A COST-UTILITY ANALYSIS AT 7 YEARS OF CHEMONUCLEOLYSIS VERSUS DISCECTOMY IN LUMBAR DISC HERNIATION

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INTRODUCTION

Low-back pain is a major cause of morbidity and economic loss in industrialized countries. However, only a small proportion of this population requires root decompression for disc herniation. Important worldwide variations of yearly rates of discectomy are found. For example, the annual incidence of disc surgery per one million inhabitants is 80 in United Kingdom, compared to 700 in the United States[1]. The number of discebtomies performed in France each year can be estimated at approximately 37 000 for 50 million inhabitants. Given proper indications and technique, disc surgery has proven an effective procedure. However, a subset of patients experience continuing or recurrent radicular pain after lumbar surgery requiring further investigations and surgical interventions. In order to avoid the distressing and complex problem of the failed back syndrome, percutaneous techniques have been developed including chemonucleolysis, manual and automated nucleotomy. Numerous studies have revealed that these new techniques have an immediate success rate comparable to that of discectomy when proper indications are made.

Evaluation of the economic consequences of disc surgery and of percutaneous techniques should not limit itself to short-term outcomes, where a relative consensus on success rates seems to prevail. The outcomes at long term including failures, recurrences as well as the rate of success of repeat surgery are more controversial. Moreover, new techniques like percutaneous nucleotomy and microdiscectomy are too recent to allow long-term comparisons. Available european series on microdiscectomy do not exceed two years and the rate of recurrences in the long run is not known. Therefore, this study is limited to discectomy and chemonucleolysis and attempts to compare short-term and long-term outcomes, in terms of QALY, as well as associated costs.

1. MATERIAL AND METHODS

1.1 Structure of the decision model

Evaluating the treatment procedures for lumbar herniated disc syndrom presupposes that we know how to conceptualize within the same schema elements which are determined by doctors' decision and elements that depend on chance. The first step in designing a decision model was to schematize events according to the choices made by doctors or dictated by the natural course of events. The branching-out corresponds either to decision nodes when they express the choice of treatment or to chance nodes when events occur whose outcomes depends on chance. In this case, the decision tree is in fact a "probability tree" with only chance nodes.
The tree involves two master branches: surgical treatment and chemonucleolysis. For each treatment, the set of events are the following :

- ***At shorl-term (1 year)***

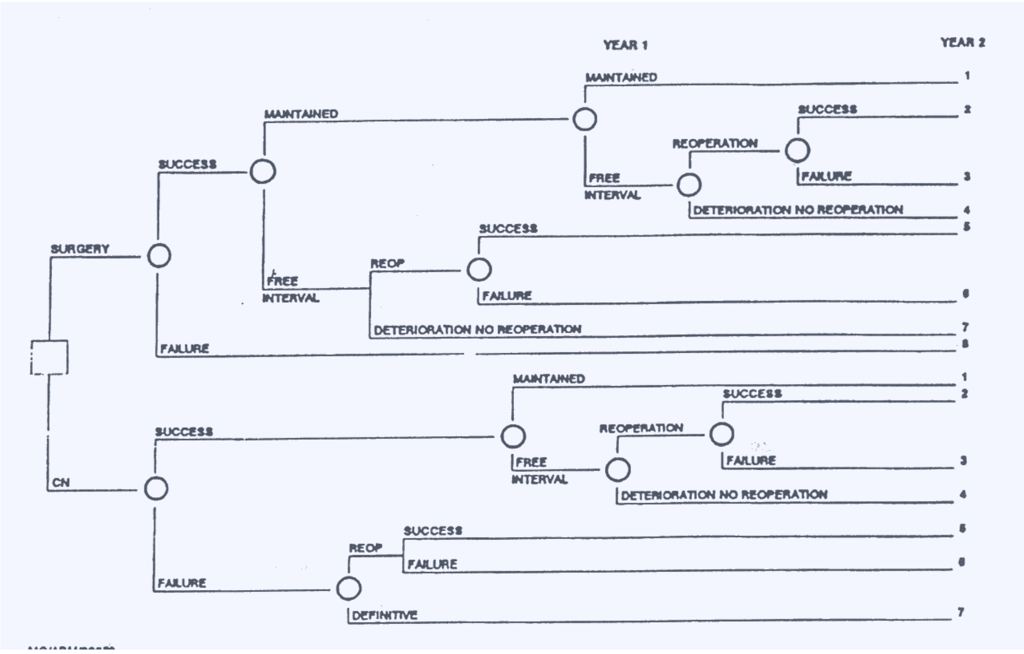
At 3 months, the treatment may succeed or fail : failures may be reoperated or not, reoperation may be a success or a failure.

