Doctoral theses at NTNU, 2022:69

Mattis Aleksander Madsbu

Surgery for Lumbar Disc Herniation

Observational studies based on data from the Norwegian Registry for Spine Surgery

Doctoral thesis

NTNU
Norwegian University of Science and Technology
Thesis for the Degree of Philosophiae Doctor
Faculty of Medicine and Health Sciences
Department of Neuromedicine and Movement Science

NTNU
Norwegian University of Science and Technology

Mattis Aleksander Madsbu

Surgery for Lumbar Disc Herniation

Observational studies based on data from the Norwegian Registry for Spine Surgery

Thesis for the Degree of Philosophiae Doctor

Trondheim, March 2022

Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Neuromedicine and Movement Science

NTNU
Norwegian University of
Science and Technology

NTNU
Norwegian University of Science and Technology

Thesis for the Degree of Philosophiae Doctor

Faculty of Medicine and Health Sciences
Department of Neuromedicine and Movement Science

ISBN 978-82-326-5546-5 (printed ver.)
ISBN 978-82-326-6506-8 (electronic ver.)
ISSN 1503-8181 (printed ver.)
ISSN 2703-8084 (online ver.)

Doctoral theses at NTNU, 2022:69

Printed by NTNU Grafisk senter

Doctoral theses at NTNU, 2022:69

Mattis Aleksander Madsbu

Surgery for Lumbar Disc Herniation – Observational Studies based on data from the Norwegian Registry for Spine Surgery

SUMMARY IN NORWEGIAN

Degenerative rygglidelser er en vanlig årsak til smerter, nedsatt aktivitetsnivå og arbeidsmulighet for mennesker i hele verden. Det er i tillegg en større økonomisk byrde for samfunnet. En av de vanligste årsakene til spinalkirurgi er for skiveprolaps i korsryggen. Dette er en degenerativ rygglidelse som vanligst rammer de mellom 40 og 50 år. Mange pasienter har et forløp som ikke trenger behandling, men hos pasienter som ikke opplever bedring av sine symptomer kan kirurgi være indisert. Kirurgi for skiveprolaps gjennomføres med mikrokirurgisk teknikk. Denne doktogradsavhandlingen handler om behandlingsresultater etter kirurgisk behandling av skiveprolaps i korsryggen.

Vi har benyttet prospektivt innsamlet data fra *Det norske kvalitetsregisteret for ryggkirurgi* (NORSpine). Det har vært gjennomført mange store randomiserte studier som sammenligner kirurgi og konservativ ikke-kirurgisk behandling. I denne avhandlingen har vi kun fokusert på pasienter som mottar kirurgisk behandling. Mer spesifikt har vi utforsket behandlingsresultater mellom ulike aldersgrupper og private og offentlige behandlingsinstitusjoner. Eldre pasienter har ofte mye komorbiditet og et mer usikkert postoperativt forløp. Dette vanskeliggjør avgjørelsen om å anbefale kirurgi eller ikke. Vi lurte på om dette påvirker behandlingsresultater etter kirurgi. Derfor valgte vi å undersøke den eldre populasjonen som ble operert for LDH.

I den første studien viste vi at pasienter som er 65 år eller eldre rapportere tilsvarende resultater som yngre pasienter ett år etter kirurgi.

I den andre studien undersøkte vi om det var noen forskjell i behandlingsresultater mellom pasienter som opereres privat eller offentlig. Vi fant tilsvarende behandlingsresultater i de to gruppene.

I den tredje studien viste vi at overvektige pasienten opplevede tilsvarende resultater som ikke-overvektige pasienter, ett år etter kirurgi.

I den fjerde studien undersøkte vi effekten av røyking på resultater etter kirurgi. Ikke-røykere rapporterte betydelig større bedring ett år etter kirurgi sammenlignet med røykere.

I den femte studien rapporterte yngre pasienter tilsvarende resultater 1 år etter kirurgi, sammenlignet med en voksen pasientgruppe.

Oppsummert har viser våre studier at det generelt er sammenlignbare resultater etter kirurgi for skiveprolaps blant ulike pasientgrupper. Vi håper at disse resultatene vil hjelpe klinikere i sin hverdag i beslutningstaking samt hva man kan forvente av resultater etter kirurgi.

Candidatus medicinae Mattis Aleksander Madsbu
Institutt for Nevromedisin og Bevegelsesvitenskap, Norges Teknisk-Naturvitenskapelige Universitet
NTNU
Hovedveileder: Sasha Gulati
Biveileder: Øyvind Salvesen
Finansieringskilde: NTNU, Institutt for Nevromedisn og Bevegelsesvitenskap

Overnevnte avhandling er funnet verdig til å forsvares offentlig for graden Doctor Philosophiae.
Disputas finner sted fredag 11.mars 2022 kl 12.15.

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

The research for this thesis was done in the period 2017–2021, while I was completing medical studies at the Norwegian University of Science and Technology (NTNU), Trondheim, Norway, and later when starting my internship at Ålesund sjukehus, Ålesund, Norway. As a doctoral candidate, I was registered at the Department of Neuromedicine and Movement Science, at the Faculty of Medicine and Health Sciences, NTNU, Trondheim. My research work originated from a medical student research project, which was later developed into a PhD thesis.

As a young medical student with a keen interest in becoming involved in a research project at the Department of Neuromedicine and Movement Science, it was a true disappointment when my first hopeful approach was rejected. Ironically, it was Sasha Gulati who rejected me, because he had too much on his plate at the time. Fortunately, Professor Linda White at the Department of Neuromedicine and Movement Science encouraged me to visit Sasha in person to query the rejection. Although I was very anxious, we had a great discussion, and Sasha accepted me as a research student.

