Long-term outcome of lumbar disc herniation surgery

Studies on different influencing factors

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Printed by Intellecta Infolog, Gothenburg, Sweden 2010

ISBN: 978-91-628-8056-9

To my family

“Du är borta mycket mamma,

men du finns alltid med mig i mitt hjärta”

Leo

Contents

1. List of publications

This thesis is based on the following papers:

I. **Clinical factors of importance for outcome after lumbar disc herniation surgery.**
Rönnberg K, Lind B, Halldin K, Zoëga B, Gellerstedt M, Brisby H
Submitted

II. **Patients´ satisfaction with provided care/information and expectations on clinical outcome after lumbar disc herniation surgery.**
Rönnberg K, Lind B, Halldin K, Zoëga B, Gellerstedt M, Brisby H
Spine (Philh Pa 1976). 2007 Jan 15:32(2):256-61

III. **Peridural scar and its relation to clinical outcome: a randomized study on surgically treated lumbar disc herniation patients.**
Rönnberg K, Lind B, Gadeholt-Göthlin G, Halldin K, Zoëga B, Gellerstedt M, Brisby H
Eur Spine J. 2008 Dec; 17(12):1714-20. Epub 2008 Oct 23.

IV. **Health-related quality of life in surgically treated lumbar disc herniation patients- Long-term follow-up.**
Rönnberg K, Lind B, Halldin K, Zoëga B, Brisby H
Submitted

2. Abbreviations

CT	Computed Tomography
EQ-5D	The 5-dimensional scale of the EuroQol
HRQoL	Health Related Quality of Life
LBP	Low Back Pain
LDH	Lumbar Disc Herniation
MRI	Magnetic Resonance Imaging
ODI	Oswestry Disability Index
PLL	Posterior Longitudinal Ligament
SD	Standard Deviation
SLR	Straight Leg Raising
VAS	Visual Analogue Scale
ZDS	Zung Depression Scale

3. Abstract

Background: A majority of patients suffering from sciatica caused by lumbar disc herniation experience a positive natural history and respond well to non-surgical treatment. Patients who fail conservative treatment and are treated surgically have been reported to get satisfactory result in about 70-90% in short-term (1-2 year) follow-up. There are few long-term follow-up studies in this patient group. The surgical success of treatment can be evaluated by different methods. Outcome based on patients' satisfaction with treatment and health related quality of life after surgery has gained increasing interest in later years. Factors as age, sex, smoking, leg pain duration, working status, type/level of disc herniation and psychosocial factors have been demonstrated to be of importance for short-term results after lumbar disc herniation surgery. The effect of epidural scar on the clinical outcome is still a controversy.

Aims: The aims of the present studies were to investigate the following factors in patients undergoing lumbar disc herniation surgery in a prospective study design:

1) Possible predictive factors for short- and long-term result (2- and 5-10 years).

2) Patients satisfaction with care/preoperative information, if expectations on surgical results and ability to return to work are related to baseline characteristics and/or can predict self-reported outcome.

3) Scar development 6 and 24 months postoperatively on MRI, relationship between postoperative peridural scar formation and clinical outcome, and the possible effect of ADCON-L (a bioresorbable carbohydrate polymer gel) on scar size and patients' outcome

4) Influence of preoperative factors on HRQoL and the postoperative change of HRQoL (EQ-5D) over time.

Patients and methods: One-hundred-eighty-three patients undergoing lumbar disc herniation surgery were recruited for the studies. Questionnaires to collect baseline data, experienced preoperative information and care, expected and present work ability, expectations on improvement of physical functions/symptoms (leg- and back pain, sensibility and muscle function) and HRQoL were filled in preoperatively. The ZDS and ODI were used to measure preoperative depression and disability. One-hundred-eight patients underwent MRI at 6 and 24 month postoperatively and an independent radiologist

graded the size, location and development of the scar, by using a previously described scoring system.

Outcomes were evaluated at 2 and 5-10 (7.3) years after surgery. At both follow-ups a self-reported (subjective) outcome score was used. In addition an objective outcome score, assessed by an independent neurologist was used at the 2-year follow-up.

Results and conclusions: In about 70 % of the patients excellent or good overall result was reported at both the short and long-term follow-up, using objective as well as subjective outcome measurements. Long preoperative sick leave predicted lower degree of satisfaction with treatment at the 2-year follow-up. At the long-term follow-up long duration of symptoms as well as time of sick leave preoperatively were identified as negative predictors. A majority of patients undergoing lumbar disc herniation surgery were satisfied with pre- and postoperative care, but to a lesser extent satisfied with given information. Furthermore, patients with preoperative positive expectations on work return and lower (realistic) expectations on pain and physical recovery had a greater chance to experience satisfaction with the result of the surgical treatment. No significant association between the size or localization of postoperative peridural scar formation and clinical outcome could be detected. Furthermore no effects on scar formation using ADCON-L were found.

Key words: Lumbar disc herniation surgery, clinical outcome, long-term follow-up, scar formation, expectation, satisfaction, predictive factors, health related quality of life (HRQoL)

4. Sammanfattning på svenska (summary in Swedish)

Bakgrund: De flesta som drabbas av diskbråck i ländryggen tillfrisknar spontant utan kirurgisk behandling. De patienter som genomgår operation rapporterar i 70-90 % ett gott resultat på kort sikt. Det finns hittills få studier gjorda med långtidsuppföljng på kirurgisk behandling av diskbråck i ländryggen. Resultatet av en operation kan mätas på olika sätt och på senare år har det blivit mer populärt att använda patientens egen bedömning av resultatet samt att analysera patientens självskattade livskvalitet efter operationen. Även patientens förväntningar på behandlingsresultatet har föreslagits kunna ha betydelse. Faktorer som visat sig ha betydelse för det kirurgiska resultatet är ålder, kön, rökning, smärt duration, arbetsförmåga/sjukskrivning, typ/nivå på diskbråcket, psykologiska faktorer och funktionsstatus. Hos en del patienter kvarstår eller återkommer dock smärtan i benet och betydelsen av ärrbildning runt nervroten har diskuterats.

Mål: Målet var att besvara följande frågor gällande patienter som genomgår operation av ett lumbalt diskbråck i en prospektiv studie:

1) Finns det prediktiva faktorer som påverkar slutresultatet på kort respektive lång tid efter operationen (2- och 5-10 år).

2) Är patienter som opereras för lumbalt diskbråck nöjda med det bemötande och den information som ges preoperativt, är förväntningarna på operationsresultat samt återgång i arbete relaterade till basfaktorer och/eller kan dessa faktorer prediktera patientens egen bedömning av operationsresultatet.

3) Hur utvecklas det postoperativa ärret i ryggkanalen över tiden (6-24 månader). Påverkar storleken av eventuell ärrbildning runt nervstrukturerna slutresultatet? Kan man med hjälp av ADCON-L (bioresorberbar kolhydrat polymer gel) påverka graden av ärrbildning.

4) Finns det någon faktor preoperativt som påverkar hälsorelaterad livskvalitet efter operationen och hur förändras livskvaliteten över tid (efter 2- och 5-8 år) efter en diskbråcksoperation.

Patienter och metoder: 183 patienter inkluderades till de olika studierna.

Patienterna fyllde innan operation i formulär med uppgifter om demografiska basfakta,

smärt duration, arbetskapacitet, sjukskrivningstid, psykologiskt och funktionellt status, förväntningar på operationsresultatet och nöjdhet med preoperativt bemötande och given information. 108 av patienterna genomgick magnetkamera undersökning (MRT) vid 6 och 24 månader, för att visualisera eventuell ärrbildningen samt följa utvecklingen av ärrets storlek över tiden. Bilderna bedömdes av en oberoende radiolog. Uppföljning skedde 2 år efter operationen med frågeformulär, kliniskt besök och bedömning av en oberoende neurolog. Långtids uppföljningen bestod av ett validerat frågeformulär med frågor avseende operations resultat, arbetsförmåga, smärta ben/rygg, psykologiskt och funktionellt status vilket skickades hem till patienterna .

Resultat och slutsatser: Ca 70 % av patienterna bedöms objektivt och upplever själva (subjektivt) att de är nöjda med operationsresultatet. Patienter med lång sjukskrivningstid före operationen uppvisade ett sämre resultat vid både kort- och långtids uppföljningen, medan lång smärt duration preoperativt påverkade 2 årsresultatet negativt. Vi fann inget samband mellan förekomst av ärrbildning (lokalisation eller utbredning av ärret), och operationsresultatet varken på kort eller på lång sikt. De flesta patienterna var nöjda med bemötandet men endast hälften var nöjda med informationen de fick innan operationen. Patienter som förväntade sig att återgå i arbete efter operationen samt hade realistiska förväntningar på smärt- och funktionsförbättring skattade sig mer nöjda med operationsresultatet. De flesta patienterna upplevde ökad livskvalitet efter operationen både vid kort och vid långtids uppföljning. Vi kunde inte finna någon preoperativ faktor som predikterade för bättre livskvalitet vid uppföljningarna. Det uppmätta värdet på livskvalitet kom inte upp i samma nivå som friska personer i samma ålder vid någon av uppföljningarna.

Nyckelord: Lumbalt diskbråck, kirurgi, kliniskt resultat, långtidsuppföljning, ärrbildning, förväntningar, nöjd, prediktiva faktorer, Hälsorelaterad livskvalitet (HRQoL)

5. Introduction

In 1934 the condition of "disc herniation" was originally described by Mixter and Barr who proclaimed that a posterior rupture of the intervertebral disc allowed nuclear material to leak and cause compression of the adjacent spinal nerve root [1]. The lifetime prevalence for lumbar disc herniation (LDH) is about 1-2 % [2, 3]. In Sweden surgery for lumbar disc herniation is performed at a rate of about 20 per 100.000 inhabitants and year and disc surgery accounts for more than 40% of all lumbar spine surgical procedures in Sweden (homepage; www.4s.nu.) [4]. The Swedish register for lumbar spine surgery document data pre- and postoperative, including leg- and back pain (VAS), HRQoL, duration of pain and baseline data [5].