Good results may persist up to the end of year 1, or deteriorate after à free interval. Two attitudes can be adopted : either the recurrence is reoperated or is medically treated. Subsequent surgery is performed after a period of unsuccessful medical treatment. It can be either a success or a failure.

- ***At long-term (years* 2- 7)**

The same process is reproduced in the course of following years: good results at the end of year 1 may be maintained until end of year 2, or a deterioration may happen after a free interval. In this case, reoperation may or may not be performed after preliminary medical treatment, and prove to be either a success or a failure etc. ..

Figure 1 : Decision tree



1.2 Assignment of probabilities

Evaluation of the short and long tenn efficacy of the 2 treatments was based upon a survey of the litterature. At short-term, most of the randomized clinical trials carried out in North-America deal mainly with laminectomy, which is no longer in use. However, two recent case studies conducted by Brown and Tomkins[2] and Alexander and al.[3] conclude to an equivalence of the two techniques respectively at 3 months and one year. In France, chemonucleolysis has been favourably compared in RCT to microdiscectomy[4] and to percutaneous manual nucleotomy[5], but no randomized trial has been led so far versus discectomy. As far as long-term evaluation is concemed, no randomized studies are available. Though we agree that the results of a mathematical model should ideally be based on comparative trials, we must not feel bound to ignore long term effects of therapies. We therefore tried to offer an analytic approach to the problem and looked for converging data extracted from available series.

Criteria for evaluation of the results, listed on table 1, include the 2 categories "success" or "failure", used in most of the papers reporting the results of the 2 procedures.

Table 1 : Criteria for evaluation of clinical outcomes

SUCCESS	VERY GOOD	NO SYMPTOMS
	GOOD	LUMBAR PAIN AND/OR SLIGHT SCIATICA NO INTERFERENCE WITH SOCIAL OR PROFESSIONAL WAY OF LIFE NO MEDICATION REQUIRED
FAILURE	POOR	INSUFFICIENT IMPORVEMENT FURTHER TREATMENT REQUIRED
	BAD	LUMBAR PAIN OR SCIATICA UNCHANGED OR AGGRAVATED

- ***Disectomy***

At short-term, a review of 7 european and american series[6-7-8-9-10-11-12] published from 1972 to 1987 and based upon 11 341 patients shows an average success rate at 3 months of 81%, ranging from 70% in Salenius study[7] to 87% in the European study[10], At one year, the results published by Lewis[8] and Bouillet[10] show a rate of success respectively of 74 and 76.4%. Therefore, two assumptions were considered :

1) a "high" hypothesis, with a success rate of 87% at 3 months and 76,4 at one year, based on the European study (BouilIet) ;
2) a "low" hypothesis, with a success rate of 80% at 3 months and 74% at one year, based on Lewis and the French series of Louyot[11]. The high hypothesis is more favorable to discectomy than that of Sicard[12], reported for 3 000 patients (83% very good/good results). The low hypothesis is also conservative, since the 74% of success quoted by Lewis is based merely upon total relief of sciatic pain, with or without remaining lumbar pain.

Assumptions on deterioration rate at one year are based on the same series, which seem to fit rather well with reoperation and recurrence rates observed in other studies[13-14-15]: in the low hypothesis (Louyot), a global rate of deterioration of 6%, leading to subsequent surgery in half of the cases (3%) ; in the high hypothesis (Bouillet), a total recurrence rate of 10.6% at one year, of which 3.20% are reoperated, and 7.40% are definite failures and receive only conservative medical treatment.

In these two series, subsequent surgery after discectomy was only perforrned on recurrences after free interval, not on failures. A review of european literature confinned that this reflected the european attitude, which is more conservative that the one generally observed in US series. Consequently, we have assumed that failures of discectomy were not reoperated.

The rate of success on reoperations after recurrences was based on the convergent results of BouilIet, Salenius and Lewis, at 0.5%.

At long term, 5 studies were analyzed[7-8-11-14-16], including a total of 2 000 patients with a folIow-up between 3 and 10 years. Overa1l, the rate of success average to 59% at 7 years. We chose this rate as a baseline probability, corresponding to a deterioration rate of 17.5%, aIso reported in the French series of Louyot between year 1 and year 7, with 7% undergoing surgery and 10.5% being considered as definitive failures.