I am forever grateful to Sasha for being my main supervisor, good friend and for his devoting mentorship. He has, throughout this entire research period, provided me with quick feedback and dedicated guidance, enabling me to complete this thesis as well as other research projects.

Øyvind Salvesen has been my co-supervisor and has given us invaluable guidance and help with our statistical challenges, preferable after a cup of jet fuel strong coffee. I would also like to thank Ole Solheim for his “open door” policy, always taking his time to answer questions and discussing both research and non-research related topics.

Further I would like to thank my co-authors Øystein Nygaard, Sven Magnus Carlsen, Steinar Westin and Lise Øie.

A special thanks to Tore K. Solberg and the Norwegian Registry for Spine Surgery (NORSpine) for collecting and sharing of data from the spine registry. None of these studies would have been possible without this material.
I would also like to extend my gratitude to the department for neurosurgery for accepting me as a colleague during my 8 months of working there.

Last but not least, I would like to thank my family and friends for their invaluable support, continuous patience and thoughtful words.

PUBLICATIONS INCLUDED IN THE RESEARCH THESIS

PAPER I

Madsbu MA, Solberg TK, Salvesen Ø, Nygaard ØP, Gulati S. 2017. Surgery for lumbar disc herniation in individuals aged 65 and older: A multicenter observational study. *Jama Surgery* 152(5): 503–506.

PAPER II

Gulati S, Madsbu MA, Solberg TK, Sørlie A, Giannadakis C, Skram MK, Nygaard ØP Jakola AS. 2017. Lumbar microdiscectomy for sciatica in adolescents: A multicentre observational registry-based study. *Acta Neurochirurgica* 159(3): 509–516.

PAPER III

Madsbu MA, Salvesen Ø, Werner DAT, Franssen E, Weber C, Nygaard ØP, Solberg, TK, Gulati S. 2018. Surgery for herniated lumbar disc in daily tobacco smokers: A multicenter observational study. *World Neurosurgery* 108: e581–e587.

PAPER IV

Madsbu MA, Øie LR, Salvesen Ø, Vangen-Lønne V, Nygaard ØP, Solberg TK, Gulati S. 2018. Lumbar microdiscectomy in obese patients: A multicenter observational study. *World Neurosurgery* 110: e1004–e1010.

PAPER V

Madsbu MA, Salvesen Ø, Carlsen SM, Westin S, Onarheim K, Nygaard ØP, Solberg TK, Gulati S. 2020. Surgery for herniated lumbar disc in private vs. public hospitals: A pragmatic comparative effectiveness study. *Acta Neurochirurgica* 162(3): 703–711.

COMPLETE LIST OF PUBLICATIONS

1. **Surgery for lumbar disc herniation in individuals aged 65 and older: A multicenter observational study** Madsbu MA, Solberg TK, Salvesen Ø, Nygaard ØP, Gulati S. *Jama Surgery* 152(5): 503–506.

2. **Lumbar microdiscectomy for sciatica in adolescents: A multicenter observational registry-based study.** Gulati S, Madsbu MA, Solberg TK, Sørlie A, Giannadakis C, Skram MK, Nygaard ØP Jakola AS. *Acta Neurochirurgica* 159(3): 509–516.

3. **Surgery for herniated lumbar disc in daily tobacco smokers: A multicenter observational study.** Madsbu MA, Salvesen Ø, Werner DAT, Franssen E, Weber C, Nygaard ØP, Gulati S. *World Neurosurgery* 159(3): 509–516.

4. **Lumbar microdiscectomy in obese patients: A multicenter observational Study.** Madsbu MA, Øie LR, Salvesen Ø, Vangen-Lønne V, Nygaard ØP, Solberg TK, Gulati S. *World Neurosurgery* 110: e1004–e1010.

5. **Risk of intracranial hemorrhage (RICH) in users of oral antithrombotic drugs: Nationwide pharmacoepidemiologic study.** Gulati S, Solheim O, Carlsen SM, Øie LR, Jensberg H, Gulati AM, Madsbu MA, Giannadakis C, Jakola AS, Salvesen Ø. *PLoS One* 13(8): e0202575.

6. **Validation of intracranial hemorrhage in the Norwegian Patient Registry.** Øie LR, Madsbu MA, Giannadakis C, Vorhaug A, Jensberg H, Salvesen Ø, Gulati S. *Brain and Behavior* 8(2): e00900

7. **Functional outcome and survival following spontaneous intracerebral hemorrhage: A retrospective population-based study.** Øie LR, Madsbu Ma, Solheim O, Jakola AS, Giannadakis C, Vorhaug A, Padayachy L, Jensberg H, Dodick D, Salvesen Ø, Gulati S. *Brain and Behavior* 8(10): e01113.

8. **Surgery for herniated lumbar disc in private vs public hospitals: A pragmatic comparative effectiveness study**
   Madsbu MA, Salvesen Ø, Carlsen SM, Westin S, Onarheim K, Nygaard ØP, Solberg TK, Gulati S. *Acta Neurochirurgica* 162(3): 703–711.

9. **Surgery for extraforaminal lumbar disc herniation: a single center comparative observational study** Madsbu MA, Polak SB, Vangen-Lønne V, Salvesen Ø, Nygaard ØP, Solberg TK, Vleggeert-Lankamp CLAM, Gulati S. *Acta Neurochirurgica* 162(6): 1409-1415.

