DIMDI Deutsches Institut für Medizinische Dokumentation und Information

Im Geschäftsbereich des Bundesministeriums für Gesundheit und Soziale Sicherung

HTA REPORT | EXECUTIVE SUMMARY

Minimal invasive procedures for the treatment of disk-prolapse

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INTRODUCTION

Back pain with or without sciatic symptoms (leg pain) is a very common disorder. Lifetime prevalence in western industrialised countries amounts up to 80 %[34]. In about 5 % of all patients with acute back pain lumbar disc herniation is thought to be causing the symptoms[1]. It is assumed that protruded disc material compromises spinal nerve roots and causes irritation. Irritation leads to pain and in some cases to neurological deficits. Surgical treatment of lumbar disc herniation aims to be causal. Protruded disc material is mechanically removed, chemically dissolved or evaporated in order to take pressure from compromised nerve roots. There is a clear indication for surgical treatment when irreversible neurological damage is to be expected (as in the case of Cauda-Equina-Syndrome, or rapidly progressing pareses) or when severe pain is not controlled by conservative measures. However, less than 5 % of patients with clinically manifested disc herniation develop these dramatic symptoms. In most cases there is only a relative indication for surgical treatment, if there is one at all.

Prospects of success, necessity and economic consequences of elective lumbar disc surgery have been debated controversially over the last decades – against the background that in most cases the natural course of the disease is lengthy and painful but benign in the end while surgery leads to high rates (up to 30 %) of unfavourable results.

Ongoing research is focussing the problem from two perspectives. One stream of research activities is trying to identify patient characteristics that determine the success of surgical results in order to refine indication criteria. So far a few risk factors for unfavourable results have been identified: back pain as a lead symptom, psychological symptoms overlaying physical symptoms, discrepancies between clinical and radiological signs, compensation payments. Newer evidence-based guidelines for the treatment of disc herniation incorporate these findings by recommending very careful selection of patients for surgery[23].

The other stream of research activities aims at optimising surgical procedures by minimising surgical trauma. Instability and scar formation resulting from tissue and bone traumatisation are thought to be the main cause of unfavourable postoperative results. This development led to microdiskectomy overcoming open diskectomy as the standard surgical procedure for the treatment of lumbar disc herniation.

Furthermore, a variety of procedures have been developed which differ from each other by the way the herniated disc is accessed, the way visualisation of the operative site is achieved and the way pressure is taken off the nerve roots.

Searching for procedures used for surgical but elective treatment of lumbar disc herniation as an alternative to standard surgery (microdiskectomy), six groups of interventions within two categories may be identified:

- Percutaneous procedures: chemonucleolysis, percutaneous manual disc decompression, automated percutaneous lumbar disc decompression, percutaneous laser disc decompression or –diskectomy and nucleoplasty.
- Endoscopic procedures with posterolateral or posterior access to the lumbar disc space (incl. Endoscopic laserforaminoplasty (ELF) and percutaneous endoscopic laser disc decompression).

There are hardly any utilisation data for minimally invasive lumbar disc surgery in Germany. According to statutory health insurance data minimally-invasive procedures were performed in about 5 % of all lumbar disc surgery cases in 2003. An increase in frequency is noted since 2000. Their real proportion is thought to be much higher - many procedures are offered by private hospitals while costs are covered by private health insurers or patients themselves.

So far no comprehensive assessment (which could serve as a basis for coverage decisions) of efficacy, safety and economic consequences of

minimal invasive lumbar disc surgery compared to standard procedures has been undertaken in Germany.

OBJECTIVE

Against this background the aims of the following assessment are:

- Assessment of efficacy and safety of minimally invasive lumbar disc surgery in comparison to standard surgery, based on the published scientific literature.
- Identification and assessment of cost-effectiveness literature comparing minimally invasive and standard procedures.
- Identification of research, evaluation and regulatory needs within the German health care system.

As more than 95 % of disc surgery is performed at the lumbar spine, the present report will exclusively focus on this location. Excluded from the assessment are:

- Procedures that are clearly in the experimental state of development (e.g. Hydrojetnucleotomy).
- Procedures that are used for different indications as the standard procedure (e.g. Disc Prostheses, Catheter Treatments, IDET = Intradiscal Electrothermal Annuloplasty).
- Procedures for which no scientific literature could be retrieved during the preparation of the assessment (nucleoplasty).