As repeat surgery is reported to be more frequent during the first two years, we assumed that the rates of recurrence reoperation were 3% in year 1 (3,20% in the high hypothesis), 2% in year 2 and 1% in each of the folIowing years.

- ***Chemonucleolysis***

At short-term, considering the convergence of european and North-American series, a success rate of 80% at 3 months seems to be very well established, with stabilization between 3 months and 1 year . According to Deburge[17], it was established that half of immediate failures undergo surgery at 3 months.

At long term, in a survey publised in 1986, Nordby[18] estirnated the average rate of success at 77% for a follow-up between 7 and 11 years. We chose as a baseline probability a lower estirnate, i.e. 67% at 7 years, based on the French series of Lavignolle and al.[19], with a rate of 12.5% of recurrences at 7 years, 10.5% of which undergoing surgery, the other 2% being considered as definitive failures. It was considered that the rate of post chymopapain surgery was twice as high in the second year as in subsequent years. By linear retropolation, the rate of post-chymopapain surgery was fixed at 3% in year 2 and at 1.5% per annum between years 3 and 7. As for non reoperated recurrences, the annual rate was supposed to be constant over time, i.e. 0.33%.

Deducting year by year alI the deteriorations from the initial successes allows to calculate the rate of persisting good results. Rates of successes of subsequent surgery vary according to authors : two assumptions were retained, one of 80% based upon the results observed in Alexander[3] and Lavignolle[19], and one of 67% corresponding to Javid[20] and Bouillet.

1.3 Hypothesis on mean time of events

In our model, distribution of events over time was made according to a number of tules. Deteriorations appeating within a period of time were assumed to occur mid-way through it.

For instance, in the first year, success has been estimated at 3 months. Therefore, deteriorations occurring in the 9 remaining months will be supposed to appear after a free interval of 4.5 months (0.375 year), the resulting bad health which will affect the remaining 4.5 months will be counted for an equivalent fraction of 0.375 year. Reoperations on reccurrences will take place after 3 months of failed medical treatment, i.e. 0.25 year. Success or failure or reoperations will then only bear on the remaining 1.5 months (0.25 year).
The following table summarizes the retained assumptions for the whole time period.

Table 2 : Mean time of duration

	YEAR 1	YEAR 2
Disectomy		
Good results maintained	0.75	1
Free interval	0.38	0.5
Recurrence	0.25	0.25
Success/failure of reoperation	0.13	0.25
Deterioration without reop.	0.38	0.5
Chemonucleolysis		
Good results maintained	1	1
Free interval	0.25	0.5
Recurrence	0.25	0.25
Success/failure of reoperation	0.75	0.25
Deterioration without reop.	1	0.5

For a cohort of 100 patients, the number of years or year fractions of good or bad health was cumulated at 7 years. In a given year and for 100 patients, the potential years of life are equal to 100 years-patients of which x years are spent in good health 1-x, in poor health.

1.4 Utility assignment

Evaluation of the quality of life was based upon the patient's own assessment of the quality of life associated with the 2 types of states, success and failure, previously described (Cf. table 1). In 1990, a survey carried out in seven public or private hospitals included 146 patients who had undergone chemonucleolysis or surgery 2 to 3 months before the data collection. All patients were over 18 years, had been treated for a sciatica with clinical signs of lumbar disc herniation, well correlated with a clear picture of an herniated disc on CT or MRI. Criteria for exclusion of the study were the classical contra-indications of chemonucleolysis including pregnancy, prior surgery, chemonucleolysis or intradiscal injections of steroïds, major neurological deficit, lumbar spinal stenosis and spondylolisthesis. Patients were recruited in order to constitute 2 groups of similar numbers corresponding to the 2 clinical results, success or failure. The investigator had to evaluate the patient's condition at 3 months follow-up, using the Rosser-Watts classification of illness states[21]. The same day, the patients were asked to fill the Dallas pain questionnaire[22] and to evaluate their condition, using the simplified health measurement questionnaire (SHMQ[23]), with "distress" measured on a 10 cm visual analogue scale.