10. **Microdiscectomy for Lumbar Disc Herniation: A single-center Observational Study.** Vangen-Lønne V, Madsbu MA, Salvesen Ø, Nygaard ØP, Solberg TK, Sasha S. *World Neurosurgery* 137: e577-e583

11. **Can a Successful Outcome After Surgery for Lumbar Disc Herniation Be Defined by the Oswestry Disability Index Raw Score?**
    Werner DAT, Grotle M, Gulati S, Austevoll IM, Madsbu MA, Lønne G, Solberg TK. *Global Spine Journal 10(1): 47-54*

12. **Accuracy and complication rates of exernal ventricular drain placement with twist drill and bolt system versus standard trephine and tunnelation: A retrospective population-based study.** Mansoor N, Madsbu MA, Mansoor NM, Trønnes AN, Fredriksli OA, Savesen Ø, Jakola AS, Solheim O, Gulati S. *Acta Neurochirurgica* 162(4): 755-761.

ABBREVATIONS AND ACRONYMS

ASA	American Society of Anesthesiologists
BMI	Body mass index
CT	Computed tomography
DDD	Degenerative disc disease
EQ-5D	(EuroQol instrument)
HRQL	Health-related quality of life
LDH	Lumbar disc herniation
LMMs	Linear mixed models (linear mixed-effects models)
MCID	Minimal clinically important change
MIC	Minimal important change
MISS	Minimal invasive spine surgery
MRI	Magnetic resonance imaging
NRS	Numerical rating scale
ODI	Oswestry Disability Index
PRO	Patient-reported outcome
PROMs	Patient-reported outcome measurements

QoL	Quality of life
SLR	Straight leg raise *(*Lasègue's test*)*
VAS	Visual analogue scale

SUMMARY IN ENGLISH

Degenerative lumbar spine disorders are a leading cause of activity limitation and work absence throughout much of the world and places an enormous economic burden on the whole society ranging from individuals, families, communities, industry and all the way to governments.
The most common reason for spine surgery is persisting and/or intolerable pain due to sciatica caused by lumbar disc herniation (LDH). This is a degenerative spinal disorder that most often presents between the fourth and fifth decade of life. For most patients, the natural course of a herniated lumbar disc is favorable, and the consensus is that surgical treatment is offered if the pain in the lower back and radiating down the legs persists despite a period of conservative treatment. Surgery for LDH is now typically performed with a microsurgical technique (i.e., lumbar microdiscectomy).

The topic of this research thesis was to study outcomes after surgical treatment for lumbar disc herniation. Our research group have used prospectively collected data from the Norwegian Registry for Spine Surgery (NORspine) for all our studies. Several previous randomized clinical trials and cohort studies has been performed, comparing surgical to non-surgical treatment. In this thesis, I focus on the surgical treatment for LDH, specifically the surgical outcomes for different age groups, lifestyle risk factors, and with regards to private and public hospitals.

In **Study I,** we investigated surgical outcomes in the elderly population. Older patients often present with more comorbidity and often need longer postoperative recovery time, ultimately making the decision of recommending surgical treatment more difficult. We questioned if this could affect outcomes at one year following surgery. We found that patients 65 years of age or older reported similar improvement one year after surgery compared to younger patients.

In **Study II,** we wanted to investigate differences in clinical outcomes between adolescent and adult patients after surgery for LDH. Adolescent patients reported similar improvement compared to the adult population at 1 year.

In **Study III,** we assessed differences in clinical outcomes between smokers and non-smokers. At 1 year, smokers experienced less improvement after surgery for LDH compared to non-smokers.

In **Study IV,** we investigated results after surgery for LDH in obese patients. After comparing the results with non-obese patients, we demonstrated that obese patients had similar results.

In **Study V,** we examined if there was any difference in surgical outcome between patients operated in private vs public hospitals. After adjusting for baseline differences, we found equivalent outcomes between the two groups one year after surgery.

In summary, we have demonstrated that results after surgery for LDH were closely comparable, although with some few minor differences. Hopefully, our results will help clinicians in daily decision making when predicting clinical outcomes after surgery.

DEFINITIONS/KEY CONCEPTS

LUMBAR DISC HERNIATION

Symptoms of lumbar radiculopathy has been described as an illness since ancient times. The clinical diagnosis of lumbar disc herniation, however, was first recognized around the mid-1700s. The understanding has transformed from pain being caused by demonic forces to the deeper understanding we have today for degenerative spinal disorders (1).

Lumbar disc herniation is defined as a disorder affecting the intervertebral disc causing protrusion of the disc or parts of the disc (annulus fibrosus and/or nucleus polposus), sometimes resulting in pressure on the dural sac or a nerve root. Although disc herniations can occur in many parts of the spinal column, they most frequently occur at the L4-L5 and L5-S1 intervertebral disc space. Pressure on a nerve root can cause sciatica. The pathophysiological understanding of disc-related pain includes both biochemical and mechanical processes (2). Sciatica is radiating pain along the lower extremities corresponding to the anatomical course of the sciatic nerve and should not be categorized as lower back pain. Lumbar disc herniation is the most common cause of sciatica, also known as nerve root pain or radiculopathy (3). An example of an extruded lumbar disc herniation is shown in Figure 1.