Assessment of medical efficacy, effectiveness and safety

METHODS

A systematic review of the literature was compiled for the assessment of efficacy, effectiveness and safety. In a comprehensive literature search 23 electronic databases were screened using search terms that covered the following topics: “disc herniation”, “minimally invasive surgical procedures”, "therapeutic studies” and “economic analyses”. Due to the continuous further development of surgical procedures our search only covered the last five years of publication (January 1998 until December 2003) and was updated once in summer 2004. The first selection of possibly relevant papers was performed by screening titles and abstracts of publications for methodological as well as content related in- and exclusion criteria. The second selection round was based on full text, applying the same criteria:

- Randomised and non-randomised controlled trials comparing the results of minimally invasive lumbar disc surgery (chemonucleolysis, percutaneous manual disc decompression, automated percutaneous lumbar disc decompression, percutaneous laser disc decompression or –diskectomy, endoscopic procedures with posterolateral or posterior access) with those of microdiskectomy or open diskectomy.
- HTA reports and systematic reviews of the study types mentioned above.
- Adult patient clientele with first time operations in one level.
- Excluded were studies in very specific patient groups (e.g. competitive athletes, patients with rheumatoid arthritis).
- Secondary inclusion criterion: Case series of minimally invasive procedures (after search for controlled trials yielded very little information).

Methodological study quality was documented using the checklists of the German Scientific Working Group for Technology Assessment in Health Care (GSWG-TAHC). Study results were summarised in a qualitative manner for each group of minimally invasive procedures. Due to the limited number and the low methodological quality of the studies it was not possible to conduct meta-analyses.

RESULTS

The literature searches yielded 1,328 publications of which eleven fulfilled the primary inclusion criteria (five systematic reviews, three HTA reports and three RTC.)

Institution / author	Title	Document type	Year
Reviews concerning more than one method			
Gibson et al.[12]	Surgery of lumbar disc prolaps	Systematic review	1999
Lühmann et al.[23]	Operative Eingriffe an der lumbalen Wirbelsäule bei bandscheibenbedingten Rücken- und Beinschmerzen	HTA report, systematic review	2003
Schmid[36]	Mikrochirurgie lumbaler Bandscheibenvorfälle	Systematic review	2000
Rasmussen et al.[33]	Lumbale skiveprolapser og radiologisk rygginterv ensjon	Systematic review	1998
Reviews and HTA reports concerning a method			
Boult et al.[0]	Percutaneous Endoscopic Laser Discectomy	Systematic review	2000
NICE[30]	Interventional procedure overview of Laser lumbar Discectomy	Rapid assessment	2003
NICE[29]	Endoscopic Laser foraminoplasty (Overview)	Rapid assessment	2003
Knight et al.[19]	Review of safety in Endoscopic Laser Foraminoplasty for the management of Back pain	Comparative study and review; registry data	2001
Kontrollierte Primärstudien			
Schick et al.[35]	Microendoscopic lumbar discectomy versus open surgery: an intraoperative EMG study	RCT	2002
Haines et al.[13]	Discectomy strategies for lumbar disc herniation: results of the LAPDOG trial	RCT	2002
Hermantin et al.[14]	A prospective randomised study comparing the results of open discectomy with those of video-assisted arthroscopic microdiscectomy	RCT	1999

The methodical quality of the review papers is very heterogeneous. The systematic reviews of Gibson at al.[12], Lühmann et al.[23], Boult et al.[0] and the National Institute for Clinical Excellence (NICE)[30, 29] as well as the RCT fulfilled most of the quality criteria of the GSWG-TAHC. The review of Schmid[36] is from a methodological point of view not corresponding to scientific standards; the overview of Rasmussen et al.[33] is lacking the transparent documentation of searches and critical appraisal of primary literature. Knight et al.[19] compare data from very heterogeneous sources (previously published RCT, own registry data). Except for Gibson et al.[12] and Rasmussen et al.[33] whose work is based upon the results of RCT only, all other authors take into account reviews and HTA reports as well as data from non-randomised controlled trials and case series.

In addition all case series published between 1998 and 2003 and reporting results of the specified minimally invasive procedures were extracted from the search results and examined. Taken together, the evidence base for the assessment of efficacy, effectiveness and safety looks as follows:

Percutaneous manual nucleotomy	Six case series (four published after 1998)
Automated percutaneous diskectomy	Two RCT (one terminated), twelve case series (one published after 1998)
Chemonucleolysis	Five RCT, five non-randomised controlled trials, eleven case series
Percutaneous laser-nucleotomy	One controlled trial, 13 case series (eight published after 1998)
Endoscopic procedures	Three RCT (two published after 1998), one controlled trial, 21 case series (17 published after 1998)

Three case series reporting results of nucleoplasty were not available.

Upon this evidence-based assessment of efficacy, effectiveness and safety of minimally invasive procedures yielded the following results:

Percutaneous manual nucleotomy

For this group of procedures there are no data from controlled trials available. Six case series with an average observation time of one year report

success rates between 52 % and 94 % while outcomes have been measured using heterogeneous instruments (modified MacNab Criteria; JOA Score; non-standardised reporting of reduction of back and leg pain). Recurrence of symptoms was noted in 4,5 % to 19 % of the operated patients. Data from case series indicate that technical (amount of disc material removed, method of visualisation) as well as patient dependent characteristics (size and location of prolapse) determine success rates. In most case series the method was used to treat small herniation not protruding the posterior ligament.