The Kind and Rosser score[24] calculated from the patient's point of view was used as an adjustment factor for weighting the years spent in success and failure states. For example, a coefficient of 0.5 for a given state of health means that a year of life spent in this conditions is not worth 12 months but only 6 months. Calculations were performed year by year, the results were calculated with and without discounting. In this case, the rate most commonly used in international studies i.e. 5% was adopted.

1.5 Expected utility of the treatments

The method included following steps :

1. Identify the sequences of potential clinical outcomes that lead to terminal branches for each treatment,
2. Associate each potential outcome occurring along a pathway with the expected duration of stay in the corresponding state of health,
3. Multiply that duration of stay with the weight for the corresponding Rosser coefficient of quality of life,
4. Add the state dependant increment of utility for each interval of time through which the patient remains to calculate the cumulated quality of life of the pathway,
5. Estimate the probability of each pathway, multiply that probability by the cumulated quality of life of the path and add across all the paths to obtain the quality-adjusted life-years of each treatment at 7 years.

1.6 Evaluation of costs

The mean duration of hospitalization for discectomy and for chemonucleolysis was determined from the survey. In order to obtain the best estimate of the true cost, evaluation in public hospitals was based upon direct medical costs. A lump sum allocation of administrative cost was added in order to calculate the full cost. The direct cost includes the cost of a day of hospitalization and the cost of the 2 procedures. The cost of an hospitalization day is calculated by dividing the direct standard costs of the unit by the number of days. This cost includes fixed charges, such as staff and depreciations and variable charges such as pharmaceutical expenses. Specific expenses directly related to the 2 procedures such as laboratory and radiological examinations are added.n These latter specific expenses are also evaluated according to their true cost. The direct cost of the 2 procedures is calculated on the basis of the detailed protocols of surgical discectomy and of chemonucleolysis.

The outpatient costs are estimated on the basis of the prescriptions made at the discharge from the hospital including the pharmaceutical and physical therapy expenses and the follow-up medical consultations.

1.7 Evaluation of cost per QALY

Instead of simply comparing the average cost-utility ratio (total costs divided by total number of QALY), we chose to measure the difference between the cost of chemonucleolysis and discectomy divided by the difference in utility of the two treatments : incremental cost-utility ratio. This gives the extra gain of QALY per extra French Franc obtained through switching from one treatment to the other.

2. RESULTS

2.1 Evaluation of the quality of life according to the clinical outcomes

Table 3 shows the Rosser coefficients and the 4 Dallas scores according to the clinical outcome. The results are divided in 2 categories, success or failure. The Rosser coefficients differ significantly ($p < 0.0001$). The higher the coefficients, the more successful is the procedure. A similar level of statistical significance was disclosed for the Dallas pain questionnaire scores. Table 3 also indicated the coefficients of quality of life according to the patient’s assessment. In case of success of the procedure, the coefficient is 0.987, which means that a year spent after a good or very good outcome is virtually equivalent to one year of good health. On the other hand, the coefficient is only 0.807 in case of poor outcome. It is also pointed out that the Rosser coefficient assessed by the patient is significantly correlated to the 4 Dallas scores ($p < 0.001$). the correlation is of course negative since, in contrast to the Rosser indicator, the high Dallas scores correspond to a lowering of quality of life.

Table 3 : Variations of Rosser and Dallas scores according to clinical outcome

INDICATORS	RESULTS		
	SUCCESS n =76	FAILURE n = 70	p
Rosser-Physician 0.933 ± 0.224	0.990 ± 0.009	0.872 ± 0.314	< 0.0001
Rosser-Patient 0.901 ± 0.369	0.987 ± 0.016	0.807 ± 0.518	< 0.0001
Dallas Daily Activities 32 ± 26	12.5 ± 13.7	53.2 ± 18.4	< 0.0001
Dallas Work 37.7 ± 31.9	15.8 ± 19.9	61.5 ± 24.7	< 0.0001
Dallas Anxiety 26.8 ± 28.7	10.5 ± 20.2	44.6 ± 26	< 0.0001
Dallas Social Relations 22.4 ± 24	9.5 ± 14.5	36.4 ± 24.6	< 0.0001

Table 4 shows the coefficients of correlation between the Rosser assessed by the patient and the assessed by the investigator. The correlation is highly significant (r = 0.705), ($p < 0.001$). There also a good correlation between the Rosser-patient and the 4 Dallas scores.