To confirm the diagnosis of disc herniation for a patient experiencing sciatic pain the patient history, including description of symptoms, the physical examination and the results of imaging investigation(s) (CT or MRI) are evaluated. A majority of the patients suffering from sciatica caused by a lumbar disc herniation experience a positive natural history and respond well to nonsurgical treatment [6, 7]. The advantages of disc surgery over non-surgical treatments have been reported to be better leg pain relief and a faster return to work [8-10]. Traditionally the evaluation of treatment (outcome) have been based on pain scales (VAS), return to work, functional status, imaging methods and surgery related complications. Recently, outcome based on patients' satisfaction with treatment [11, 12] or patients´ health related quality of life [10, 13, 14] after surgery has become popular.

Surgical treatment of symptomatic lumbar disc herniation has been reported to have a high success rate (70-95%), evaluated by validated outcome scores and patients satisfaction [9]. Outcome for surgically treated patients compared to conservative treated patients have been demonstrated to be superior at short-term follow-up (up to 1 year) but no differences has been demonstrated between treatments at long-term follow-up [15]. However, surgically treated patients have been demonstrated to experience a faster pain relief, improvement of function and satisfaction than non-surgical patients [16, 17].

Residual back- and leg pain and recurrent disc herniation remain the major postoperative problems [18].

6. Background

6.1 Disc anatomy and pathology

6.1.1 *Anatomy of the disc*

The intervertebral disc is the largest avascular structure in the human body and is mainly composed of proteoglycans and collagen (type 1 and 2) [19]. Its major role is mechanical, to bear and/or transmit loads arising from body weight and muscle activity. The intervertebral disc consists of three anatomical structures; nucleus pulposus, annulus fibrosus and the vertebral endplates. The nucleus pulposus is the water-rich (80%), gelatineous center of the disc. Annulus fibrosus encircle the nucleus pulposus and is made of collagen sheets, usually named lamellae. These are held together by proteoglycans and help to maintain the fluid within the tissue of the disc. The proteoglycan aggregates within the annulus fibrosus and the nucleus pulposus and gives the young disc its strengths and pliability.

Both the top and the bottom of each vertebra are capped with a thin cartilaginous pad called the vertebral endplates. The endplates are avascular and aneural in a healthy adult disc [20].

6.1.2 *Disc Degeneration*

Intervertebral disc degeneration visualized on MRI is commonly found in asymptomatic individuals over 50 years of age [21]. Natural degeneration due to aging cause the nucleus pulposus to become more fibrotic and less gel-like and initially the disc height is preserved [22, 23].

Pathologic disc degeneration is also named “deteriorated disc” [23] and are believed to start with a disruption or tear of the annulus fibrosus. A local inflammation thereafter occurs and macrophages, mast cells and growth factors infiltrate the injured disc and try to initiate repair of the annulus fibrosus [24]. However, there are no diagnostic methods

available to clearly differentiate between a normal aging of the disc and pathological disc deterioration.

Various factors have been suggested to influence disc degeneration; mechanical, genetic, shear stress or toxic factors [25, 26]. The most significant biochemical change and critical factor in intervertebral disc degeneration is the loss of proteoglycans [20, 27] . The decrease in proteoglycans leads to a lower water binding capacity of the disc. These biochemical changes has a major effect on the load bearing and commonly cause a degenerated lumbar discs to bulge posterior when the spine is loaded.

6.1.3 *Lumbar disc herniation*

Herniation of an intervertebral disc occurs when the outer layer of the disc, the annulus fibrosus, ruptures and allows disc material from the inner part, nucleus pulposus (NP) and sometimes also annulus fibrosus and material from the end plate, to leak out. If the leakage occurs posterior it leaks into the epidural space and may cause pressure on nervous structures and thereby initiate symptoms including sciatic pain.

A disc bulge may be the first step towards a disc herniation but may also stay as a bulge without any further rupture of the annulus fibrosus (figure 1a).

There is different ways to classify disc herniations and one of the most common classifications separate between protrusion, extrusion or sequestration of the disc (figure 1b-d) [23].

Herniated discs can take the form of ”protrusion” or “extrusion” based on the shape of the displaced material and they can be “contained” or “uncontained”. A contained disc herniation has an intact outer annulus.

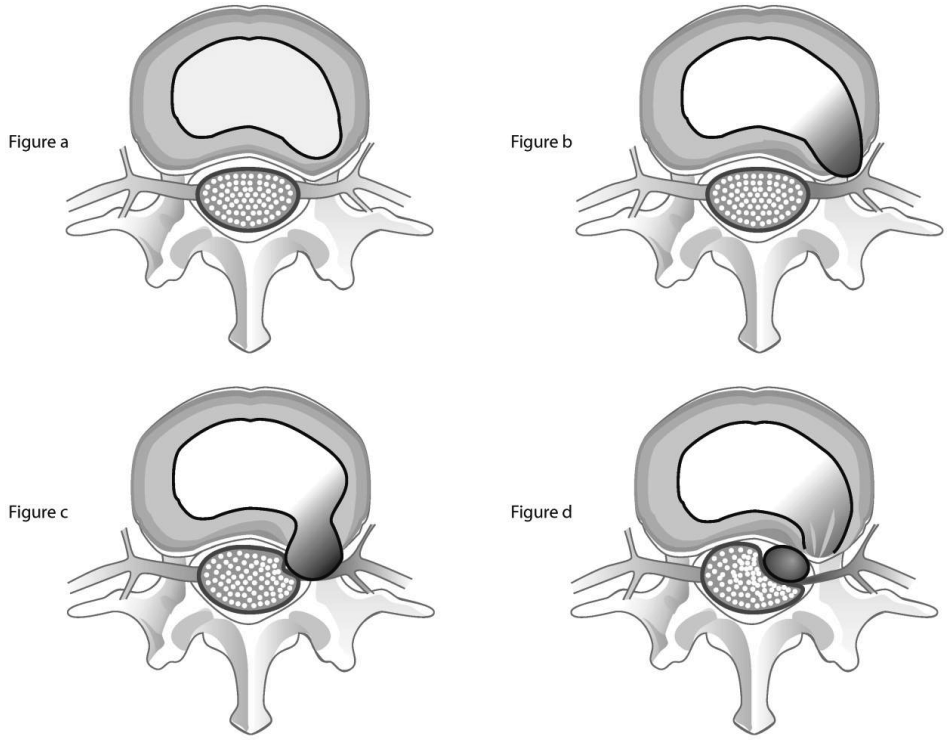

Figure 1a-d. a) *Disc bulge,* ***b)*** *Disc protrusion (located extraforaminal),* ***c)*** *Disc extrusion (located intraforaminal) and* ***d)*** *Sequestration (located within the spinal canal).*

Disc protrusion (figure 1b)

Disc protrusion is seen in about 30% of the normal non-symptomatic population [20]. The posterior longitudinal ligament (PLL) is still intact. The protrusion is focal or broad based, never wider than the base of the disc.

Extrusion (contained or un-contained, figure 1c)

Due to the classification of disc herniations by Fardon et al a disc extrusion is present when anyone distance between the edge of the disc material beyond the disc space is greater than the distance between the edges of the base, or when no continuity exists

between the disc material beyond the disc space and that within the disc space. Disc extrusion is less often seen in an asymptomatic individual.

Sequestration (free fragment, figure 1d)

The extrusion is named sequestration if the displaced disc material has lost continuity with the disc and loose disc material is present in the epidural space.

These larger disc lesions (sequestration and extrusions) have a great chance to be reabsorbed by the body, called "shrinkage phenomenon" [28, 29].

Most commonly a disc herniation that causes symptoms occur posterior or posteriolateral into the spinal canal. A disc herniation can also occur more lateral, without involvement of the spinal canal, but may here still be able to influence a nerve root (intraforaminally or extraforaminally).

Another type of disc herniation is the intraspongious disc herniation also known as Schmorl´s Nodes. These are herniation of nucleus pulposus into the trabecular bone of the vertebral endplates caused by weakness in the endplates. They have also been suggested to occur secondary to infection, metabolic diseases or trauma [30-32].

In studies on surgically treated patients, shorter duration of sciatica and significantly better functional outcome were seen in patients with contained herniations compared with patients with uncontained (sequestered or extruded) herniations [6, 9]. However, Halldin et al found no relation between the distribution or size of the herniation and outcome at 2-year follow-up in surgically treated patients [33]. Matsui et al. investigated the natural history of lumbar disc herniations using MRI in conservatively treated patients who were followed for 7 years. They did not find any association between the size of the herniation and clinical outcome [34].

Approximately 90 % of lumbar disc herniations occur at the two most caudal levels of the spine, the L4-L5 and L5-S1 level [35, 36].

Incidence

The lifetime incidence for lumbar disc herniation (LDH) with nerve root compression is about 1-2 % [2]. The incidence ranges from 1-10% [37]. For sciatica the lifetime incidence is about 40% [3].

Risk factors

A disc herniation occurs as a consequence of an annular rupture and can be viewed as a special form of disc degeneration. As described earlier the etiology of disc degeneration and thereby also disc herniation is multifactorial and related to factors as heredity [38-41], lifting/carrying and extreme forward bending [42, 43], hard-working [40, 41], lumbar load [40], cumulative physical workload [44], BMI over 25.7 [41], lack of sport activities and night shift works [45]. The main factors associated with LDH in children are trauma or sport activities with subsequent axial loading of the spine [46].

6.2 Symptoms

LBP is believed to often be the first symptom of a LDH and may also possibly be the only symptom. Sciatica is the most classical symptom, characterized by radiating pain with a dermatomal distribution, typically affecting one nerve root in the lumbar or sacral spine. Sometimes it is associated with sensory and/or motor deficits in the leg in accordance to the affected nerve root. The cauda equina syndrome is a special form of LDH where the herniated disc material occupies most of the space in the spinal canal. This serious condition involves sacral nerve roots and besides leading to uni- or bilateral sciatic pain, can cause bowel and/or bladder disturbances, lowers extremity muscle weakness and loss of sensibility and perineal or saddle paresthesia. This condition demands a more urgent attention compared to when a single nerve root is affected [47-49].