Due to heterogeneity of patients, outcome measures used and technical variation of treatment methods these results cannot be generalised to the whole group of percutaneous manual nucleotomies, especially not in comparison to standard procedures.

Automated Percutaneous Lumbar Diskectomy (APLD)

There are two RCT comparing the efficacy of APLD to the efficacy of microdiskectomy or open conventional diskectomy. Both trials include patients with small disc herniations or protrusions suffering from sciatic symptoms resistant to conservative treatment. Both studies had to be terminated ahead of time. The RCT of Chatterjee et al.[5] was terminated after inclusion of 71 patients (aiming for 160 patients) when interim analyses after six months showed significantly worse result for patients treated with APLD (MacNab: 29 % success for APLD vs. 82 % success for microdiskectomy, $p < 0{,}001$). The second RCT performed by Haines et al.[13] aimed to compare the efficacy of automated (APD) and endoscopic percutaneous diskectomy (EPD) to the efficacy of conventional diskectomy: It was terminated early because of recruitment problems (instead of 330 patients only 34 were included). There were no statistically significant differences in success rates (Mac Nab) among the groups at six months. Authors explain the recruitment problem by the fact that only a small fraction of patients with lumbar disc herniation qualify for APLD if generally accepted indication criteria (e.g. Criteria of the Food and Drug Association) are used.

Success rates between 56 % and 92 % as reported in twelve case series are rather contrasting to the RCT results.

In conclusion it may be stated that the efficacy of APLD is probably inferior to that of microdiskectomy. Furthermore our results demonstrate that data from case series do not contribute to a valid comparison of efficacy of different procedures.

Percutaneous Lasernucleotomy / Laser Disk decompression

One trial reports inferior results for patients (sciatica; monosegmental, non-sequestrated, non-extruded herniated disc) treated with lasernucleotomy in comparison to historical controls treated with open diskectomy (65 % excellent and good results versus 85 % excellent and good results)[3].

13 case series report varying success rates between 56,5 % and 91,5 %. There is considerable heterogeneity among the studies concerning technical details of procedures, observation time and methods of outcome assessment. Most patients included suffer from sciatica with radiologically confirmed protrusions or disc herniations not protruding ligaments. In most trials a period of unsuccessful conservative treatment preceded the intervention.

Taken together it must be stated that there is no valid evidence-base to draw conclusions on the efficacy or effectiveness of lasernucleotomy procedures in comparison to standard techniques.

The British institute NICE recommends the intervention to be used within the National Health System only under trial- and audit conditions and with the obligation of informing patients about the lack of efficacy data.

Chemonucleolysis

Among all minimally invasive procedures the assessment of efficacy and effectiveness of chemonucleolysis compared to microdiskectomy or open diskectomy is the only one that is based on RCT data. Five RCT[6,9,0,28,41] include patients with symptoms of root compression, radiologically confirmed disc protrusion and a period of unsuccessful conservative treatment. Observation times vary between one and two years. Outcomes assessed are: necessity for a second operation;

success as judged by the operating surgeon; success as judged by the patient and success judged by an independent observer. In the Cochrane Review[12] results of the studies were compiled by metaanalysis. These results demonstrate inferior results for chemonucleolysis when compared to open diskectomy (higher rates of failure after twelve months; higher probability for re-operation after six to 24 months).

In the same Cochrane Review furthermore five studies were analysed comparing chemonucleolysis to placebo treatment (+ continued conservative therapy)[7, 10, 11, 16, 38]. The studies of high methodologically quality demonstrate superior results of chemonucleolysis compared to continuing conservative care (rated by patients, surgeons or independent observer). The authors of the Cochrane Review are concluding that chemonucleolysis might be an intermediate treatment option between conservative and surgical care. These conclusions are supported by the study results of van Alphen et al.[41] who found identical success rates when comparing chemonucleolysis with optional diskectomy versus diskectomy alone (patient rated outcomes).

Chymopapain is at the moment not available in German pharmacies.

Endoscopically assisted minimally invasive disc surgery

So far, three RCT examined the efficacy of endoscopic procedures compared to microdiskectomy, including the terminated study by Haines et al.[13] whose results cannot be used.

One RCT[27] includes 40 (20 per study group) patients with sciatic symptoms (including slight neurological deficits) resistant to conservative treatment and radiologically proven small subligamental herniations. Due to the small number of patients no statistically significant differences in success between the treatment groups could be made. There was a tendency noted towards a quicker postoperative improvement in the endoscopic group, which were most profound looking at return to work rates. On the other hand three out of 20 endoscopically treated patients had to undergo a second operation, in the group treated with microdiskectomy only one out of 20 needed a second procedure.