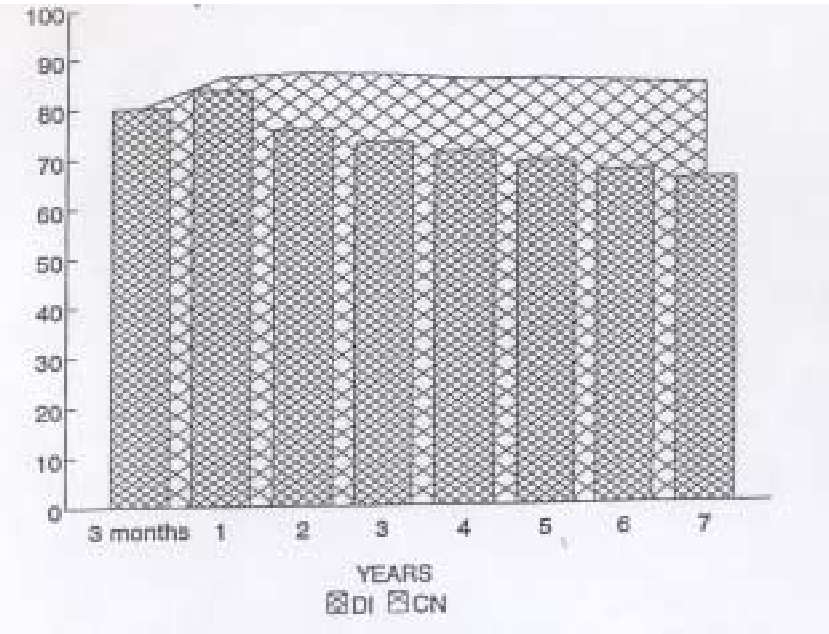
Table 4 : Convergent validity of Rosser and Dallas scales

INDICATIORS	COEFFICIENTS OF CORRELATION	P
Rosser-Physician/ Rosser-Patient	0.705	< 0.001
Rosser-Patient/ Daily Activities	- 0.391	< 0.001
Rosser-Patient/Work	- 0.322	< 0.001
Rosser-Patient/Anxiety	- 0.374	< 0.001
Rosser-Patient/ Social Relations	- 0.328	< 0.001

2.2 Years of life spent in good and poor conditions of health

Calculation of the fraction of years spent in good health for a cohort of 100 patients year by year is shown on Fig. 2. This graph compares the score of the patients having undergone chemonucleolysis with that of the operated patients in the high hypothesis. At year 7, the score of the chymopapain patients in the high or low hypothesis is respectively 84 and 81 year-patient of good health, 68 of which are attributable to maintenance of an initial successful outcome and 16 to success of post-chymopapain surgery in case of initial failure or recurrence. In the case of disectomy contribution of the maintained initial success at 7 years is 60 years, the 5 remaining years being attributable to the success of repeat surgery. Reasoning no longer on a cohort basis but on an individual basis, the probability for a patient of being in good health in the 7^{th} year is 0.84 after chemonucleolysis and 0.65 after disectomy.

Figure 2 : Clinical success over 7 years (Number of years per 100 patients)



2.3 Quality-adjusted life-years (QALY)

As previously described, QALY are calculated by attribution of the Rosser coefficients to the previous results, and accumulation over-time. The results before and after adjusting are summarized in table 5. At year 7, the potential years of life lost due to reduction of the quality of life is 27.36 for chemonucleolysis patients and 44.24 for discectomy patients in the high hypothesis.

Table 5 : Results at seven years in QALYs for a cohort of 100 patients

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
NON DISCOUNTED QALY's							
CHEMONUCLEOLYSIS (high hypothesis)	96,17	192,51	288,76	384,89	480,92	576,83	672,64
CHEMONUCLEOLYSIS (low hypothesis)	96,00	192,51	288,03	383,02	479,47	574,98	670,44
DISCECTOMY (high hypothesis)	95,72	190,07	283,82	377,41	470,55	563,33	655,76
DISCECTOMY (low hypothesis)	94,78	188,70	282,10	375,15	467,84	560,18	652,17
DISCOUNTED QALY's							
CHEMONUCLEOLYSIS (high hypothesis)	96,17	187,88	275,18	358,24	437,27	512,37	583,84
CHEMONUCLEOLYSIS (low hypothesis)	96,00	187,48	274,50	357,26	435,98	510,76	581,98
DISCECTOMY (high hypothesis)	95,72	185,54	270,66	351,44	428,09	500,74	569,69
DISCECTOMY (low hypothesis)	94,78	184,19	268,90	349,30	425,58	497,89	566,51