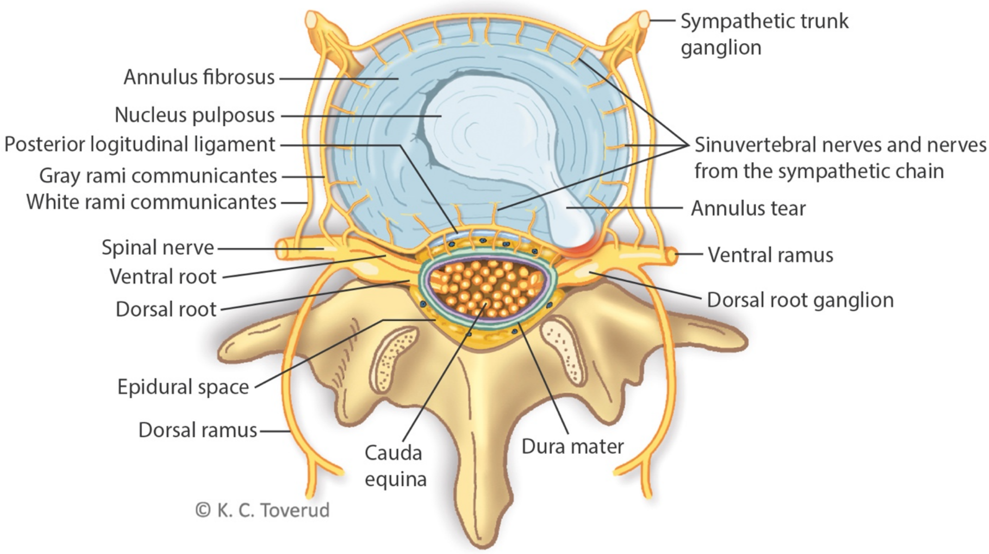

Figure 1: Anatomical illustration of an extruded lumbar disc herniation. Reproduced with permission from K. C. Toverud

EPIDEMIOLOGY: WHO SUFFERS FROM LUMBAR DISC HERNIATION?

Lumbar disc herniations are most common in people between 30 and 50 years of age(4). It is difficult to estimate the true prevalence of a lumbar disc herniation, as most are asymptomatic and estimated in epidemiological studies vary (5). The increased availability of MRI (magnetic resonance image) and CT (computed tomography) has led to increased diagnoses of bulging discs, and as a consequence the condition is now recognized as quite common. Several studies show that, at any given time, more than 50% of adults have bulging discs and up to 35% have asymptomatic lumbar disc herniations diagnosed on the basis of MRI (6-8). With regard to risk factors, some studies have linked disc herniation to cigarette smoking and vigorous physical activities. Genetic predisposition and environmental factors have also been suggested as potential causes(9).

DIAGNOSIS

Diagnosis of lumbar disc herniation is based on clinical consultation (patient history, neurological examination, specific tests such as the straight leg raise (SLR) test). If necessary, patients are referred to an MRI or CT to confirm the clinical suspicion, which potentially will initiate further treatment.

CLINICAL PRESENTATION

The most frequent patient complaint is sciatica. The debut of symptoms could be acute or progressively worsening over time. Sciatica can be described as sharp radiating pain, often starting at the level of the lower buttock, commencing down in one of the lower limbs. The exact pattern of radiating pain may vary depending on the level of the herniated disc and orientation (left, right, middle). A patient with a herniated disc at the L5 level would typically have a sharp aching pain starting at the buttock, radiating down dorsolateral in the corresponding leg. Patients may also experience paresthesia and loss of sensation in the dermatome, corresponding to the compressed nerve root (Table 1). Weakness in the foot can be present, and is often considered a more alarming symptom, where clinicians more often are faced with the dispute between surgical or non-surgical treatment.

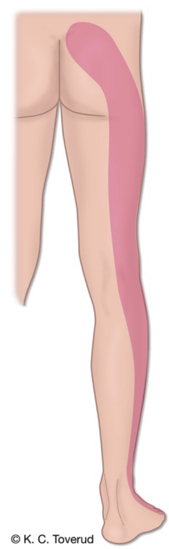

Figure 2: Illustrating L5 pain pattern
Reproduced with permission from K. C. Toverud

Table 1: Lumbosacral root affection

Localization	Sensory loss	Motor deficit	Reflexes
L1-L2	Anterolateral hip, anterior to medial aspect of thigh	Hip flexion Adduction of hip	-
L2-L3	Anterior aspect of thigh	Hip flexion Knee extension Adduction of hip	Adductor
L3-L4	Knee and medial aspect of leg	Knee extension	Patellar
L4-L5	Lateral leg to medial aspect of dorsal foot	Dorsal flexion of ankle and toes	Medial hamstring reflex
L5-S1	Lateral malleolus, lateral aspect of foot to 5. Toe	Plantar flexion of ankle and toes. Foot eversion	Achilles

Acute onset neurological symptoms such as substantial weakness in the lower limb or symptoms of cauda equina syndrome (Table 2) are emergency situations requiring hospital admission, and depending on radiological imaging potentially, immediate surgical intervention.

Table 2: Symptoms of cauda equina syndrome

Clinical diagnosis of cauda equina syndrome
Dysfunction of bladder, bowel, or sexual function Sensory changes in saddle or perianal area
Other possible symptoms
Back pain (with or without sciatic-like pain) Sensory changes or numbness in the lower limbs Lower limb weakness Reduction or loss of reflexes in the lower limbs Unilateral or bilateral symptoms

In the diagnosis of lumbar disc herniation, it is essential to evaluate if the pain is caused by spinal nerve root compression or if other causes of lower back pain/sciatica is more likely. This is especially important to evaluate the need of radiological imaging or other diagnostics measures. A clinician can perform several tests. The Lasègue´s test is probably the most common test. It is often referred to as “straight-leg raise” (SLR) test and is easily performed in an office setting. The patient is required to be in a relaxed supine position whilst the examiner raises the leg, fully extended. The test is considered positive if the patient experiences sciatic pain radiating from the buttock and below the knee with the leg raised between 30-70 degrees. Ultimately, a negative test makes the diagnosis of disc compression less likely, with a sensitivity of 90% and specificity of 28% (10). The examination findings must be interpreted with caution, taking the patient history into consideration.