Another RCT[14] includes 60 patients (30 per study subgroup) with root symptoms and radiologically proven lumbar intracanalicular disc protrusions. While clinical results (success rates, satisfaction with the operation results) were identical there were some advantages for the endoscopically treated patients noted concerning postoperative recovery.

Both studies used a posterolateral or transforaminal access to the disc space for the endoscopic procedures.

Schmid[36] compiled the results of two case series and one non-randomised controlled study to assess the efficacy of endoscopically assisted lumbar disc surgery. In these studies satisfactory results were noted in 72 % to 91 % of treated patients[18, 22, 37]. The compilation does not take into account technical heterogeneity of the procedures used.

Between 1998 and 2004, 14 case series were published, especially reflecting the permanent further development of operating techniques and the widening of indication criteria. This reduces the comparability of study results. In nine studies with endoscopic procedures using posterolateral and transforaminal access to the disc space success rates between 69 % and 90 % are reported. Five studies reporting on endoscopic procedures using access to the disc space from posterior find success rates between 90,5 % and 94 %. Patients with all types of disc protrusion or – herniation were in included in the studies.

Percutaneous Endoscopic Laserdiskectomy (PELD) which uses a combination of endoscopic and laser technique is taking a special position among the endoscopic treatments. Its efficacy compared to standard techniques could not yet be proven in controlled studies. Four case series and time comparisons report success rates between 60 % and 87 %.

The ELF (Endoscopic Laser Foraminoplasty) which was originally developed to treat stenoses of the lateral recesses is also taking a special position. There are no efficacy data from controlled trials yet, data from published case series (all originating from one operating centre) indicate success rates around 70 %.

In conclusion it may be stated that endoscopically assisted minimally invasive procedures constitute a group of medical technologies with a lot of ongoing further development and research. For these procedures two RCT comparing results to standard operations are available. They do not find significant differences concerning efficacy (success rates), but point out a tendency towads faster postoperative recovery. The results are referring to patients with small and subligamental disc protrusions. The results of case series including patients with non-covered, dislocated and / or sequestered protrusions suggest high success rates for this indication as well. Still, results from case series are hardly generisable.

Based on the data available, no conclusion can be drawn concerning the efficacy of ELF or PELD in comparison to standard procedures.

Safety

Compiling data on the safety of the minimal invasive procedures compared to standard procedures is even more difficult than the comparison of their efficacy. In most trials the assessment of complications is less standardised than the assessment of surgical outcomes - in most cases it is a purely anecdotal description of single adverse events. Due to the rarity of events studies with a low number of participants are not suitable for analysing complication rates from a statistical point of view. The careful interpretation of trial results indicates that complication rates of minimal invasive treatments are at least not higher than those of standard procedures.

DISCUSSION

Amount and quality of available evidence, transferability of results

There is a far-reaching consensus among researchers and policy makers that assessment of efficacy of a treatment should be based on the results of high quality controlled trials, preferably RCT. The proof of efficacy is a necessary component for the assessment of benefit which incorporates further qualities such as safety or access and further perspectives such as patients, clinicians, payers or society's view.

Only nine randomised trials on three of the six groups of technologies assessed here are available, their results being partly compromised by methodological difficulties. Methodological problems include low patient numbers, insufficient description of randomisation techniques, unblinded and non-standardised assessment of outcomes as well as short observational times.

Five RCT assess the efficacy of chemonucleolysis compared to standard surgical techniques. In Germany this procedure is currently not performed at all, due to the unavailability of chymopapain. Three RCT focus the efficacy of endoscopic procedures compared to open surgery. One RCT is reporting non-clinical outcomes only[35]. The results of the two remaining RCT are hardly comparable due to technical differences among the surgical procedures used (interventional – as well as comparison techniques), the outcomes assessed and time of observation. For the Automated Percutaneous Lumbar Diskectomy (APLD) results of one RCT are available[5]. This trial had to be terminated early due to highly inferior results of APLD compared to the standard technique. A second RCT[13] investigating APLD was terminated due to recruitment difficulties. There are no RCT available for manual percutaneous nucleotomy or lased diskectomy.

All other data on the efficacy of minimally invasive lumbar disc surgery derive from case series. Even within the procedure groups the studies demonstrate great heterogeneity concerning included patient groups, the technical specifications of procedures, the setting, the outcomes assessed, the duration and the completeness of observations. Under optimal conditions (clearly specified procedure, adequate indication, documented additional treatment, objective and standardised assessing of outcomes, almost complete follow-up observation) a statement about the efficacy and or safety of a specific procedure in that highly specific situation can be made. Conclusions for the entire group of technologies may not be based on the results of case series.