The radiating pain, sciatica, is not always caused solely by compression of the nerve root. It has been suggested to be a combination of chemical radiculopathy (neurotoxic agents) [50-53] and/or discogenic sciatica [54-56].

The symptoms of LDH in children are more often limited to LBP than in the adult but can also present as more classical radiculopathy. The diagnosis in young individuals may also be delayed by their somewhat different description of the pain experience and the fact that LDH is a rare diagnosis in children. The lumbar pain may only be present when coughing or bending forward. Neurological examinations are often negative and it is rare with bladder and genital dysfunctions [46, 57].

6.3 Diagnosis

The diagnosis is based on patient history (typically low back pain and/or dermatomally distributed sciatica), clinical examination (positive findings involve decreased tendon reflexes, sensory and/or motor deficits and positive SLR), and imaging findings (computed tomography (CT) or magnetic resonance imaging (MRI)). Most patients suffering from lumbar disc herniation have a positive straight leg raising test (SLR) or Lasegue´s sign [58-61]. The MRI technique has advantages compared to the CT with a better visualization of the soft tissue and the neural structures. However, the relationship between a disc herniation visualized by MRI (or CT) and the experience of sciatica are complex. Some patients have a disc herniation with possible nerve influence on images, but experience no pain [20, 34, 62, 63]. In addition patients who completely recover from an episode of back pain and sciatica, can demonstrate an unchanged disc herniation appearance on a follow-up MRI [29].

6.4 Treatments

6.4.1 *Non-surgical treatment*

A majority of the patients suffering from sciatica caused by a lumbar disc herniation experience a positive natural history and respond well to nonsurgical treatments [6].

The patients are recommended to live as normal as possible. Conservative treatment usually are based one or a combination of medical treatments (analgesics and NSAID) [64] and physical therapy, including some form of back exercises (e.g. McKenzie) [65] and stretching. Sometimes alternative treatments such as bone setting manipulation are used [66, 67]. The goals of non-surgical treatment strategies include both relief of sciatica pain and prevention of future sciatica symptoms.

6.4.2 *Surgical treatment*

In patients where conservative therapies have failed to gain improvement of leg pain and disability surgery may be performed. Persisting sciatic pain is the main reason for surgical treatment [68]. In children, surgery should be considered when neurological deficit or incapacitating pain occur [46]. The optimal timing of surgery is still a subject of debate. One study suggests that patients with sciatica for more than 12 months have a less favorable outcome [6] and in a recent study by Blazhevski et al the best result were found in patients with < 3 months duration of sciatica [69]. Sometimes sub-acute surgical treatment is necessary, when the patient suffer from great motor function loss or excruciating sciatic pain. However acute surgical treatment is indicated only in patients with a cauda equina syndrome [47, 48].

Surgical procedure

The goal of disc hernaition surgery is to decompress the affected nerve root by removing the herniated disc tissue. Most commonly open partial discectomy are performed. The patient is placed in a kneeling position or on the stomach on a bridge formed table. The level of LDH is usually marked using an imaging intensifier before the skin incision. A minimal midline approach is used to dissect the paravertebral muscles unilaterally down

to the laminae and thereafter the interlaminar ligament is resected. A partial laminotomy is performed when necessary. When the ligamentum flavum is resected the neuronal structures and the disc are visualized. Herniated disc material and loose fragments in the disc is removed to decompress the affected neural structures. The surgery is performed with or without microscope, due to the surgeons' preference. It has previously been demonstrated that the use of microscope does not effect the short-term (1-year) result [70]. The duration of hospital stay depends on the patient's mobility after surgery. The aim is that patients should be ambulated already at the day of the surgery. In some centers elective disc herniation surgery is planned as day surgery.

Results of surgical treatment

Reported early results of surgical discectomy have shown success rates of over 90% [9, 18, 71, 72]. Further, patients treated surgically have been reported to have better short-term outcome than conservative treated patients [9, 73]. Long-term results have been less positive with success rates of 40-79 % [74, 75]. Both short- and long-term studies have demonstrated higher recovery rates and more complete relief of leg pain, higher improvement of satisfaction with treatment and perceived recovery compared with patients treated non-surgically [16, 17, 72].

However, in the study by Weber et al. no significant differences in clinical outcome between surgically and non-surgically treated patients were found 4-10 years after surgery [15].

6.5 Outcome

6.5.1 *Predictive factors for outcome*

Many different parameters have been studied to identify predictive factors for outcome after LDH surgery. Some of these factors are intensity and duration of leg pain, Physical examination, gender, age, work and education level, social and psychological factors and type of herniation [76] [77-83]. Factors that have been identified to predict a positive

outcome (leg pain relief and/or satisfaction with surgical result and/or return to work) are short duration of preoperative leg pain [6, 84], no preoperative co-morbidity, male gender [85], age [86] and short time to surgery [69, 87]. Longstanding preoperative leg pain has been demonstrated to be a predictor for a less favorable outcome [6, 84, 88]. Heavy manual work and low education level [74, 89], female gender [13, 85, 86, 90, 91] contained herniation [9], disc protrusion [87] and central lumbar disc herniation [92] are other factors that may affect the outcome negatively.

6.5.2 *Outcome measurement*

There are many different ways to evaluate the outcome after lumbar disc herniation surgery. Traditionally the effect of treatment have been based on pain scales (VAS), return to work, functional status, imaging measurements and surgery related complications.

Outcome was earlier commonly assessed by the surgeon but in later year an independent observer (objective) or the patient itself (subjective) has been introduced to evaluate the outcome [93].

6.5.3 *Objective outcome*

The risk for bias decrease when using an independent observer not involved in the treatment of the patient, for assessment of surgical outcome. Objective outcome is often classified by scales related to postoperative pain relief, work capacity/sick leave, daily activity or analgesics consumption. These scales often use the scale; excellent, good, fair or poor. Odom`s criteria [94] and Mcnab`s classification of outcome [95, 96] are two such validated scales used in spinal surgery. They are demonstrated to correlate well with other validated outcome scores based on subjective outcome and patients´ satisfaction with treatment [12, 97].

6.5.4 *Subjective outcome*

There are several validated patient administered multi-item questionnaires used for patients surgically treated for spinal disorders. Most of them are based on back- and leg pain relief, daily living, physical activity, disability and social restriction.

The "Visual Analogue Scale" (VAS) is a pain scale used for visualizing the patients' pain in the clinical care of patients but also a well known outcome instrument for pain assessment often used in orthopedic conditions (e.g. in spinal surgery). Clarke and Spear introduced this instrument in medical science 1964, for assessment of wellbeing [98].

The "Oswestry Disability Index" (ODI) describes back-related disability with a combination of physical and social restrictions [99]. It has emerged as the most commonly recommended condition specific outcome for spinal disorders [100, 101]. ODI was developed by John O`Brian in 1976 and is based upon interviews by an orthopaedic surgeon and an occupational therapist of back pain patients. Based on these interviews they constructed a questionnaire made of 10 questions covering different dimensions of daily living.

Another patient based outcome measure is the global assessment scale where patient rate their satisfaction with the result or improvement of preoperative pain as satisfied, partly satisfied or not satisfied, or grade their improvement/no improvement with treatment as much better, better, unchanged or worse [11, 12, 102].

A good correlation has been demonstrated between patient based assessments and earlier validated objective outcome scores [102].

Expectations

Patients' expectations on a given treatment have been demonstrated to be associated with the success rate of the treatment and directly related to patients' satisfaction with the given treatment [12, 103-107]. Patients´ expectations appears to influence the postoperative outcome [108, 109] . There are different factors that can influence preoperative expectations, such as given information and care and influence from relatives and friends [12, 110-112]. Patients with high or positive expectations on surgical treatment of lumbar disc herniation have been demonstrated to have a better outcome, based on pain relief and recovery time [103, 113].

To assess patient expectations it is common to use preoperative questionnaires about expected improvement in physical function or expected ability to return to work and daily living.

Health related quality of life

WHO´s definition of health is "a state of complete physical, mental and social well-being and not merely the absence of infirmity" [114]. Quality of life is defined as "The individuals´ perceptions of their position in life, in the context of the cultural and value system in which they live and in relation to their goals, expectations, standards and concerns" [115]. The concept of health status and quality of life in medicine are widely used in different diagnoses [10, 13, 14, 80, 116-123]. In later year patients HRQoL has gained an increasing interest in health care evaluation and is often used in studies of patients undergoing spinal surgery [10, 13, 14, 74, 124, 125].

HRQoL measure an individual's health in the aspects of physical, psychological, social and spiritual role function as well as general well being [126]. These instruments are validated and for the patient easily used self-completed questionnaires.

A number of instruments have been development to measure HRQoL during the last years.

Disease specific instrument

Disease specific instruments are used for a specific disease or health problem.

Validated disease specific instrument commonly used in spinal disorders are the Million Index [127], the Oswestry Disability Index [99], the Low Back Outcome Score [128] and the Roland Morris Disability Index [129, 130].

Generic instrument

These instruments focus on descriptions of health status and allow comparisons between different study populations and disease groups.

The Medical Outcomes Survey 36-item Short-Form (SF-36) is one of the most used HRQoL questionnaires. The SF-36 includes 8 health concepts of functional health and well-being scores divided in equal amount of physical and mental components [131, 132].

Other instruments used in spinal research are Nottingham Health Profile [133] and the Duke Health Profile [134, 135].

Utility instrument

Utility instruments are designed to weight several dimensions into a single index which is used as a score expressing the total health state. With non-disease specific HRQoL instruments it is possibility to compare the effect of different medical conditions on the quality of life and these instruments all allows comparisons between different treatments on a specific condition.

Available instruments are, The Health Utility Index (HUI) [136], the Quality of Well-Being [132] and the EQ-5D [137].

