). Unfortunately, the relief provided by medical therapy generally decreases over time and is frequently resistant to multidrug regimens. Moreover, many patients quit medical therapy because of side effects, while drug intolerance is particularly common in elderly patients (Zakrzewska et al 2002).

Nonrespondent patients can be surgically treated through microvascular decompression (MVD), an invasive procedure that relieves the vascular compression on the trigeminal nerve (Burchiel et al 1988; Barker et al 1996; Broggi et al 2000; Sindou et al 2002; Theodosopoulos et al 2002). Even though MVD represents the first choice for those patients (Fujimaki et al 1990; Lee et al 1997; Apfelbaum et al 2000), less invasive procedures such as radiofrequency rhizotomy (Taha et al 1995; Kanpolat et al 2001; Tronnier et al 2001), glycerol rhizotomy (Lundsford et al 1984; Saini 1987; Burchiel 1988; Young 1988; North et al 1990), balloon compression (Brown et al 1993; Skirving et al 2001) and gamma knife stereotactic radio surgery (Kondziolka et al 1996; Rogers et al 2000; Maesawa et al 2001; Pollok et al 2002; Brisman et al 2002) are preferred for elderly patients suffering from significant comorbidities, or with recurrent facial pain after prior surgery (Pollock et al 2005).

In all those cases, CKR is a valid alternative to surgical treatments for TN. However, in times of resource constraints, costs and benefits of CKR are to be evaluated against its closest comparator in order to provide decision makers with relevant information as to the impact of the new technology in the hospital system.

In order to perform that, a study on direct healthcare costs and clinical outcomes of CKR vs. MVD for TN was conducted, in collaboration with the Italian Diagnostic Centre (CDI), where a CKR system has been installed since July 2004, and the teaching clinic "C. Besta" National Neurological Institute (Besta Institute), a highly specialized neurological and neurosurgical centre in Milan, Italy.

The main objective of the study was to estimate the incremental cost-effectiveness ratio of CKR vs. MVD for patients non respondents to medical treatment.

Materials and methods

Study design and perspective

An observational, incidence-based cost effectiveness study was designed to compare CKR vs. MVD in treating medically unresponsive TN patients. The perspective taken was that of the hospital and the costs included in the analysis were direct healthcare costs, borne by hospital.

Patient selection

Patients were recruited in the two selected hospitals: Besta Institute and CDI. More specifically, Besta Institute was in charge of recruiting medically unresponsive TN patients treated with MVD surgery, while CDI was in charge of medically unresponsive TN patients treated by CKR.

All CKR patients were enrolled consecutively in the period September 2004 (when CKR was first used) until June 2005, and then followed-up for a period of 6 month. MVD patients were recruited retrospectively (February – August 2004) by going through medical records. Patients were recruited in the study (both arms) if non respondents to medical treatment (Barrow National Institute Scale scores IV or V; see below), and were excluded if they suffered from a typical pain, multiple sclerosis, younger than 18, or with a follow-up duration of less than 6 months.

Outcome measurement

Outcome assessment referred to pain at baseline and at follow-up (6 months) in the two groups of patients. Pain was scored level I to V according to Barrow Neurological Institute (BNI) pain intensity scoring criteria (Table 1) (Rogers et al 2000). Outcome was evaluated by a standardized personal questionnaire administered to patients by physicians. For CKR patients, the questionnaire was prospectively administered at follow-up visits. As to MVD, clinicians interviewed the patients by phone, after a period not inferior of 6 month

Table 1 Barrow Neurological Institute (BNI) Pain Intensity Scoring Criteria

Score	Description
I	No trigeminal pain
II	Occasional pain, not requiring medication
III	Some pain, adequately controlled with medication
IV	Some pain, not adequately controlled with medication
V	Severe pain/no pain relief

from surgery. In both cases, the questionnaires were answered uniformly, as the same investigators scored the pain intensity in the two arms.

Costs evaluation

The full costing methodology was used to measure resource consumption, and the approach used was the bottom-up micro-costing. The latter is known to be the most rigorous approach since it requires data collection for all single components of care supplied by the hospital (Shuman et al 1992; Wolff 1998; Heerey et al 2002; Tarricone 2006). In the micro-costing approach, estimation of costs can be divided into three steps: the first is to identify the health inputs involved in the procedure (personnel, drugs, disposables, equipment, length of stay, etc.), the second is to estimate the quantity provided, and the third step is to estimate the unit costs for each input.

According to the full costing approach, costs of hospital care were calculated summing up variable and fixed direct costs exclusively associated with the operations of the wards, and a fair share of overheads (generally administrative and other central services). The latter was retrieved from the hospitals' accounting department: for Besta Institute, overheads accounted for 18% of the direct costs, while for CDI, overheads accounted for 15.4%.