When it comes to transferring international research results into the context of the German health care systems, national specificities are not as important as three content related problems which make a comparison of study results and their interpretation difficult:

- Ongoing further development of technologies leads to a variety of methods "on

the market" which prohibits giving recommendations concerning a whole group of technologies. This variety is not only noted among the minimally invasive procedures but also among the standard surgical techniques against whose results the new procedures are to be compared.

- The second problem is concerned with the heterogeneity of patients included in trials and case series. One inclusion criterion applied in almost all studies is the persistence of sciatic symptoms despite conservative treatment. Differences are noted when taking into consideration results of radiological investigations. Even within the groups of technologies differing inclusion and exclusion criteria are used concerning radiological findings (e.g. dislocation or size of herniations, sequestration or penetration of ligaments).
- The third problem is concerned with the lack of standardisation in outcome assessment which is furthermore performed in variable intervals after the operations. The most frequently used dichotomous judgement of success and failure is based upon a variety of different assessment instruments and procedures. Among those many rely on the subjective judgement of results by the surgeon himself or the patient (MacNab Criteria in various modifications). Validity and generisabilitiy of these measurements especially in settings with different social-cultural background has never been systematically reviewed.

In 1999 in their conclusion of the Cochrane Review Gibson et al.[12] point out the need for methodologically rigorous RCT in order to assess the efficacy of minimally invasive disc surgery compared to standard techniques. This conclusion is shared by the authors of all the literature reviews[0, 23, 30, 29, 33] analysed in this volume.

Efficacy

From a methodological point of view the most valid information is available for the assessment of the efficacy of chemonucleolysis. RCT results suggest that considering chemonucleolysis as an intermediate treatment option between conservative and surgical yields results as favourable as standard diskectomy alone. However, chemonucleolysis is rarely performed in Germany (and also in the USA). The main reason for this is, beside the pharmaceutical not being available in Germany, that severe allergic and severe neurological complications (severe infections) are feared[36, 39]. Taking into consideration published data on complication rates, this fear is hard to substantiate. Reanalysis of all chemonucleolysis trials of the Cochrane Review[19] and two large post-marketing studies (USA 1984: 29,057 cases; Europe 1987: 18,925 cases) report complication rates. According to their results less than 2 % of treated patients experience allergic reactions, the rate of anaphylactic reactions with circulatory problems is not even 1 %. Deaths due to anaphylactic complications were reported in 0.07 % of cases in the American data and in the European trials not at all.

The second group with RCT data on efficacy compared to standard techniques are the endoscopically assisted procedures. It has to be noted though that this group comprises a number of very heterogeneous surgical techniques. The two RCT available[27, 14] demonstrate comparable success rates for endoscopic procedures and standard technology. As concerns return to daily routines and work a trend towards faster recovery was observed for the endoscopic procedures. These conclusions refer to techniques using a posterolateral access to the disc space in patients with a small, non-sequestered disc protrusion. Furthermore, it is not clear whether these results from ten year old trials are generisable to procedures used now.

All further information on clinical efficacy and safety of endoscopic procedures are based on the results of case series. In these studies the great variety of endoscopic procedures performed as well as the heterogeneity of the patients included prevents an overall conclusion for the whole group of technologies. A certain time related tendency can be observed though: whereas older studies (published before 2000) are performing minimal invasive treatments on patients with small and covered protrusions, more recent studies also include patients with large, dislocated or sequestered protrusions. Success rates for the minimally invasive procedures (assessed by heterogeneous

assessment tools) do not differ very much from those reported for standard procedures.

The interpretation of data on the safety of minimally procedures is even more difficult. While for measuring success some standardisation is at least tried by using scales like the Mac Nab Criteria, the measurement of adverse reactions or events is totally unstandardised. Most reporting is unsystematic and anecdotal. A differentiation of complications according to severity and specificity for the procedure assessed is hardly applied. The frequency of severe complications (injury of the dura / durafistula, nerval root injury) reported in case series of endoscopic procedures is markedly less than 5 % and therefore ranges in the same order of magnitude as for standard procedures[15].

Assessment of the (comparative) efficacy of APLD is mainly based on the results of one RCT which demonstrates markedly inferior results for APLD (29 % primary successes) as compared to microdiskectomy (80 % primary successes). These results are contrasting to the results reported case series which vary between 56 % and 92 %. Various explanations for these observation have been discussed (age and state of hydration of the protrusion; form of the protrusion: wide vs. narrow based; preceding treatments) without leading to clarification. Against this background two conclusions may be drawn:

- APLD does not seem to be an appropriate treatment alternative for patients with small lumbar disc herniations.
- Results of case series are not a valid base for conclusions on the efficacy of treatments, especially not in comparison to alternative options.