EQ-5D Questionnaire

The EQ-5D is a non-disease specific instrument and thereby allows comparison between different medical conditions. The instrument consists of two different parts, EQ-5D score and EQ-VAS and is a patient self-administered multidimensional questionnaire [137].

The EQ-5D score comprises 5 dimensions; mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each of the dimensions is divided into three levels of severity; no problems, moderate problems or severe problems. This instrument creates 243 health states that have been ranged as EQ-5D index scores by a large UK population sample. The EQ-5D score thereby range from 0.00 (worse possible health state) and 1.00 (best possible health state). Some states are considered as "worse than death" and given negative values [138].

EQ-VAS is a global assessment of patient health, ranges from 0-100 representing "worst-best imaginable health state".

The result of the two-part questionnaire can be presented as a health profile or as a global health index. It has good reliability and validity [139]

6.5.5 *Radiological/imaging outcome*

Magnetic Resonance Imaging (MRI) is the preferred investigations for spinal diseases. The high resolution of MRI for soft tissues allows illustration of the intervertebral disc morphology and the nervous structures[140]. MRI makes it possible to classify the LDH preoperatively and to evaluate any eventual disc degeneration.

There are different ways to classify LDH by MRI. Komori et al graded the herniation after continuity of nucleus tissue to the remaining disc [141].

The relationship between different type or size of the herniation and outcome following lumbar disc herniation are well studied for both conservative and surgically treated patients [76, 92, 142].

The postoperative period after lumbar disc herniation surgery use to be divided into early (<6 months) and late stages. In the early stage it is difficult to interpret postoperative MRI following lumbar spine surgery and it is hard to differentiate recurrent disc herniation from post-surgical fibroses [143, 144].

The clinical significance of postoperative scar formation and outcome is debated.

Some authors have demonstrated a relationship between extensive peridural fibrosis diagnosed by MRI and increasing low back pain and/or recurrent radicular pain [145-147] whereas others have not [148]. To prevent or reduce postoperative peridural scar formation numerous synthetic and natural materials have been evaluated in both animal and human studies [149-155].

One of the materials is ADCON-L, a bioresorbable carbohydrate polymer gel. The purpose of this material is to cover the dura and nerve root(s), to form a protective membrane, until the fibrosis formation is completed [156-158].

7. Aims of the study

Overall the aim of the study was to study long-term result and different factors influencing the result in patients undergoing surgical treatment for a lumbar disc herniation using different outcome instruments.

More specific the aims of the study were to:

- Investigate the long-term result after lumbar disc hernaition surgery and possible predictive factors for surgical outcome, such as demographics, psychological, social or physiological.

- Investigate patients satisfaction with given care and given information in surgically treated disc herniation patients. To study possible relationships between baseline characteristics and expectations of surgical results and ability to return to work and if these expectations are related to self- reported global assessment (subjective) 2 years after surgery. To compare the patients' self-reported global assessed outcome with the independent observer´s (objective) assessed outcome 2 years after surgery.

- Study if there is any relationship between the size and/or location of peridural formed scar and clinical outcomes 2-year after lumbar discectomy. Analyze scar development between 6 and 24 months postoperatively by MRI and to study if ADCON-L has effect on scar size or and/or patients' outcome.

- Study the influence of preoperative factors on HRQoL and the postoperative development of HRQoL at 2-year and long-term follow-up, using the EQ-5D instrument, in lumbar disc herniation surgery patients.

8. Summary of studies

8.1 Materials and methods

Between September 1996 and March 2002, 183 consecutive patients surgically treated for a CT or MRI verified one-level disc herniation on L4-L5 or L5-S1 level, were recruited for the studies. Patients with other spinal disorders, previous spinal surgery, recurrent herniation at the same level, extra foraminal herniations, perioperative negative exploration or language difficulties were excluded.

The Regional Ethical Review Board approved all the studies and the patients gave their informed consent for participation.

Surgery

All patients were treated surgically at the department of Orthopaedics, Sahlgrenska University Hospital in Gothenburg. Six different spine surgeons performed the surgery.

By using a midline approach the paravertebral muscles were dissected down to laminae and the interlaminar ligaments resected. A partial laminotomy was performed when necessary. Herniated disc material and loose fragments from the disc was removed to decompress the affected neural structures. Postoperatively the patients were ambulated already at the end of the day of surgery.

Study I:

Patients

From the initially 183 recruited patients, 171 were included in this study. Twelve patients were excluded initially because of confusion of language, perioperative negative exploration, other spinal disorders or previous spinal surgery. One-hundred fifty-four (90%) of the patients completed the 2-year follow-up and 140 (82%) of the patients completed the long-term follow-up. Surgery was performed at L4-L5 level in 77 (45%) of the patients and 94 (55%) at L5-S1 level. The mean age was 39±11 years and 76 (44%) were women. Mean time to long-term follow-up was 7.3± 1.0 (5.1-9.3) years.

Preoperative data

For baseline data preoperative questionnaires were used. Gender, age, smoking habits, duration of leg pain, intensity of leg- and back pain (VAS), analgesics consumption, time to sick leave, degree of depression/anxiety (ZDS), disability (ODI) and employment status was recorded.

2-year follow-up data

Patients were followed-up by an independent observer, a neurologist, at the hospital. The independent observer assessed outcome (objective) based on Mcnab´s classification of postoperative outcome and graded the result as excellent, good, fair or poor.

Patients rated their satisfaction (subjective) with treatment as; satisfied, partly satisfied or not satisfied. Questionnaire about improvement in pain intensity (VAS), analgesics consumption, eventual sick leave, degree of depression/anxiety (ZDS), disability (ODI), and employment status was recorded.

Long-term follow-up data (5.1-9.3 years)

Follow-up questionnaires were sent by mail, and if the patient did not respond, up to two reminders were sent by mail after telephone contact.

Again patients rated the satisfaction with treatment, filled in questionnaires including pain intensity (VAS), sick leave, employment status, degree of depression/anxiety (ZDS) and disability (ODI).

Primary outcomes at 2-year and long-term follow-up

Objective outcome assessed by independent observer (at 2-year follow-up).

Subjective outcome based on patients´ satisfaction with treatment (at 2-year and long term follow-up).

Secondary outcomes at 2-year follow-up

Change in leg- and back pain (VAS), working capacity, analgesics consumption and need for sleeping pills.

Predictive factors investigated

Gender, age, smoking habits, level of disc hernia, use of analgesics, time on sick leave, duration of leg pain, baseline leg- and back pain (VAS), ZDS and ODI.

Statistical analysis

Objective and subjective outcome were dichotomized in the analyses. Objective outcome was categorized as excellent/good or fair/poor and subjective outcome was categorized as satisfied or partly/not satisfied. Potential relationships with predictors were analyzed by using chi-square test (categorical predictors), t-test (baseline data as a predictor) or the Mann Whitney U test. For multivariate analyses logistic regression was used and analyzed with a forward stepwise selection procedure to find the most influential predictor.

Study II:

Patients

This study included 172 patients. One-hundred forty-eight (86%) completed the 2-year follow-up (study population). The study population had a mean age of 40 (18-66) years, 68 (46%) of the patients were women and 66 (45%) underwent surgery at the L4-L5 level.. The originally included 172 patients in study II included one more patient than study I (171). This "extra" patient was a patient with negative exploration preoperatively. However this was not noticed until the analyze for study I which was performed after study II. The exclusion of this patient in study II would not in any way have changed any of the results.

Preoperative information and care

Preoperative the patient received information from the surgeon regarding the planned surgery about the surgical procedure, risks, expected time to sick leave and result.

Regarding the result the patient received information of expected improvement in pain relief, especially leg pain and of sensibility and muscle function.

A physiotherapist gave instruction and information about daily living postoperatively.

Information was also given by spine educated nurses employed at the ward.

Satisfaction with given information and care was evaluated by a non validated questionnaire composed of six different questions about information (figure 2) given preoperatively and seven different questions about given care (figure 3) with yes/no response.

"Have you received enough information about";

1. -Disc herniation?
2. -Your operation?
3. -Expected results after the operation?
4. -Eventually risks with the operation?
5. -Time for sick leave after the operation?
6. -Postoperative regimes?

Figure 2. *Questions about satisfaction with given information preoperatively*

1."Are you satisfied with the contact with your doctor"?
2. "Do you feel that you have got adequate information about your disease"?
3. "Do you feel that doctors and nurses care about you"?
4. "Do you feel that doctors and nurses understand your problems"?
5. "Do you understand what's wrong with you"?
6. "Do you feel that the doctor spent enough time with you"?
7. "Would you like to meet the same doctor again"?

Figure 3. *Questions about satisfaction with given care preoperatively*

Depending on how many “yes/no” answers the patient had they were deployed as “satisfied” or “dissatisfied” and dichotomized into two groups. To be assessed as “satisfied” with given information > 3 out of 6 questions must be answered as “yes” and likewise >4 out of 7 for given care.

Expectations

Before surgery patients were asked about their expectations on surgical result regarding pain intensity (leg- and back pain), sensibility and muscle function.

Expectations were assessed by using a non graded line with descriptions expected to “become worse”, “stay the same” or “become better” at the left, middle and the right of the line. Patient’s expectations were then graded as low, medium or high.

By using the same non graded line improvement at the two follow-up occasions was assessed as “got worse”, “no change” or “got better”. Preoperatively questions were asked about expectations on work ability postoperatively. Postoperatively the patients were asked about if they had returned to their workplace (or a similar work) after surgery.

Subjective and objective outcome

The patient rated their subjective outcome;”global assessment of satisfaction with treatment” as satisfied, partly or not satisfied. An independent neurologist assessed objective outcome based on Macnab´s classification on surgical outcome as excellent, good, fair or poor.

Preoperative data

Baseline data and degree of preoperative depression (ZDS), leg- and back pain intensity (VAS), duration of pain, disability (ODI), satisfaction with information and care, expectations on surgical result and work ability was collected from questionnaires.