In addition to the straight-leg raising test, there is a crossed straight-leg test, also known as the “Fajersztan´s test”. The test is performed in similar matter as the former. The test will be positive if sciatic pain is experienced in the affected leg, when the unaffected leg is raised. Compared with the SLR test, the crossed straight-leg test has a low sensitivity of 28% and a high specificity of 90% for disc herniation (10).

Table 3: Potential spinal and non-spinal causes of sciatica

Conditions causing sciatica
Spinal
Lumbar disc herniation
Osteoarthritis
Spinal stenosis
Spondylolisthesis
Synovial cysts
Arachnoid cysts
Spinal tumors
Inflammatory conditions
Non-spinal
Piriformis syndrome
Muscle spasms
Hip and pelvic fractures
Pregnancy related
Diabetes – peripheral neuropathy and polyneuropathy
Vascular impingement

Another commonly performed clinical examination is the Slump test. To perform the test, the patient is placed in a sitting position, with their back slightly flexed/slumped and with hips and both knees flexed to 90 degrees. Then, one knee is fully extended, and the patient is asked to flex the cervical spine. If pain is experienced in a radicular pattern, the test is considered positive. To increase the neural tension yet further, the examiner may also dorsiflex the ankle. The sensitivity and specificity of the Slump test is somewhat lower that Lasègue´s test and SLR test. In one study the sensitivity and specificity was estimated to be 84% and 83% respectively (11).

While all three tests are designed to reveal lumbar nerve root impingement or irritation, it is important to keep in mind that a positive test does not always indicate a herniated disc. The list of non-spinal causes of sciatica is long (Table 3) and can be a challenge for any clinician to differentiate from spinal causes.

RADIOLOGICAL IMAGING AND FINDINGS

Patients with lower back pain and/or sciatica are often referred to radiological imaging. MRI has become the gold standard and is the modality of choice for making the radiological diagnosis. Furthermore, high quality imaging is important for preoperative planning. However, one should emphasize the importance of only referring patients with a strong indication, where the results should influence further management. Coincidental findings on MRI scans (e.g disc bulges and protrusions) are quite normal, and can be confusing in asymptomatic patients or patients with a diffuse patient history (12). In worst case, undefined/minor changes could be interpreted as the cause of a patient´s complaints and potentially lead to unnecessary surgery/treatment. The main symptom leading to an MRI referral should be sciatica. However, many patients with lower back pain also experience radiating pain. In a study from Barzouhi et al. 91% of patients with sciatica alone, had a disc herniation on MRI, compared to only 76% of patients experiencing sciatica with disabling back pain in combination (13). Patients with progressive neurological deficits with acute onset radiculopathy or signs of cauda equina syndrome, should always be considered for an emergency MRI/CT.

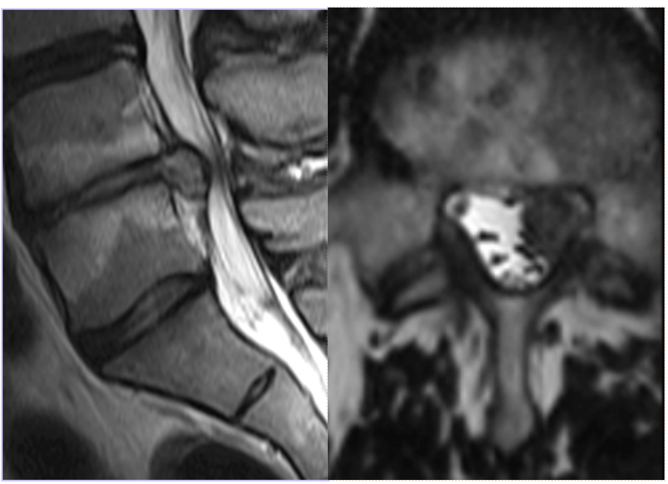

Figure 3: MRI showing a herniated lumbar disc in the L4-L5 disc space compressing the left nerve root. Reproduced with permission from Øystein Nygaard

SHOULD ALL DISC HERNIATIONS BE TREATED AND HOW?

The natural course for patients with symptomatic lumbar disc herniations is generally favorable. Most patients get symptom relief within a period of 3 months. Surgery is often offered to patients with persistent sciatica despite a period of conservative treatment, with a radiological image corresponding to the patient's complaints. (14).

NON-SURGICAL TREATMENT STRATEGIES

Most patients experiencing sciatica will be relieved of their symptoms within a relatively short amount of time. It is estimated in several studies that within 6-8 weeks, the majority of patients will experience a significant improvement of their leg pain (15-17). Even patients with initial paresis have been shown to have a high probability of recovery without surgery (18). Hence, the natural course of sciatica is in general considered to be favorable. Based on data from the Norwegian Registry for Spine Surgery (NORSpine), it is known that only approximately 5% of Norwegian patients with lumbar radiculopathy are operated, which similarly reflects that the condition has a favorable course.

For most patients, conservative treatment includes pain medication and physical therapy. NSAIDs, opioids, acetaminophen, glucocorticoids and other medications are often prescribed. However, it has been difficult to determine the true effect of pharmacological treatment in clinical studies (19-21). Epidural injections of glucocorticoids are also a conservative strategy that patients often are offered. Although it has been shown that it might provide a short-term relief of pain, the clinical evidence is somewhat inconsistent and long-term results are lacking. Conclusions about the true effect of epidural injections of glucocorticoids is therefore uncertain (22, 23).