As for MVD, direct fixed costs were represented by the usage of the operating theatre and equipment, the cost of labor (ie, surgical, anesthesiologist, and nursing teams), and the hospital stay, while variable direct costs were drugs, disposables, specialist visits, laboratory tests, and other diagnostic investigations done during hospitalization and follow-up.

As for CKR, direct fixed costs referred to capital investment (CKR needs a separate bunker to be built or made available), equipment, and labor costs. The latter was calculated on the basis of the observed time actually worked by each type of professional directly involved in the procedure (nurse, physician, radiology technician, and health physicist), multiplied by the cost per unit of time. Variable direct costs were represented by disposables, specialist visits, imaging tests (in particular, brain magnetic resonance imaging [MRI], and brain computed tomography [CT] scans), for treatment and follow-up.

In order to assign a monetary value to diagnostic procedures, the national fee-for-service system adopted by the National Health Service to fund public and private providers was used whenever full costs were not available from the accounting department. Drug costs for antibiotics were based on official ex-factory prices per unit in Italy (Agenzia Italiana del Farmaco 2005).

A threshold analysis was performed in order to test the robustness of cost differences between the two treatments.

Results

Globally, 40 patients were enrolled in the study: 20 for each arm. The sample characteristics are presented in Table 2.

CKR patients resulted 12 years older than MVD patients (p-value 0.002). Gender distribution is similar, female being the larger group in both the procedures (60% and 55%, respectively). Fewer patients in MVD group had undergone prior TN treatment compared with the CKR group (30% for MVD and 40% for CKR). The most frequent treatment before CKR was thermal rhizothomy (62.5%); followed by MVD (37.5%), whilst for MVD patients the most frequent procedure (67%) was another MVD.

At baseline, all patients ranked high in the BNI scale but CKR patients were the highest with 85% in the V class (p-value 0.0001).

At follow-up, 90% of patients in both groups experienced a reduction of severity, passing from levels V and IV to levels I, II, or III; while only 10% of patients in both arms did not experience a significant pain reduction, still non respondent to medical treatment (Table 3). Nevertheless the difference was not statistically significant (Chi-test p-value >0.05). No adverse events or major complications were registered

Table 2 Sample size and characteristics

Procedure	**CKR (N = 20)**		**MVD (N = 20)**	
Age (at the time of the treatment)	**Years**		**Years**	
Mean (SD)	74.2 (12.8)		61.9 (9.7)	
Range	(40–88)		(41–75)	
Gender	**N.**	**%**	**N.**	**%**
Female	12	60%	11	55%
Male	8	40%	9	45%
Previous TN treatment	**N.**	**%**	**N.**	**%**
Yes	8	40%	6	30%
No	12	60%	14	70%
Type of previous TN treatment	**N.**	**%**	**N.**	**%**
MVD	3	38%	4	67%
Thermal rhizothomy	5	63%	1	17%
Radiosurgery	–	–	1	17%
BNI Score at Baseline	**N.**	**%**	**N.**	**%**
IV. Some pain, not adequately controlled with medication	3	15%	15	75%
V. Severe pain/no pain relief	17	85%	5	25%

Table 3 Clinical outcome at follow-up – BNI Scale

BNI score at baseline	**CKR (N = 20)**		**MVD (N = 20)**	
	N.	**%**	**N.**	**%**
IV. Some pain, not adequately controlled with medication	3	15%	15	75%
V. Severe pain/no pain relief	17	85%	5	25%
P-value (Chi-square test)	0,0001			
BNI Score at FU	**CKR (N = 20)**		**MVD (N = 20)**	
	N.	**%**	**N.**	**%**
I. No trigeminal pain	6	30%	9	45%
II. Occasional pain, not requiring medication	4	20%	7	35%
III. Some pain, adequately controlled with medication	8	40%	2	10%
IV. Some pain, not adequately controlled with medication	2	10%	2	10%
V. Severe pain/no pain relief	–	0%	–	0%
P-value (Chi-square test)	0,17			

in the two arms, such as toxicity. In CKR treatment group the number of patients recording a follow-up BNI level III is significantly higher than in MVD group (8 cases compared with 2 cases), this could be explained by the fact that in CKR arm baseline BNI level V was also more frequent than in MVD arm (17 cases compared with 5 cases).

As for resources consumption, the results show that MVD full cost is Euro 6,641.0 (SD 1,798.8) per patient while CKR treatment is Euro 4,388.5 (SD 12.7) (Table 4). The difference of Euro 2,252.5 is mostly explained by two factors: the cost of the surgical procedure, which takes on average 3.5 hours of operating theatre, compared with 70 minutes of radiation for CKR, almost a standard procedure time for TN – thus explaining the minimum full cost variance; and the cost of hospital stay for MVD patients. Indeed, the length of stay is on average 10 days per patient (±7.4 SD); while no hospital stay is required for CKR patients, being it an outpatient service.