2-year follow-up data

Improvement in leg- and back pain, sensibility, muscle function and work capacity was recorded. Patients rated their global assessment of satisfaction with treatment (subjective). Objective outcome was assessed as in study I.

Statistical analysis

All correlation coefficients (cc) presented are Spearman's rank correlations. Cross-tables were analyzed with standard chi-square tests or Fishers exact test. For analyses the relationship between dichotomous variables Mann-Whitney-U´s rank-sum test was used.

Study III:

Patients

Initially 128, out of the total 183 patients, were recruited for this study. The patients were peroperatively randomized into two groups, treated with ADCON–L (n=60) or not (controls) (n=48). During the follow-up period 6 patients underwent surgery for a recurrent herniation and 3 patients underwent spinal fusion surgery. Eleven were lost to follow-up. Of the remaining 108 patients (ADCON–L (n=60), controls (n=48)) 103 (95%) completed the MRI examination at 24 months, 99 (92%) filled in questionnaire about satisfaction at 2-year follow-up and 102 (94%) was examined by the independent observer.

The mean age was 39 years (18-66), 51 (47%) women and 48 (44%) underwent surgery at the L4-L5 level.

Surgery

All patients underwent the procedure of partial discectomy described above. Before closure of the surgical site the patients were randomized by envelope to receive ADCON-L (treated) or not (controls). For the treated group 3g of ADCON-L was applied to the surgical site, surrounding the nerve root, the thecal sac and the posterior longitudinal ligament, up to the lower surface of the lamina.

Magnet Resonance Imaging

All MRI scans were obtained at the same University Hospital. Most examinations were performed with 0.5-T imagers on Philips Gyroscan T5-NT. A small number of the examinations were made with 1.5 T imagers, Siemens Magnetom Vision Plus or Philips Gyroscan Inera T 15 due to technical reason.

Sagittal T2- and T1- weighted images and axial T1- and PD- weighted images were used and after intravenous Gadolinum injection, the sagittal and axial sequences were repeated. The T1 sagittal sequences were obtained using parameters of TR 492 ms/TE 10 ms with turbo spin echo (TSE), 35 cm field of view (FOV), a 256x189 matrix and 3 mm slice thickness with 0.3 mm spacing, T2 sagittal sequences by 3224 ms/130 ms (TR/TE) with TSE, a 35 cm FOV, a 256x170 matrix, 3.0 mm slice thickness with 0.3 mm spacing. PD axial sequences were acquired in the plane of the disc by a 1654 ms/40 ms (TR/TE) with TSE, 26 cm FOV, a 256x190 matrixes and 4.0 mm slice thickness with 0.4 mm spacing.

Slice thickness was 3 and 4 mm for sagittal and axial sequences, respectively for examinations with Philips Gyroscan T5-NT, and 4 mm for both sagittal and axial sequences for the other two imagers. The PD-weighted axial sequences were stacked slices, including the three most caudal lumbar intervertebral disks through the inferior aspect of S1. Axial T1-weighted sequences before and after Gadolinium were angled according to the lumbar disks L4-L5 and L5-S1.

An experienced independent neuroradiologist, blinded to treatment and clinical findings evaluated all the MRI images.

Scar evaluation

The evaluation included scar size, formation around the circumference of the nerve root, scar compression of the nerve and/or dura. The amount of scar was evaluated according to the grading system described by Ross et al. by using a score ranging from 0-4 (corresponding 0->75% scar) (figure 4) [146].

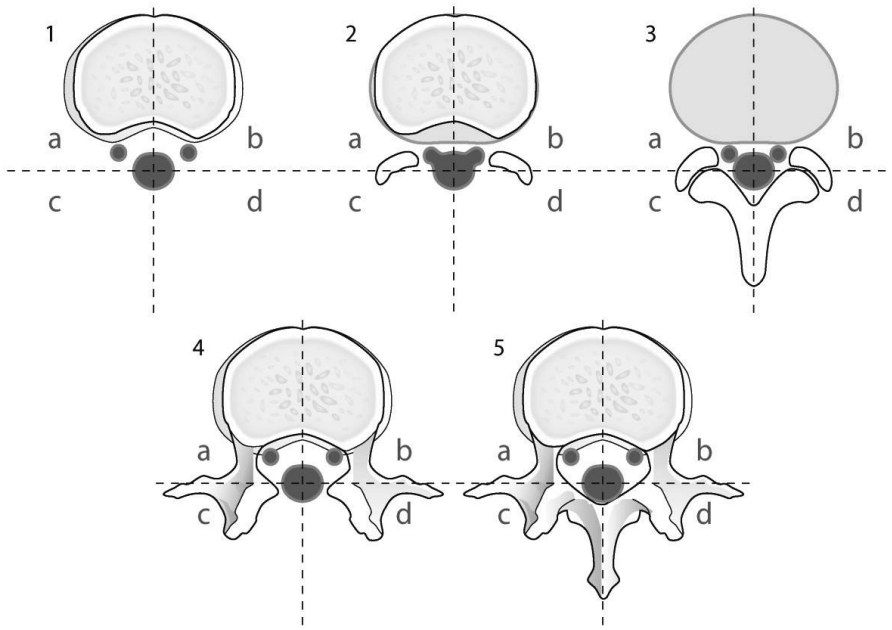

Figure 4. *Each MRI slice was divided into 4 spatial quadrants, 5 slices were available for evaluation (2 slices above-, 1 at- and 2 below the disc). For each patient this made 20 MRI quadrants available for evaluation. The quadrant with the most pronounced scar formation got the highest score and was used for calculation.*

Preoperative

Patients reported radicular pain by using VAS. Disc herniation was confirmed by a CT or MRI evaluation.

6 months follow-up

All included patients were examined with MRI using the "ADCON-L" protocol.

2-year follow-up

Examination with MRI was done with the "ADCON-L" protocol. Radicular leg pain was reported by using VAS. Satisfaction with treatment (subjective outcome) was rated by the patients as satisfied, partly satisfied or not satisfied. Objective outcome was examined by independent observer according to Macnab classification.

Statistical analysis

Non parametrical tests were used for qualitative data. For paired data, Wilcoxons signed rank test were used. For comparison between two independent groups, Mann-Whitney-U´s test, Kruskal-Wallis or a chi-square test was used.

Study IV:

Patients

In this study 117 consecutive patients surgically treated between September 1998 and March 2002 were included. One of the inclusion criteria was to complete the EQ-5D questionnaire preoperatively. The study population comprised 54 (46%) women and 49 (42%) men, mean age of 39±11 years. Forty-nine (42%) of the patients underwent surgery at the L4-L5 level and 68 (58%) at the L5-S1 level. Ninety-six (82%) of the patients completed the EQ-5D questionnaire at 2-year follow-up and 89 (76%) at the long-term follow-up.

Preoperative data

Baseline data questionnaires (gender, age, surgical level, duration of leg pain) and intensity of leg- and back pain (VAS) were filled in. HRQoL was measured with EQ-5D.

2-year follow-up data

VAS was used for reporting the intensity of leg- and back pain. EQ-5D was used for measurement of the patients HRQoL.

Long-term follow-up data

Leg- and back pain intensity (VAS) and HRQoL (EQ-5D) follow-up questionnaires were sent home to the patients by mail. If the patient did not respond up to two reminders were sent by mail.

Statistical analysis

SPSS software was used for statistical analyzes. Paired Samples t-test was used for analyzing differences in HRQoL at baseline and follow-ups. When comparing groups, Independent Sample t-test or ANOVA was used. For correlations between different variables nonparametric Spearman rank correlation test was used.

8.2 Results

Study I:

Preoperative baseline data

Baseline data are presented in table 1.

Primary outcomes: objective (2-year) and subjective (2-year and long-term)

Objective outcome was reported as excellent/good for 67% of the patients at 2-year follow-up. The same results was seen for subjective outcome where 67% of the patients rated their satisfaction with treatment as "satisfied", 28% "partly satisfied" and 5% as "not satisfied". At long-term follow-up 72% were satisfied, 24% partly satisfied and 4% not satisfied.

Predictive factors for primary outcome: objective (table 2)

Preoperative duration of leg pain less than 6 months (p=0.039) and preoperative time on sick leave shorter than 2 months (p=0.001) predicted for excellent/good result at the 2-year follow-up. Higher analgesics consumption (p=0.022) and a higher mean age (p=0.028) also predicted for excellent/good result at two year after surgery.

Predictive factors for primary outcome: subjective (table 2)

Time on sick leave less than 2 months preoperatively predicted a better satisfaction with treatment at both follow-ups (p=0.015 and p=0.028 respectively).

At long-term follow-up a preoperative duration of leg pain less than 6 months predicted for a higher degree of satisfaction (p=0.019).

Table 1. *Baseline data for patients included in study I*

Baseline data N=171	
Gender *(%)*	
Female	76 (44)
Male	95 (56)
Age *(years, mean ± SD)*	39 ±11
Smokers *(%)*	45 (27)
Surgical Level *(%)*	
L4-L5	77 (45)
L5-S1	94 (55)
VAS leg pain *(mean±SD)*	59±19
VAS back pain (mean±SD)	50±23
Duration leg pain *(months, %)*	
<6	61 (39)
6-12	49 (31)
>12	46 (30)
Employment status *(%)*	
Employed	123 (75)
Apply for job	15 (9)
Disability pension (because of back pain)	3 (2)
Disability pension (other reason)	4 (2.5)
National basic (old age) pension	4 (2.5)
Student	15 (9)
Analgesics *(%)*	
>1/day	92 (55)
1/day	22 (13)
Rarely	34 (20)
None	20 (12)
Length of sick leave *(months)*	
<2	42 (26)
2-3	71 (43)
>3	50 (31)
Zung Depression Scale *(20-80) Mean (range)*	43(46)
Oswestry Disability Index *(0-100)Mean (range)*	53(90)

Secondary outcomes and predictors (at the 2-year follow-up) (table 2)

VAS leg pain

Improvement of leg pain (VAS) was reported by 88% of the patients at the 2 year follow-up. There was a relationship between the improvement of VAS leg and a higher VAS leg baseline (p=0.008).