Patients with lower back pain are often referred to physical or manual therapy. In several guidelines, the general recommendation is to stay active and avoid bed rest (24-27). Depending on the severity of each patients' symptoms, activity is often self-limiting. Some studies have provided evidence that bedrest is neither better or worse than either physiotherapy or no therapy (watchful waiting) (16, 17, 28). With regard to patients with lower back pain combined with sciatica, one recent randomized trial with 220 patients compared early physiotherapy with "usual care" and found that patients referred to early physiotherapy reported better outcomes (change in ODI), in both 6 months and 1 year follow-up studies (29). However, further evidence in supporting these findings is scarce.

SURGICAL INTERVENTION

There is general consensus that surgery should be offered to patients with persistent sciatica/radiculopathy after a period of conservative treatment (14). There are no clear guidelines on how long a patient may try conservative treatment before surgery should be offered. In cases where the pain is incapacitating and the patient is bedridden with strong pain medication, or in cases of severe progressive paresis, there are sometimes indication for earlier intervention. The goal is then to relieve the patient of pain and to prevent late sequela, such as permanent paresis and neuropathic pain. While surgical interventions have varied over time, the goal is still to relieve patients of symptoms and enable them to return to work and other daily activities more rapidly. However, the decision should be made jointly between the surgeon and the patient.

SURGICAL TECHNIQUES

Surgery for back pain and radicular pain has been frequently explored throughout history (1). The first acknowledged surgery for a ruptured interverbal disc was performed in 1932 by neurosurgeon Mixter and orthopedic surgeon Barr (30) performing an open discectomy. Over the next decades, the procedure became one of the most performed procedures by both neurosurgical and orthopedic surgeons.

Open discectomies are typically performed making a skin incision on the back, corresponding to the affected vertebrae. Further, muscle layers are retracted in order to visualize the bony structures of the spinal canal. A laminectomy is often performed to further identify the affected parts of the dural sac or nerve root, finally removing the herniated disc, either in parts or in toto. Visualization may be aided with the use of loupe magnification.

For a long time, open discectomy was the only surgical alternative. It was not until the late 1970s where Yasargil (31) and Caspar (32) independently introduced the technique of microdiscectomy for treating disc herniation, closely followed by Williams (33). The surgical technique is similar to the open discectomy but requires a smaller skin incision, thus making the procedure itself less traumatic for the patient and offers better visual control of the operation field. In most cases, a laminotomy/arcotomy (removing only parts of the lamina for better visualization) is adequate. While open discectomy still is an alternative for selected patients, microdiscectomy is now the most common procedure.

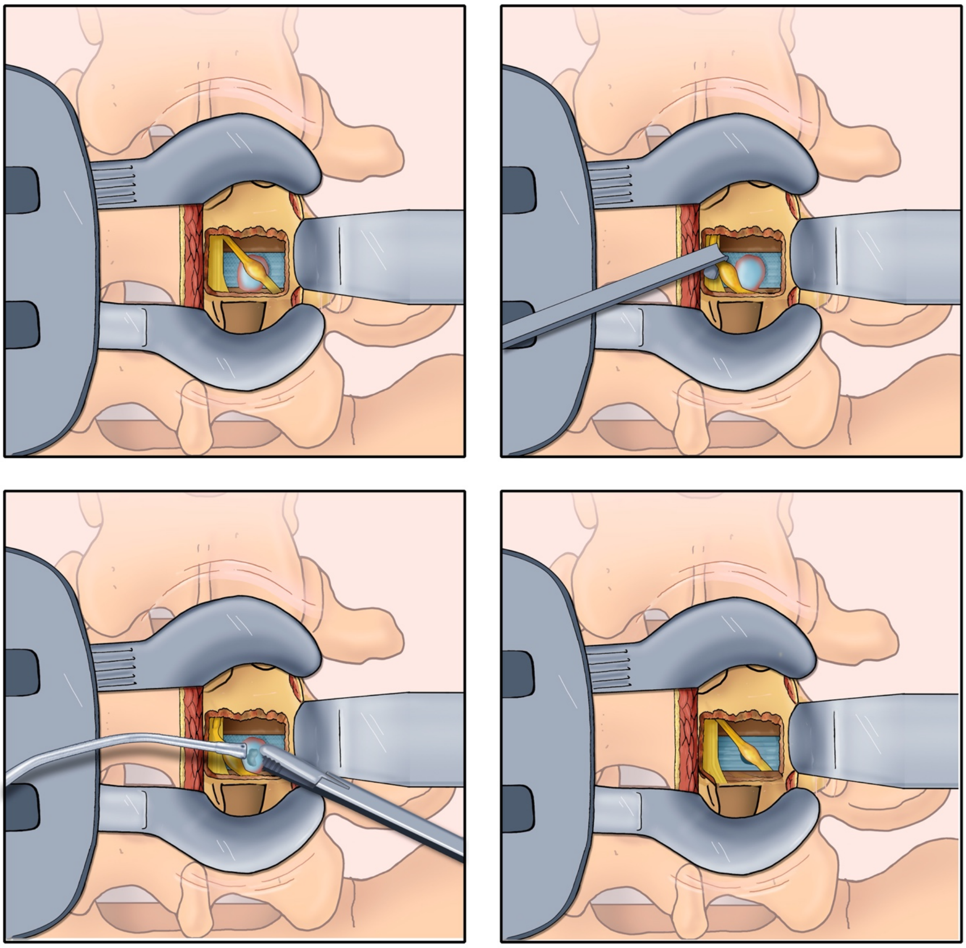

Figure 4: Illustrating a microdiscectomy approach using Caspar retractors. Reproduced with permission from K. C. Toverud

Several less invasive techniques have been developed since microscopes were first used during surgery. While Yasargil, Caspar and Williams introduced the popular microdiscectomy technique, several spinal surgeons have explored the use of other variants, such as the less invasive muscle splitting technique of Foley and Smith(34). Minimal invasive techniques include: microendoscopic discectomy, endoscopic discectomy, tubular discectomy, percutaneous manual nucleotomy and radiofrequency nucleoplasty.