Notably, no drugs or laboratory tests are used specifically for CKR procedure, whilst MVD required drugs for both the surgical intervention and post-operation (on average 170 doses per patient over the observation period) and laboratory tests (patients averaged 5 tests each). Outpatient visits per patient were more frequent for CKR than for MVD during the observation period (2.5 units vs. 1.1); on the contrary, imaging tests resulted less frequent in CKR compared with MVD (2.2 units vs. 3.1), nevertheless these were more expensive ones (higher frequency of CT Scans, MRIs for CKR vs. chest X-rays, ECGs for MVD).

A threshold analysis was performed in order to determine how much key baseline variables would need to change to equalize the resources consumption for the treatments (Table 5). MVD costs would break even CKR costs if the time of utilization of the operating theatre decreased by 71%: 1.0 hour instead of 3.5 hours. As to the length of stay, CKR would still result cost saving even if MVD required no hospital stay at all. Conversely, CKR costs would break even MVD costs if the annual activity of the machine decreased by 46%: 155 patients per year instead of 289, or equally, 402 fractions instead of 749.

Discussion

Technological innovation is one of the main determinants of healthcare costs and its rapid changes require decision makers to take allocative decisions in relatively short time. Economic evaluations are intended to support the health-related decision making process by informing decision makers as to allocative decision aimed at maximizing patients' health by estimating

Table 4 Average direct healthcare cost per patient

Full Cost	**CKR**		**MVD**		**DELTA**	
Cost category	**Euro**	**%**	**Euro**	**%**	**Euro**	**%**
Outpatient visits	47.4	1%	17.6	0%	–29.8	–1%
Imaging tests	437.2	10%	157.9	2%	–279.3	–12%
Radiation/Surgical procedure	3,903.9	89%	4,317.0	65%	413.1	18%
Drugs (related to procedure/TN)	–	0%	118.6	2%	118.6	5%
Laboratory tests	–	0%	73.3	1%	73.3	3%
Hospital stay costs	–	0%	1,956.7	29%	1,956.7	87%
Total	**4,388.5**	100%	**6,641.0**	100%	**2,252.5**	100%

Table 5 Threshold analysis

Variables	% Variation	Absolute variation	Treatment full cost	Preferred strategy
			MVD	
Operating theatre utilization for MVD patients (hours)	–71%	Form 3.5 to 1 hour	Euro 4.388,5	Equal
LOS for MVD patients (days)	–100%	From 10.0 to 0.0 days	Euro 4.684,3	Dominated
			CKR	
CKR annual activity (treated patients)	–46%	From 289 to 155 patients	Euro 6.641,0	Equal
Incidence of overheads in CKR Center (considered as a proxy of efficiency)	+2.6%	From 15.4 to 18 percentage points	Euro 4,483.21	Cost Saving

costs and benefits of the new technology and comparing it to the prevalent clinical practice.

Stereotactic radio surgery has become an important treatment alternative to surgery for a variety of intracranial diseases (Andrews et al 2006). In TN disease, MVD surgery is still considered the first line treatment for medical unresponsive TN (Fujimaki et al 1990; Lee et al 1997; Apfelbaum et al 2000), nevertheless radio surgery cyberknife system could represent a feasible first line option for TN in the close future, once its effectiveness has been robustly investigated, being it less costly than MVD, as emerged from this study.

Europe is experiencing a fast growth of CKR technology: eight CKR systems are already working in its countries at the time of the study, but – with the exception of the present study – no economic evaluation analysis has been done on CKR and its potential applications.

Economic evaluation analysis could be useful as to decide whether and how much of the technology the European countries can afford and for what indications it results to be most effective and efficient. The present study certainly goes in this direction and represents an important basis for building further and wider evidence.

This study has some limitations. The two groups of patients are not directly comparable, therefore it is not possible to conclude that CKR is as effective as MVD. CKR group was significantly older than the MVD group, even if age has not been found to be a predictor of success/failure for either radio surgery or MDV procedures (Pollock et al 2005), and patients in MVD group had typically less severe facial pain at baseline. The difference in patients' characteristics is explained by the fact that CKR is not seen as an alternative to MVD for the time being but, rather, as a second line strategy whenever MVD is not possible to deliver.

The cost analysis does not include those associated with patients' productivity losses during admission time, and informal care. Had these costs been evaluated, the difference between the two treatments would have resulted even bigger in favor of CKR, being an outpatient service.

Finally, more data are needed to assess the effectiveness of CKR considering follow-ups longer than six months in order to account also for recurrent trigeminal pain. The results obtained can be considered as preliminary, and would need to be further verified by larger samples and longer follow-ups as long as the technology develops.

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