Further, improved leg pain at the 2-year follow-up was related to preoperative analgesic consumption (p=0.002), time on sick leave and ODI (p=0.04).

VAS back pain

Improvement in back pain (VAS) was reported by 77% of the patients. Patients with improved back pain (VAS) at 2-year follow-up reported a higher degree of back pain (VAS) at baseline (p=0.001).

Improved back pain (VAS) was also related to higher value on ZDS (p=0.045) and higher ODI (p=0.04).

Working capacity

53% reported full working capacity, 20% with minor limitations, 16% part-time and 11% were not able to work at all at the two year follow-up. Shorter duration of preoperative leg pain and a preoperative sick leave time less than 2 months was related to full working capacity at two year (p=0.014 and p<0.001 respectively).

Analgesics

Consumptions of analgesics were distributed as follows; 4% of the patients consumed analgesics more than once a day, 10% once a day, 38% rarely and 48% at the two year follow-up.

Higher VAS leg pain at baseline related to a higher consumption of analgesics at the two year follow-up (p=0.046) and a sick leave time less than 2 months was related to lower consumption of analgesics (p=0.002).

Sleeping pills

Sex percent of the patients reported a regular consumption of sleeping pills At the two year follow-up The use of sleeping pills regularly was related to time to sick leave longer than 3 months (p=0.008) and higher baseline value on ZDS (p=0.02) and on ODI (p=0.007).

Table 2. *Summary of significant predictors*

Outcomes	**Relations**
Primary outcome	**Significantly related to:**
Objective outcome at 2-year follow up	Age, duration of leg pain, sick leave, analgesics
Patients´ satisfaction at 2-year follow up	Sick leave
Patients´ satisfaction at long term follow up	Duration of leg pain, sick leave
Secondary outcome	**Significantly related to:**
Improved leg pain	Baseline leg pain, Analgesics, Sick leave, ODI
Improved back pain	Baseline back pain, ZDS, ODI
Working capacity	Duration of leg pain, sick leave
Analgesics	Baseline leg pain, Sick leave
Sleeping pills	Sick leave, ZDS, ODI

Multivariate analyses and forward stepwise regression model

The multivariate analyses showed no significant predictors either for objective or subjective outcome when using the full model of potential predictors.

The forward stepwise regression model selected time to sick leave as the most influential predictor for both objective outcome (p=0.014) and subjective outcome (p=0.017) at 2-year follow-up.

For improvement in VAS leg pain significant predictor was baseline VAS leg pain (p=0.039) for both multivariate analyze and forward stepwise regression model.

Regarding improvement in VAS back pain, ZDS was the only predictor for both models (p=0.049).

For working capacity (p=0.007) and analgesic consumption (p=0.002) time on sick leave was the only predictors for both models.

Finally, for use of sleeping pills time on sick leave followed by level of disc hernia and age was the most influential predictors.

Study II:

Information and care

Satisfaction with information and given care was reported by 46 % and 82 % respectively. Answers for each asked question about information and care pre- and 2 years postoperatively are presented in figure 5 and 6. High ZDS value correlated to a lower degree of satisfaction with given information (cc=0.202, p=0.031).

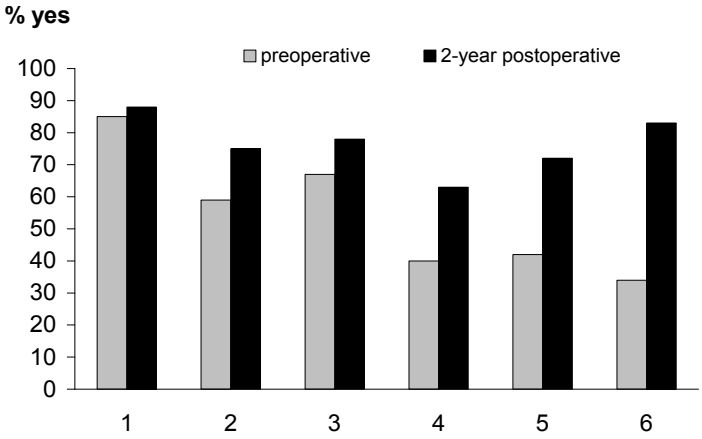

Figure 5. *Answers about given information, preoperative and 2-years follow-up.*

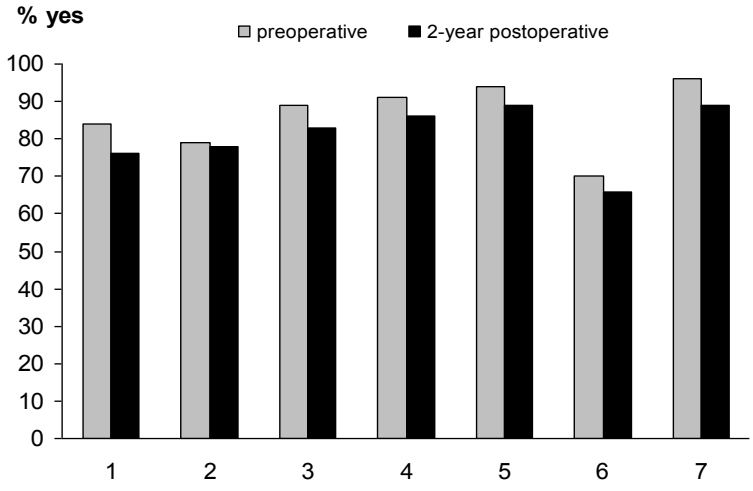

Figure 6. *Answers about given care, pre- and 2-years postoperatively.*

Expectations

A majority of the patients had high expectations on the surgical results, leg pain (94%), back pain (81%), sensibility (71%) and muscle function (72%). High expectations preoperatively were found to predict a better patient reported result 2 years postoperatively.

Expectations on ability to return to previous or similar work after surgery had a good correlation with the result at 2 year. 76% of the patients expected to return to work and 24% expected not to return and out of these respectively 78% and 26% returned to work ($p=0.021$). Patients who expected to return to work were more often satisfied with treatment (67%) than patients with low expectations where only 45% were satisfied with treatment after 2 years ($p=0.029$).

Patients with high value on ZDS had a lower degree of expectations on leg pain recovery ($p=0.022$) and ability to return to work ($p=0.046$).

Subjective and objective outcome

A high agreement between patients' satisfaction (66% satisfied) with result and independent assessment (67% excellent/good) was found ($p<0.001$). 86 % of the satisfied patients were assessed as excellent/good. In the small group of patient (6%) "not satisfied" no one was assessed as excellent/good by the independent observer.

There was a also a high agreement between satisfaction with treatment and recovery of all physical functions and symptoms ($p<0.001$)

Study III:

There were no significant differences in baseline parameters between ADCON-L- and the control group. The scar size decreased between 6- and 24 months in 49%, were unchanged in 42% and increased in 9% of the patients. Scar score at 6- and 24 months are presented in figure 7.

No relationship was found between scar size or scar location and clinical outcome (VAS leg pain, subjective and objective).

In this study no positive effects on scar size, or outcome in ADCON-L treated patients could be seen.

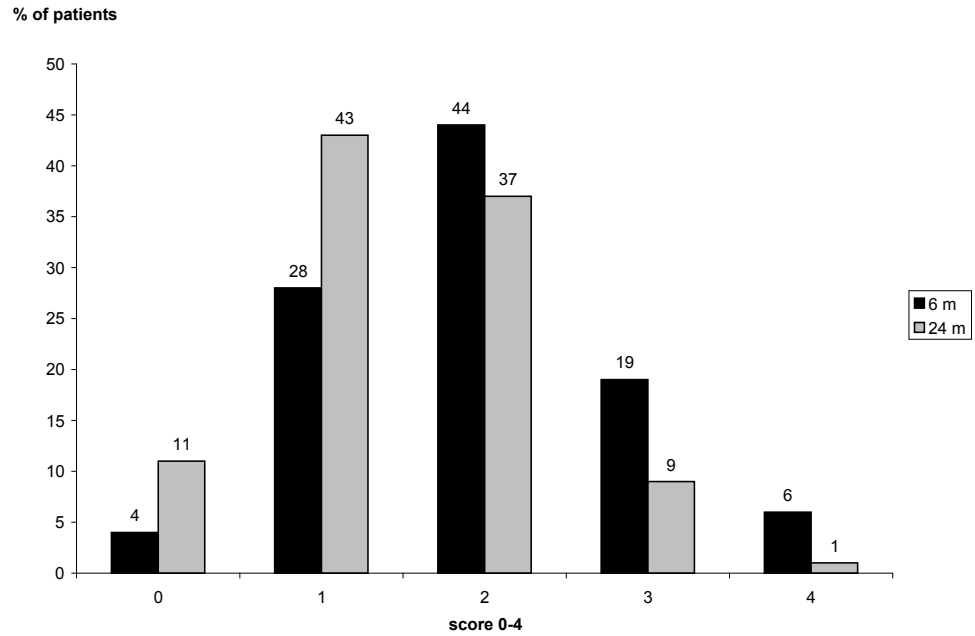

***Figure* 7**. *Scar score at 6 and 24 months postoperatively.*

Study IV:

EQ-5D

The mean follow-up time at long-term was 6.9 SD 1.0 (5.1-8.4) years. The EQ-5D score at baseline was 0.09 and improved significantly to 0.69 at 2-year follow-up ($p<0.001$) and from 0.12 to 0.73 at long-term follow-up ($p<0.001$). However, there was no correlation between baseline EQ-5D and the score at any follow-ups.

85% of the patients reported improved EQ-5D between baseline and 2-year follow-up and 91% between baseline and long-term follow-up.

There was a significant change in EQ-5D score between baseline and both follow-ups ($p<0.001$).

Baseline parameters and EQ-5D

None of the baseline factors predicted a higher improvement of EQ-5D score.

EQ-5D dimensions (figure 8a-c)

Severe problems were reported by a majority of the patients preoperative for the dimensions pain and mobility.