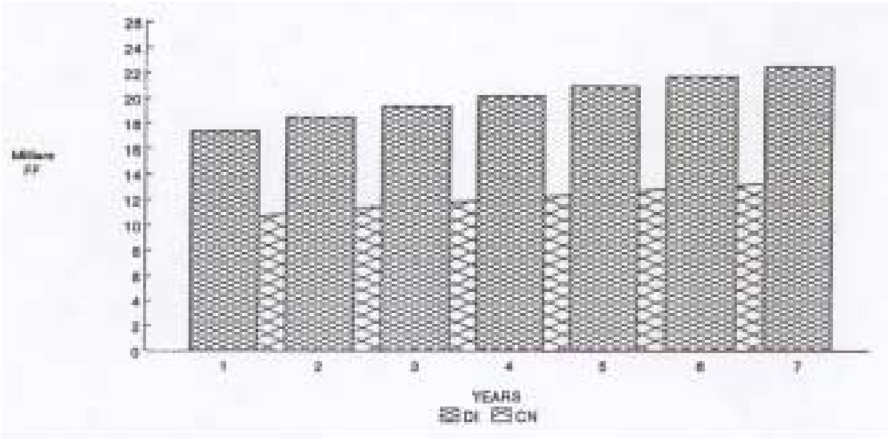
2.4 Evaluation of costs

The total cost of discectomy and chemonucleolysis was calculated by adding the cost at the time of the 2 procedures to that of their long term failure at 1 year and 7 years.

The mean hospitalization duration was 2.2 ± 0.60 days for chemonucleolysis and 7.7 ± 1.6 days for discectomy. The total cost of discectomy at the time of the survey (1990) in a neuro-surgery unit of a public hospital was 15,400 French Francs. The total cost of chemonucleolysis at the same period was 8,000 French Francs.

Financial consequences of the failures were evaluated for the 2 procedures and total costs were compared for the high and low hypothesis of outcomes at 7 years. Figure 3 compares the cost of chemonucleolysis and of discectomy, year by year, and at a seven end-point.

Figure 3 : Chemonucleolysis versus discectomy : discounted medical cost at 1 and 7 years per patient (CN and DI in neurosurgery)



2.5 Cost-per QALY

Comparison for a cohort of 100 patients of the indexed cumulative costs and of 7-year quality-adjusted life years {QALY) can be used to calculate the cost-benefit ratio for each method. In the high hypothesis for chemonucleolysis, the mean cost per year of good health to a 7-year end-point is 2,299 French Francs in a neurosurgery unit. The cost of discectomy is 3,958 French Francs. These results, reformulated in terms of additional cost and additional efficacy, are even more striking. The additional cost per patient of discectomy compared to chemonucleolysis is 9,126 French Francs. The additional benefits associated with the use of chemonucleolysis is equivalent to 0.142 years of life at 7 years, i.e. 52 days.

3. DISCUSSION

The Rosser coefficients measure a certain quality of life of the patient, based on two dimensions, pain and disability. The Dallas index expresses the impact of pain on daily activities, work, psychological state and relationship-related activities. This study has shown that these two indicators are closely linked. Also, the Rosser coefficients and the four Dallas scores have been shown to differ significantly as a function of the outcome of surgery or chemonucleolysis. It can be concluded that these indicators are valid criteria for assessing the quality or efficacy of treatments of intervertebral disc hernia, even though they are only indirect indicators. In subsequent studies, it would be quite possible to add them to the "conventional medical criteria" and to take them into account as secondary assessment criteria if the main ones are not sensitive enough to discriminate between treatments.

This paper attempts to estimate cost-benefit ratio of surgical discectomy and of chemonucleolysis in the treatment of intractable radicular pain caused by discal herniation at a 7 year end-point. This estimation was necessarily based upon careful analysis of the litterature, since no prospective study providing long-term follow-up is available. Obviously, the accepted hypothesis regarding the clinical results may be subject to controversy, due to the variability of the reported results from numerous studies. However, this variability in itself suggests that a synthesis of the published results may provide a more realistic appraisal of outcomes in general practice, in that it highlights points of consensus about key issues such as the range of short-term results, frequency of recurrences, rates and outcomes of repeat surgery. Whenever a divergence was detected in the literature for a given parameter, we included the possible extreme hypothesis in a sensitivity analysis.