There are no data from controlled trials for the assessment of the efficacy of percutaneous manual diskectomy in comparison to the standard procedures. Six case series (three published after 1998) report variable success rates between 52 % and 94 %. Some of the result indicate that success might depend on anatomical characteristics of the disc protrusion (prolapse vs. protrusion) and technical specifications of the procedures used (e.g. amount of disc tissue removed). Nevertheless these are only observations from single studies which cannot form the base for an overall conclusion on the efficacy of this group of technologies. There are hardly any data on safety available so no overall conclusion can be drawn.

For the assessment of efficacy of percutaneous lasernucleotomy there are no data from controlled trials either. Case series results do not permit conclusions on the significance of these procedures among the treatment options for lumbar herniated discs. Like the endoscopic procedures the group of laser procedures comprises a number heterogeneous technologies. Different lasers are used in different doses with different instruments of application, with the help of different visualisation techniques and on different settings (radiological departments vs. microsurgery or orthopaedics, outpatient vs. in-patient). Very low complication rates (< 1 % discitis) are reported in three cases series.

Effectiveness

There are five sources for information for effectiveness of medical treatments: so called controlled “pragmatic” trials, observational studies with population or regional reference, systematic observations of utilisation, surveillance data and registry data.

There are no such data (to date) on the effectiveness of minimally invasive lumbar disc surgery procedures. For chemonucleolysis older surveillance studies[31] are yielding information on frequency and type of complications, but not on effectiveness. The Swedish registry for disc surgery collects data on all surgical procedures performed on the spine, completeness ranges around 85 %. Aim of the registration is to improve effectiveness, efficiency and quality of spinal surgery. Individual patient data on diagnosis, treatment performed and outcome (one and two years after the operation) is registered, analysed and fed back to the operating departments. For this volume the annual report of 2003 (based upon 2002 data) of the Swedish registry was made available. So far no specific analyses on minimally invasive procedures have been performed but will be available in the coming years as it was communicated by the head of the registry.

To date it must be concluded that the question of whether minimally invasive surgical procedures to treat lumbar disc herniation are effective cannot be answered on the basis of the published literature.

Research Needs

The use of minimally invasive surgical treatment as an alternative to microdiskectomy or open diskectomy is characterised by a paradoxical situation: on the one hand there is a large amount of procedures being heavily advertised and marketed and on the other hand, there are hardly any data which allow patients, clinicians and payers to undertake a realistic estimate on the risk / benefit ratio. This situation creates an urgent demand for research and evaluation in two directions:

First of all, RCT are needed to investigate efficacy of the technologies compared to standard surgical procedures and, if needed also to conservative treatment options.

Second, a monitoring system should be installed to collect information on performance and safety of the technologies under routine care conditions.

ECONOMICAL EVALUATION

METHODS

For the systematic review of the economical literature results of the literature searches reported above are screened using specific inclusion and exclusion criteria. Transparency and methodological quality of economical studies are assessed and documented using catalogues developed by the GSWG-TAHC. Results are presented, referring to single documents first and afterwards summarised for the different groups of technologies in a qualitative manner. Extraction of cost determinants from recent case series data is also tried in this part. The available data did not permit the calculation of metaanalyses.

RESULTS

The literature searches yielded two economic analyses and one HTA report including an economic analysis of minimally invasive surgical technologies for lumbar disc herniation. Two economic studies dealing with chemonucleolysis[17, 20] were identified from reference lists – both were due to their early publication date not included in the results of the electronic literature searches. Assessment of transparency and methodological quality of all publications included ranged far below the maximum achievable scores.

APLD

There are two economic analyses[8,0] comparing the cost-effectiveness of automated percutaneous nucleotomy to that of open diskectomy. The two analyses report contrary results. The paper by Dullerud[8] favours APLD as the clearly more cost-effective procedure while the work of Stevenson et al.[0] concludes that open diskectomy is more cost-effective. The discrepant results are explained by methodological as well as content related issues.

The main difference is caused by the largely differing success rates of APLD that were included in the calculations. Stevenson[0] includes success rates from the only available RCT which includes a study population matching widely accepted in- and exclusion criteria for APLD[32]. Dullerud[8] bases his calculation on more favourable data from two case series with unclear inclusion criteria for the patients treated. Heterogeneity of patient populations probably accounts for the largest part of variability in results. Results furthermore reflect the observation that case series often report more favourable results than controlled trials. More difficulties for the interpretation of results arise from the control procedure selected and from intransparently documented generation of cost data.