COMPARISON OF SURGICAL TECHNIQUES

In a large pooled analysis in which open discectomy, microdiscectomy, and tubular discectomy were compared, it was not possible to determine whether one technique offered better results than other techniques (35).

The role of minimal transmuscular tubular discectomy and endoscopic discectomy is still unclear (36). Minimal invasive discectomy has shown a tendency to generate less pain for the patients, but possibly with suggested higher recurrence rates of LDH (37).

Table 4: Characteristics of different surgical techniques

Open discectomy	Microdiscectomy	Minimally invasive
Standard incision	Smaller skin incision	Smaller or no skin incision
Visualization may be through loop magnification	Excellent visualization in the field through microscope	Indirect visualization
Potential laminectomy	Potential laminotomy or hemilaminectomy	Minimal muscle/tissue trauma. Offers potentially quicker recovery
Hospitalization generally required	Outpatient treatment if suited	Outpatient treatment possible

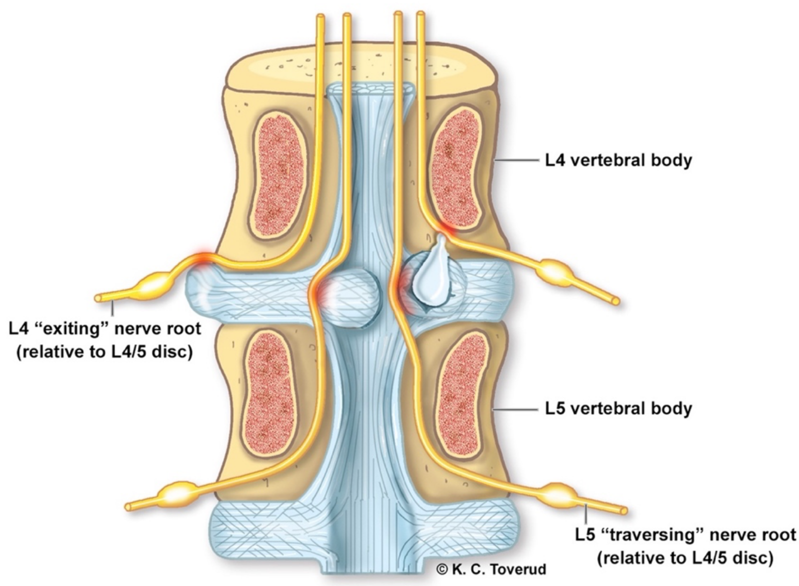

Figure 5: Illustrating different anatomical locations of disc herniations. Reproduced with permission from K. C. Toverud

RESULTS AFTER SURGERY FOR LUMBAR DISC HERNIATION

One of the most acknowledged randomized clinical trial on surgical treatment for lumbar disc herniation was the SPORT study, published in 2006. The study included 501 patients randomized to receive either surgery (“standard open discectomy”) or non-surgical treatment. All patients had a confirmed disc herniation with persistent sciatica of minimum 6 weeks. In addition to the randomized trial, they prospectively included a cohort consisting of initially eligible patients who had refused for undergo randomization.
Both studies had a follow-up time of 2 years, with outcomes assessed at 6 weeks, 3 months, 6 months, 1 year and 2 years. Outcomes were assessed using Short-Form 36 (SF-36) and a modified version of the Oswestry Disability Index (ODI).

The researcher concluded that after two years both groups reported similar improvement. The study had some important limitations, and the results must be interpretated with caution, especially considering the large amount of crossover from both surgical (50%) to non-surgical (30%) groups. In the separate cohort study, consisting of patients who refused to be randomized, surgery turned out to have superior outcomes for patients compared to non-surgical intervention. Conflicting results between these two studies, each of which had flaws and biases, ultimately made it difficult to claim superiority of one treatment modality.

In 2008, the same researcher used the combined data from both the SPORT trial and cohort study to produce a 4-year retrospective study, which demonstrated better outcomes for patients who had been treated surgically. Based on the same material, the authors presented the results of a 8-year results in 2014, and again the results were in favor of surgical intervention (38).

In the following years, several studies were published, each of which aimed to address the same study question: surgical or non-surgical intervention for LDH? Most of these studies found that surgical intervention resulted in faster relief of patients´ symptoms, but over time the differences in the outcomes of surgical and non-surgical management diminished (39-41).

The results of a large trial consisting of 283 patients who had had experienced severe sciatica for 6–12 weeks and had been randomized to early surgery vs. conservative treatment were presented by Peul et al. in 2007 (42). In the main analysis, utilizing the Roland-Morris Disability Questionnaire, pain relief was faster for patients who had received surgery, but after 1 year the outcomes were similar for the two groups. In a 2-year follow-up study, the investigators found that the clinical outcomes had remained unchanged between the two groups (41).

In a small, randomized trial that included only 56 patients randomized to either microdiscectomy or conservative treatment, no differences were found after 2-years follow-up (39). However, patients in the surgical group reported faster relief of symptoms compared with patients who received conservative treatment for only 6 weeks after surgery.

Two earlier prospective cohort studies, each with a 10-years follow-up period, led to conclusions mainly in favor of surgical treatment (43, 44). Both of these observational studies must be interpreted with caution considering the possibility of potential confounding factors.