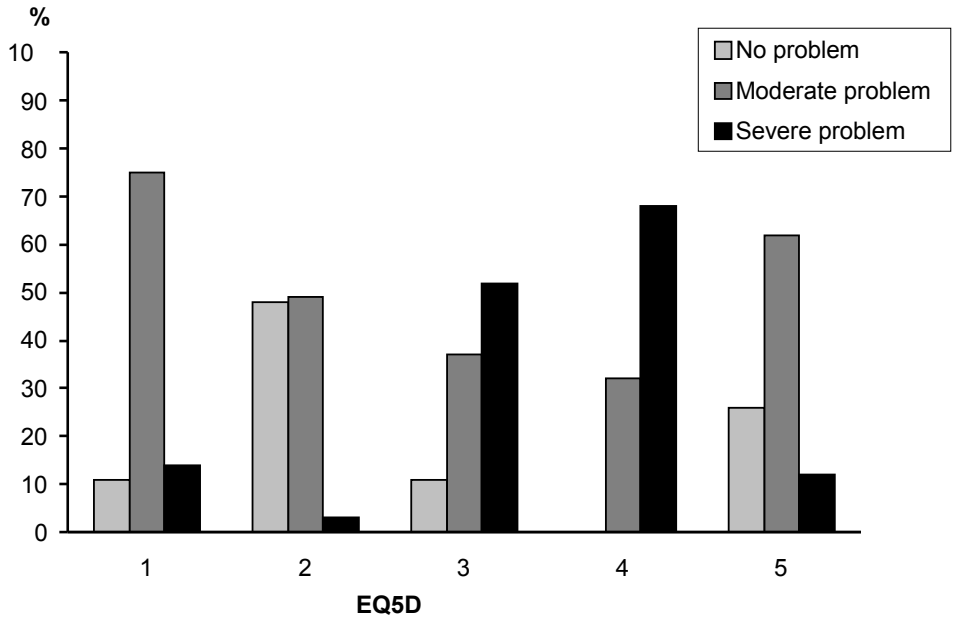

Figure 8a. *EQ-5D preoperative (N=117). 1=mobility, 2=self-care, 3=usual activities, 4=pain/discomfort, 5=anxiety/depression*

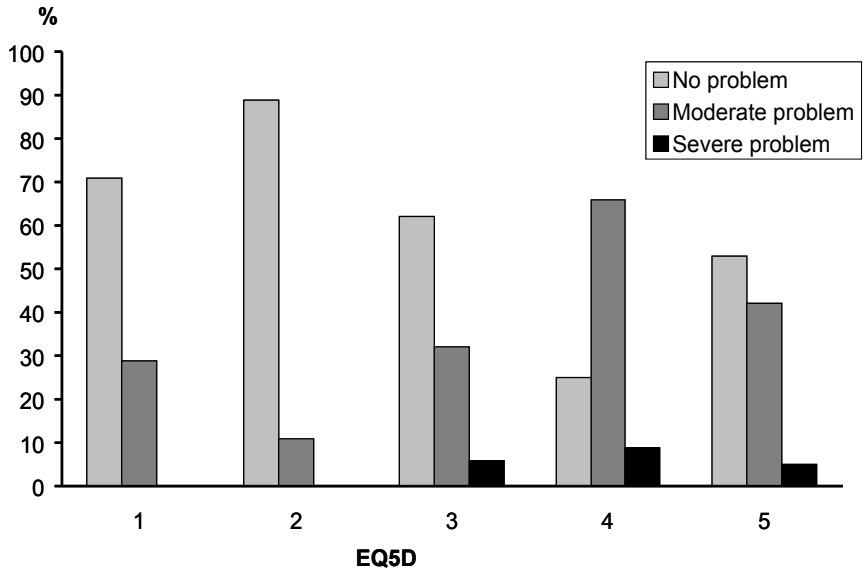

Figure 8b. *EQ-5D at 2-year follow-up (N=96). 1=mobility, 2=self-care, 3=usual activities, 4=pain/discomfort, 5=anxiety/depression*

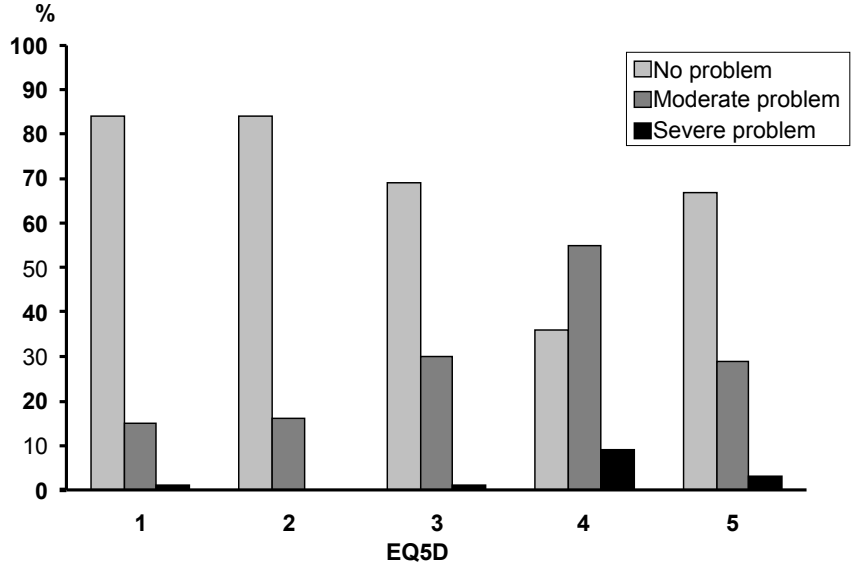

Figure 8c. *EQ-5D at long-term follow-up (N=89). 1=mobility, 2=self-care, 3=usual activities, 4=pain/discomfort, 5=anxiety/depression*

EQ-VAS

86% of the patients reported higher EQ-VAS after both follow-ups compared with baseline. The mean EQ-VAS improved from 38 to 71 at 2-year ($p<0.001$) and from 37 to 72 at long-term ($p<0.001$).

Correlation between EQ-5D score and back/leg pain (VAS)

There was a correlation between EQ-5D score and VAS back-and leg pain both preoperatively and at both follow-ups; VAS back pain (preop. R= -0.338, $p<0.001$, 2-year R=-0.750 $p<0.001$, long-term R=-0.692, $p<0.001$), VAS leg pain (preop. R= -398, $p<0.001$, 2-year R=-0.721, $p<0.001$, long-term R=-0.545, $p<0.001$)

Preoperative VAS leg pain correlated with EQ-5D change for both follow-ups, (2-year R=0.329, p=0.002, long-term R=0.230, p=0.036).

For preoperative VAS back pain no correlations with EQ-5D change at any of the follow-ups were seen. Neither, any correlations were seen between preoperative VAS back- or leg pain and EQ-5 D score at follow-ups.

Patients with limited increase/decrease in EQ-5D score

Patients (37%) with <0.5 increase of the preoperative EQ-5D score at long-term follow-up had a significant higher baseline EQ-5D score than patients with increase in score ≥0.5 . There were no significant differences in baseline data between these two groups but in the group that increased <0.5 we found a significant higher VAS back- and leg pain at both follow-ups (p=0.006).

9. General Discussion

In summary, the long-term result after lumbar disc herniation surgery is in our study satisfactory in about two out of three patients, based on patient satisfaction with treatment. Preoperative sick leave time was found to be a clinically important predictor for both subjective and objective outcome in the investigated patients. No association between peridural scar and clinical outcome was seen in this patient group. Neither could any association between the localization of scar formation in relation to nervous structures and clinical outcome be detected.

The patients in the present study were mostly satisfied with care pre- and postoperatively but to a lesser extent satisfied with given information preoperatively. Patients with preoperative positive expectations on work return and realistic expectations on pain and physical recovery had a greater chance to be satisfied with the results after lumbar disc herniation surgery compared to patients with negative and/or unrealistic expectations.

Based on HRQoL, more than 90% of the patients reported an improvement at both 2-year and long-term follow-up. However, they do not, as a group, obtain the health related quality of life level (as measured by EQ-5D) as a normal population at as long time as 5-8 years postoperatively.

Clinical outcome

In the present study 67% of the patient reported satisfaction with treatment after 2 year, 28% was partly satisfied and 5 % not satisfied. Objective assessment of the patients was in accordance with these findings. Further, more than 90 % of the patients reported an increase in EQ-5D score. The short-term results after surgical treatment of symptomatic lumbar disc herniation has previously been reported to have a high success rate (70-95%), evaluated by validated outcome scores, HRQoL and patients satisfaction [9, 10, 12, 18, 71]. The result from the present study is within the lower range of previous reports with both a somewhat low satisfaction with treatment rate and excellent/good objective assessed outcome frequency.

Long-term follow-up results were studied in study I and IV using subjective outcome, measured as satisfaction with treatment and as change in EQ-5D score (HRQoL).

Satisfaction with treatment was here reported by 72% of the patients and more than 90% of the patients reported improvement in HRQoL.

However, patients assigned to early surgery have previously been demonstrated to obtain a faster pain relief and recovery in short-term but less in long-term [15, 17, 72, 159]. Our study was in agreement with previously reported studies on long-term follow-up. Short-term result was less positive with a quite low satisfaction and objective assessed outcome. The explanation for the finding that our patient group, with a long mean waiting time for surgery, reached similar outcome levels at long-term, but had somewhat less improvement than in previous studies at the first follow-up, might be that the benefit from early surgery seen in other studies decrease over time. Our short-term results are in agreement with studies comparing conservative patients with surgically treated patients followed at long-term.

Predictive factors

Patients who fail to recover from sciatic pain are at risk to develop chronic pain syndromes which emphasizes the importance of identifying factors that can predict the outcome, both regarding short-term and long-term results. Therefore possible predictive factors for the surgical outcome are of interest.