Chemonucleolysis

Two economic analyses from the 1990ies compare cost-effectiveness of chemonucleolysis and open diskectomy[17, 20]. Javid[17] based a cost-effectiveness analysis on results of a prospective cohort study. Launois[20] presents a modelling study comparing cost-effectiveness of chemonucleolysis and conventional diskectomy. In spite of methodological differences they arrive at same core conclusion: for carefully selected patients (with sciatic symptoms resistant to conservative care; non-dislocated, non-sequestered lumbar disc herniation) chemonucleolysis seems to be the more cost-effective treatment option.

Endoscopically assisted technologies with posterior access to the disc space

One HTA report from CEDIT (Comité d' Evaluation et de Diffusion des Innovations Technologiques)[25] reports a cost–minimisation analysis concerning this group of procedures based on data from the French hospital association Assistence Publique Hopiteaux de Paris (AP-HP). The authors conclude that the total perioperative costs for the endoscopic procedure in spite of necessary investments for new equipment may be lower than the costs for a standard procedure, due to shorter postoperative

stay in hospital. For several reasons these results can hardly be transferred to the German health care context: the procedure assessed (MED®, Sofamor-Danek) is not marketed any more; there are no long- or medium term efficacy data; costs obtained within the French hospital association are not comparable to those arising in the German context.

Our searches retrieved no studies analysing health economic consequences of manual percutaneous nucleotomy, percutaneous laser nucleotomy or endoscopically assisted procedures with postero-lateral access to the disc space.

Results from recently published case series indicate a permanently ongoing refining and remodelling of technologies as well as a widening of indication for minimally invasive surgery. Therefore, data from case series are not suitable to describe overall cost determinants.

DISCUSSION

Amount and quality of health economic data

Evidence to demonstrate efficacy and safety of the six groups of technologies assessed in this volume is very scarce. So it is not surprising that there are only a few studies assessing their economic implications. A comprehensive search strategy detected five economic analyses altogether (two for chemonucleolysis, two for APLD and one for endoscopically assisted surgery with posterior access).

Assessment of methodological quality using checklists developed by the GSWG-TAHC detected profound methodological and content related deficits. In part these deficits result from the scarcity of efficacy data which prohibits the use of sophisticated methods for economic evaluation. The deficits relate to insufficient description of qualitative and quantitative health effects and the lack of precisely defined time frames for analysis. In only one paper modelling of cost-effectiveness over a medium term time period (seven years) is undertaken[20]. Other deficits refer to conception and performance of analyses. The main problems here are non-transparent or superficial assessment of cost determinants and costs. This prohibits transferral of results into other health care systems. Further severe problem are the lack of sensitivity analyses and the only superficial discussion of possible bias in the economic analyses.

Content related problems are elicited by the choice of input data (costs, effectiveness data) and selection of the comparator (open diskectomy or microdiskectomy) for economic analyses.

The relevance of the published economic analyses for decision making in the context of the German health care system is further reduced by the fact that chemonucleolysis and APLD are hardly in use in Germany[39] and the MED® technology on which cost calculations by Maiza et al.[25] are based is not even marketed anymore.

Direct and indirect costs of minimally invasive lumbar disc surgery in the published literature

Information from the published literature concerning costs of minimally invasive surgical procedures is for the reasons named above rather scarce and hardly reliable.

All publications consistently state that direct medical costs of chemonucleolysis and APLD are lower than the costs of standard procedures. In case of endoscopically assisted procedures the same tendency is noted when length of hospital stay after the intervention is taken into consideration (this statement is based on the data from one French cost minimisation analysis.

A differential and quantative interpretation of economical data is hampered by the following problems:

- In some of the analyses DRG-based flat rates for costs are given without explanation of their quantity structure.
- In some of the analysis elicitation of costs for surgery is mentioned without documentation of quantity structure or prices.
- Not given or outdated basic years prohibit conversion and comparison of prices given in different currencies.

Direct non-medical and indirect costs were not analysed in the five economic publications.

For four (manual percutaneous nucleotomy, laser nucleotomy, endoscopically assisted procedures with posterolateral access, Laserforaminoplasty) of the six groups of technologies assessed in this volume no economic analyses were retrieved from

the published literature. For these technologies it was attempted to describe a quantity structure of direct costs from data derived from currently published case series.

Analysis of 26 case series published after 1997 demonstrated that the reports included only very few data that could be used to construct a quantity structure for economic analysis. Furthermore, data were extremely variable so that no generalisable information could be extracted.

So it must be concluded that there are no valid cost data for minimally invasive lumbar disc surgery available from the published literature.

Cost effectiveness of minimally invasive lumbar disc surgery

Cost-effectiveness analyses were retrieved from the literature for two of the six groups of procedures assessed: APLD and chemonucleolysis.