We consider the short-term performance of chemonucleolysis, i.e. 80% of very good/good outcomes to be firnly established. The success rate of this method has steadily increased as a result of better selection of candidates for nucleolysis. Thus, according to a review of the North-American studies of chemonucleolysis published by CINH[25], the mean success rate rose from 67% for 75 centers in the USA between 1963 and 1975, to 80-89% after 1981 in 37 centers. In Europe, the mean success rate reported before 1981 in 13 centers was 70%, but more recent studies show the same progression. In 1986, Deburge[4] and Clère[26] reported success rates of 77.5% at 6 months and 81% at 3 and 6 months respectively. In 1990, Lavignolle[19] highlighted the impact on the outcome of chemonucleolysis of good patient selection : the short-term success rate rose from 78% with discography (200 cases between 1978-1980) to 82% with dicometry (500 cases, 1981-1984) to 92% with discomanometry, which has been used since 1985 in 300 cases. We did not include these very favorable results, since they were observed in centers of excellence, some of which routinely use patient selection methods which are not yet available under normal conditions of practice and also the follow-up for these very recent studies has not yet reached the end-point selected, i.e. 7 years. Likewise, assuming that good results are maintained between 3 months and one year is conservative, since some authors such as Nordby[27] and McDermott[28] report improvement between 3 and 6 months. Wiltse, cited by Nordby, found that 52% of patients recovered at 4 months, 33% at 6 months, and 12% took 12 months.

In contrast, there is some divergence concerning the success rate of surgical repair of failures and recurrences following chemonucleolysis. This is why two outcome hypotheses have been tested.

Surprisingly, the short and long-term results of discectomy have been investigated to a lesser extent than those of chymopapain. Again, some centers of surgical excellence have reported higher success rates at 3 months than ther 87% of our high hypothesis. However, it would have been iI1ogical to base ourselves on the most favorable results obtained by surgery, when we had not done this for chemonucleolysis. We therefore used the major studies, the results of which were obtained under normal working conditions, and we evaluated them on criteria defined on similar bases for both methods. The high hypothesis was based on the work of Bouillet, which seemed to be more favorable to discectomy than that of Sicard, reported from 3 000 patients (83% of very good/good results). As for the low hypothesis, i.e. 80% of good results observed by Louyot at 3 months, this is not the worst : Salenius and even the very respected study of Lewis report worse results. In any case, the long-term projections based on these data, i.e. 62 to 65% ofvery good/good results in year 7, are very close to the long-term results published by Rish (64% at 3-8 years) and by Lewis (62% at 7 years).

Finally, the results obtained in function of the various high and low hypotheses adopted differ little. According to our estimations, the probability for a given subject of being in a satisfactory state of health (very good or good) during the 7th year ranges from 0.81 to 0.84 after chemonucleolysis and from 0.62 to 0.65 after discectomy. This therapeutic benefit is essentially attributable to the good outcome of the surgical repair of failures and recurrences, which provides a second chance for chemonucleolysed patients. The clinical results, reformulated in term of QALY for a cohort of 100 patients, reveal an additional gain of 14 years of good health after the use of chemonucleolysis. Per patient, the additional benefit associated with the use of this method is equivalent to 0.142 years of life at 7 years, i.e. 52 days of good health.

The hospital cost of the procedure itself and the cost to the 7-year end-point has been calculated for both methods, including repeat surgery for failures and recurrences and the long-term medical costs for non-reoperable deteriorations. It was found that the hospitalization costs associated with chemonucleolysis were about half those associated with discectomy: when the patient was admitted to a rheumatology service, the hospital cost of chemonucleolysis was only 48% of that of discectomy; it was still only 51.5% of that ofdiscectomy when the post-nucleolysis hospitalization took place in a neurosurgery unit. At one year , after integrating the cost of the repeat surgery for failures, the global medical costs after chemonucleolysis were no more than 56.6% and 60% of those following discectomy depending on whether the initial hospitalization was in a rheumatology or neurosurgery unit. At 7 years, the ratios remained unchanged. Thus, the indexed additional cost per patient of discectomy compared to that of chemonucleolysis was, at 7 years, 9,721 French Francs or 9,126 French Francs, depending on whether the chemonucleolysed patient was hospitalized in a rheumatology or surgery unit. The use of chemonucleolysis resulted in a saving of nearly 10,000 Francs.

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