In study Ⅰ we found that preoperative duration of leg pain less than 6 months were related to excellent/good outcome at both 2-year and long-term follow-up. Longstanding preoperative duration of leg pain has also previously been described as a predictor for bad outcome after lumbar discectomy [6, 84, 85].

The length of preoperative sick leave was identified as the most influential predictive factor, both for objective outcome and subjective outcome and for several of the secondary outcomes as well, in our study. In patients with a sick leave period shorter than 2 months the satisfactory outcome frequency at 2 year follow-up was about 80% both using objective and subjective assessments. Furthermore full working capacity was three times more common among patients with the shortest sick leave (<2 months) compared to patients with the longest sick leave period (>3 months). Analgesics consumption was also related to time on sick leave.The need for analgesics was twice as high in the group with a sick leave period >3 months compared to patients with sick leave time <2 months.

Finally, the chance to have an improvement of leg pain was higher (97% versus 78%) in the group with <2 months of sick leave compared to sick leave time >3 months.
In a previous study patients with long preoperative sick leave time were found to have less favorable outcome [160]. Further, in a study on work return after lumbar discectomy long preoperative sick leave also were demonstrated to be a negative predictor for work return [161].

Patients' satisfaction
The overall level of patient satisfaction with treatment was found to be in accordance with objective outcome assessed by the independent observer in the present study. Agreement between patient satisfaction and other outcome instruments has previously been demonstrated in studies on patients with chronic low back pain [102].
We found in study II further that only 46% and 75% respectively of the patients were satisfied pre- and 2-years postoperatively with the information regarding the procedure (disc herniation surgery) that was given. It has previously also been reported that patients are dissatisfied with the degree of information that they receive from their healthcare provider [159].
As could be expected the amount of satisfaction with information increased over time when the patients had obtained their own experience. This is in agreement with a study by MgGregor at al.[110]. Almost 80% of the patients in the present study were satisfied with given care both pre- and 2 years postoperatively.

The Quality theory suggests that, if an obtained result after an intervention is equal or better than a customer expects he or she will be satisfied. This theory seems applicable for medical treatments of patients where satisfaction has been demonstrated to be directly related to patient expectations [104, 106, 107].

Expectations

Almost all patients in the study had high expectations on recovery regarding reduced leg pain 2 years after surgery, which is in agreement with given information.

Different factors can influence expectations, such as known success rate with a given treatment, given information and care, personality trait, health and mood status and influence from relatives/friends [110, 111, 162]. In this study mood status was the only baseline characteristics that influenced the expectation on clinical outcome. A high value on ZDS was related to a low degree of expectations on leg pain recovery ($p=0.022$) and expectations on ability to return to work ($p=0.046$). Preoperative high expectations on reduced leg pain, improved sensibility and muscle function were all associated with better postoperative subjective outcome. Further, positive expectations on work return were associated with higher postoperative work return, increased physical function and satisfaction with treatment. Positive expectations have also in earlier studies been demonstrated to be associated with better health outcomes and have further been suggested to influence clinical outcome independently of the treatment itself [103, 106, 113, 163].

Postoperative scar formation

In study III we investigated the possible relation between postoperative scar formation and clinical outcome. There was a reduction in the presence and amount of scar tissue between MRI at 6 months compared to 24 months but no association between scar formation (size or localization) and clinical outcome at any time point was demonstrated. The relationship between the fibrotic tissues and the epidural structures (thecal sac and nerve roots) and clinical symptoms have been extensively debated. Some previous studies suggest that scar tissue is responsible for unfavorable outcome results after spinal surgery [145, 146, 164]. Our study is in agreement with the findings by Nygaard et al where no associations between the amounts of postoperative peridural scar formation or nerve root displacement and outcome 1 year after microdiscectomy for lumbar disc herniation was seen [148]. There has been an interest to investigate if anti-adhesion barriers would make a difference if applied peroperatively in patients undergoing disc herniation surgery. An effect of such a material would indirectly support the theory that the peridural scar causes

problems. One of the materials, ADCON-L, have been demonstrated to reduced scar formation and improved clinical outcome[146, 165] In the present study we could not find any positive effects of the anti-adhesion gel used, ADCON-L. It did not reduce the scar size nor did it improve the clinical outcome. This is in agreement with some other studies on ADCON-L [157, 166].

Health Related Quality of Life

A majority of the patients improved dramatically and significantly in HRQoL, measured by EQ-5D after surgical treatment of lumbar discectomy. There was a large improvement, expressed as a change in EQ-5D score, between baseline and the 2-year follow-up which then stayed relatively stable until the long-term follow-up.

The mean preoperative EQ-5D score in our patients was only 0.09 which is lower than been reported in previous studies on patients suffering from lumbar disc herniation [10, 13]. This could be related to the long waiting time for surgery. And when comparing the EQ-5D score to a previously described age correlated normal population our study group of operated disc herniation patients had a lower EQ-5D score at both follow-ups [167].

A strong correlation between EQ-5D and VAS back- and leg pain at baseline, 2-year and long-term follow-up was seen. Our results suggests that despite a significant improvement in EQ-5D score that the overall inferior result in this patients group are caused by a subgroup of patients still suffering from pain many years postoperatively. We did not find any correlation between the preoperative EQ-5D score and the postoperative score at any of the follow-ups.

10. Conclusions

- Long-term result after lumbar disc herniation surgery is in our study satisfactory in about two out of three patients based on patient satisfaction with treatment. Time on sick leave was an important predictor for outcome both at 2-year and at long-term follow-up (5.1-9.3 years)

- Dissatisfaction with preoperative information was found. Associations between expectations and lower mood, experienced surgical result and subjective outcome were found. Subjective outcome demonstrated high agreement with objective outcome at 2-year follow-up

- No association between peridural scar and clinical outcome were seen. No effect on ADCON-L at scar size and/or patients outcome.

- There was a strong correlation between EQ-5D and VAS back- and leg pain at baseline, 2-year and long-term follow-up. More than 90% of the patient reported an improvement in EQ-5D at both 2-year and long-term follow-up.

11. Future

Patient satisfaction is an important outcome after surgically treated lumbar disc herniation and satisfaction is closely related to both expectations and given information in this patient group. This highlights the importance of having the patient in focus when evaluation a given treatment.

If a decision is made about surgery, when conservative treatment have failed it is important to give disc herniation patients appropriate information which cause realistic expectations. Patients of today themselves seek information from many sources e.g. the internet and health-care providers need to be aware of this and advice and discuss more around this than traditionally has been done.

The findings that both sick leave time and leg pain duration influence postoperative results in this patient group indicates, what also previously has been suggested, that surgery should be performed after a relative short waiting time.

This highlights the importance of a well functioning health care organization, where time on the waiting list for clinical appointments as well as surgery do not delay the treatment.

12. Acknowledgements

I wish to express my sincere appreciation to all those who have helped and supported me in my research and with this thesis. Thanks especially to:

Helena Brisby, MD, Associate Professor, Department of Orthopaedics, Sahlgrenska University Hospital at University of Gothenburg, my tutor and friend, for exceptional encouragement and endless support in both clinical and scientific work.

Bengt Lind, MD, Associate Professor, Gothenburg Spine Center, co-tutor and former tutor, for guidance and support. For making me interested in spinal research and letting me start with my thesis.

Bjorn Zoëga, MD, PhD, Landspitali University Hospital, Reykjavik, Island, co-tutor, for exceptional guidance and relevant points of views.

Klas Halldin, MD, PhD, Department of Orthopaedics, Sahlgrenska University Hospital at University of Gothenburg, co-author, for sharing clinical and scientific experience and for being a fun former room-mate.

Martin Gellerstedt, PhD, Trollhättan/Uddevalla, co-author and statistical analyzes. So many times I wanted to give up with all these statistical "things" but you gave me so much support and pushed me further.

Gro Gadehol-Göthlin, MD, PhD, Department of Radiology, Sahlgrenska University Hospital at University of Gothenburg, co-author, thank you for making study III possible!

Lena Rutberg, MD, Department of Neurology, Sahlgrenska University Hospital at University of Gothenburg, for assessment of patients at 2-year follow-up.

Björn Rydevik, MD, Professor, Department of Orthopaedics, Head Section of Anesthesiology, Biomaterials and Orthopaedics, The Sahlgrenska Academy at University of Gothenburg, for your kind help and support.

Jón Karlsson, MD, Professor and Chairman, Department of Orthopaedics, Sahlgrenska University Hospital at University of Gothenburg, for good advice and support.

Jonas Thanner, MD, PhD and **Peter Nyberg**, MD, PhD as former Head of the Department of Orthopaedics, Sahlgrenska University Hospital
All my colleagues at the Spine section, Department of Orthopaedics and all other colleagues and friends at the Department of Orthopaedics, Sahlgrenska University Hospital.
Linda Johansson, secretary for academic guidance and help.
Jill Fallénius, secretary for help with editorial work, miss you!
Eva Fermén, secretary, for help with editorial work at long-term follow-up and for laughing and giving friendly support.
Pontus Andersson, for professional illustrations.

Barbro Rönnberg, my sister-in-law, for endless friendship and guidance through life, in good times and in bad.
Erika Löfstedt, my dearest friend. I told you so!
Carina Floberg, my close friend, for wonderful friendship.
All my friends in the military, KS14 medical platoon, NBG08 surgical unit and FS17. You are always on my mind!
Louise Lindblad, for everything we've been through during the last years, so many happy moments!
Monica Hyttmark Niska, FS17 FST, my room-mate, we did it!

My mother, **Ingrid**, for endless love and for always being there!
My father, **Arne**, who is not with us anymore, you are in my mind and in my heart!
My sisters, **Kicki, Ulla, Annika, Ulrica, Cilla** and my brothers, **Peter** and **Stefan,** for all your support in life.

My husband, **Mattias**, what would life be without you?
Finally to my dearest treasures, **Hanna**, **Emma** and **Leo** for all love and happy moments!

The studies were financially supported by grants from the Gothenburg Medical Society, Doktor Felix Néubergh Foundation , Marianne and Marcus Wallenberg Foundation and government grants under the LUA agreement.

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