APLD

The two published Analyses yield contrary results. One favours APLD[8] the other one[0] favours microdisectomy as the more cost-effective intervention. The difference is mainly explained by the underlying different estimates of efficacy of APLD (29 % vs. 66 %). It has to be noted though that the more favourable estimates are derived from case series results, the unfavourable estimates are based on the results of the only published RCT. Cost estimates contribute to the differing results as well. Dullerud[8] and his co-workers use flat-rate prices for conventional diskectomy while calculating pure surgical costs for APLD. These two circumstances inevitably produce biased results in favour of APLD. Cost effectiveness calculations by Stevenson et al.[0] are possibly biased in favour on conventional surgery by giving high cost estimates for secondary procedures after failure of APLD.

Although methodological quality of Stevenson's[0] analysis is superior to that of Dullerud[8] its results can still not yield a basis for estimation of cost-effectiveness of APLD within the context of the German health cared system. On the one hand transferability of clinical data is doubtful on the other hand cost calculations are intransparently documented so that they are not comparable to costs arising in the German system.

Chemonucleolysis

Cost-effectiveness of chemonucleolysis was compared to that of open diskectomy in two analyses from the 1990ies. Despite of conceptual and content related differences both arrive at the core conclusion that chemonucleolysis, including the option of open re-operation after failure of the minimally invasive procedure, is more cost effective than primary open diskectomy. Both analyses are subject to methodological problems that compromise the validity of the core conclusion. Problems include use of open diskectomy as comparison (standard today is microdiskectomy), heterogeneity of patients included as well intransparent documented cost data. The model of Launois et al.[20] does not consider clinical improvement after failure of primary open diskectomy. All problems tend to bias the analyses to favour chemonucleolysis. The papers are not valid as a base for decision making in the context of the German health care system, especially against the background that chymopapain is currently not available in regular pharmaceutical trade.

Costs of minimally invasive surgery for lumbar disc herniation in Germany

This point cannot be clarified by data from the published literature. Economic analyses do not report transparent cost calculations which could be translated for the German context. Case series do not yield data that allow the construction of a quantity structure.

Publications from Germany reporting detailed cost information for lumbar disc surgery were not retrieved by our literature searches.

Research needs

As long as there are no valid data on efficacy, effectiveness and safety of minimally invasive disc surgery it makes little sense to ask for economic evaluations. Only against the background of valid effectiveness data cost-effectiveness can be calculated which could serve as a basis for decision-making. The conclusions of the medical assessment in this volume asked for more RCT and systematic evaluation of performance under conditions of routine care. Both types of evaluations could be accompanied by economical analyses.

CONJOINT CONCLUSIONS

Conclusions that can be drawn from the results of the present assessment refer in detail to the specified minimally-invasive procedures of lumbar disc surgery but they may also be considered exemplary for other fields where optimisation of results is attempted by technological development and widening of indications (e.g. total hip replacement[24]).

1. Compared to standard technologies (open diskectomy, microdiskectomy) and with the exception of chemonucleolysis, the developmental status of all other minimally-invasive procedures assessed must be termed experimental. To date there is no dependable evidence-base to recommend their use in routine clinical practice.

2. To create such a dependable evidence-base further research in two directions is needed:
   a) In order to validly clarify safety and efficacy of minimally invasive procedures compared to standard procedures RCT data are needed. The studies need to include adequate patient populations, use realistic controls (e.g. standard operative procedures or continued conservative care) and use standardised measurements of meaningful outcomes after adequate periods of time. These demands do not only express the view of decisionmakers and payers – they are also devised by the professions themselves[43, 42, 2, 26].

   b) Studies that are able to report effectiveness of the procedures under everyday practice conditions and furthermore have the potential to detect rare adverse effects are needed. In Sweden this type of data is yielded by national quality registries. On the one hand their data are used for quality improvement measures and on the other hand they allow comprehensive scientific evaluations.

3. Since the year of 2000 a continuous rise in utilisation of minimally-invasive lumbar disc surgery is observed among statutory health insurers. Examples from other areas of innovative surgical technologies (e.g. robot assisted total hip replacement) indicate that the rise will probably continue - especially because there are no legal barriers to hinder introduction of innovative treatments into routine hospital care. Upon request by payers or providers the "Gemeinsamer Bundesausschuss" may assess a treatments benefit, its necessity and cost-effectiveness as a prerequisite for coverage by the statutory health insurance. In the case of minimally-invasive disc surgery it would be advisable to examine the legal framework for covering procedures only if they are provided under evaluation conditions. While in Germany coverage under evaluation conditions is established practice in ambulatory health care only (“Modellvorhaben") examples from other European countries (Great Britain, Switzerland) demonstrate that it is also feasible for hospital based interventions. In order to assure protection for patients and providers and at the same time not hinder the further development of new and promising technologies provision under evaluation conditions could also be realised in the private health care market - although in this sector coverage is not by law linked to benefit, necessity and cost-effectiveness of an intervention.

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