Table 5: Selected studies comparing surgery to non-surgical intervention for LDH

Author	***Year***	***N***	***Study type***	***Primary outcome***	***Follow-up***	***Favoring results***
Weinstein et al (1)	*2006*	*n = 501*	*RCT*	*SF-36 and ODI*	*2 years*	*Inconclusive*
Weinstein et al (2)	*2006*	*n = 743*	*Obs. Cohort*	*SF-36 and ODI*	*2 years*	*Surgery*
Weinstein et al (3)	*2008*	*n = 1244*	*RCT + Cohort*	*SF-36 and ODI*	*4 years*	*Surgery*
Lurie et al (4)	*2014*	*n = 1244*	*RCT + Cohort*	*SF-36 and ODI*	*8 years*	*Surgery*
Peul et al (5)	*2007*	*n = 283*	*RCT*	*Roland disability Questionnaire*	*1 year*	*Inconclusive*
Peul et al (6)	*2008*	*n = 283*	*RCT*	*Roland disability Questionnaire*	*2 years*	*Inconclusive*
Lequin et al (7)	*2013*	*n = 231*	*RCT*	*Roland disability Questionnaire*	*5 years*	*Inconclusive*
Österman et al (8)	*2006*	*n = 56*	*RCT*	*Back & Leg pain*	*2 years*	*Inconclusive*
Bailey et al (9)	*2020*	*n = 128*	*RCT*	*VAS leg pain*	*6 months*	*Surgery*
Weber et al (10)	*1983*	*n =*	*Obs. Cohort*	*-*	*10 years*	*Surgery*
Atlas et al (11)	*2005*	*n = 400*	*Obs. Cohort*	*Back & Leg pain*	*10 years*	*Surgery*

The timing of surgery is always a difficult question, and scientific evidence is somewhat inconclusive in this regard. The biggest clinical trials have mainly included patients in the surgical intervention group with symptoms lasting from 6 weeks to 3 months (39, 41, 42, 45, 46). Furthermore, the authors of a systematic review of five different studies concluded that early surgery for patients with sciatica might provide better short-term relief of leg pain compared with prolonged conservative care (42). However, the supporting evidence is weak given that only one of the studies was examined in depth.

It is still uncertain as to how best to treat patients with symptoms persisting more than 3 months. Prolonged sciatic pain before receiving surgery has even been recognized to have a negative effect on the outcome (47, 48). A recent trial examining patients with radiculopathy lasting 4-12 months revealed that patients who underwent surgery showed greater improvement at 6 months of follow-up compared with patients who had received conservative treatment (49). Considering the results from other trials with longer follow-up time, long-term outcomes are needed before any firm conclusions can be drawn.

The cost-effectiveness of surgical intervention vs non-surgical intervention is difficult to measure. However, a study by van den Hout et al. found that early surgery resulted in faster return to work and was more cost-effective compared with conservative treatment (50). The cost-effectiveness of surgery has also been evaluated based on data from the SPORT study, where surgery was found to have higher costs than non-surgical management, but resulted in better health outcomes at two years (51).

Postoperative management regimes vary. Patients are frequently referred to physiotherapy or other forms of rehabilitation, either immediately after discharge or as a routine follow-up strategy some weeks later. Different active postoperative management strategies have been studied with variable results based on low-quality to moderate quality studies (52). In a recent multicenter randomized trial, early rehabilitation for 6-8 weeks vs. no referral immediately after discharge, was not found to be neither more effective nor cost-effective (53).

AIMS AND METHODOLOGICAL CONSIDERATIONS

PATIENT POPULATION

Data were collected through the Norwegian Registry for Spine Surgery (NORSpine). All patients in papers I-V are included in this registry. Norway has a public health care system with equal distribution of resources and uniform training and licensing of health care personnel. The population is homogenous and has been relatively stable. NORspine is a comprehensive registry for quality control and research. Currently, all 40 centers performing lumbar spine surgery in Norway report to NORspine. According to the Norwegian Directorate of Health approximately 63% of all patients who underwent lumbar spine surgery in Norway during the study period, January 2007 to May 2014, were included in NORspine. In general, the treatment centers that participated in this study had the same preferred surgical strategy for LDH without radiological instability. Surgery was performed by ipsilateral paravertebral muscle retraction and removal of the disc herniation under microscope magnification using a unilateral transflaval approach. It was not mandatory for data relating to either health care providers or patients to be reported to the NORspine registry. Moreover, neither patients' access to health care nor providers' payment was conditional upon reporting data to the registry. We screened patients who underwent surgery between January 2007 and May 2014 for eligibility. Follow-up time from the date of the operation was one year.

We considered patients eligible for inclusion in the study if they had a diagnosis of symptomatic paramedian lumbar disc herniation, surgery had been performed as a single-level lumbar microdiscectomy, and their data were included in the NORspine registry. Patients were excluded if they had undergone previous surgery on the lumbar spine, undergone fusion and/or open laminectomy as a surgical approach, or had associated spinal conditions (degenerative spondylolisthesis and/or scoliosis).

AIMS

Data from NORspine provided us a unique opportunity to assess surgical outcomes in patients that are typically omitted from randomized controlled trials. Using data from NORspine we wanted to investigate the following:

1. Outcomes following lumbar microdiscectomy in elderly patients
2. Outcomes following LDH surgery in adolescents
3. Outcomes following LDH surgery in tobacco smokers
4. Outcomes following surgery for LDH in obese patients
5. Outcomes following surgery for LDH in private vs public hospitals

OUTCOME MEASURES

PATIENT REPORTED OUTCOME MEASURES (PROMs)

In treating degenerative spinal disorders, it is our mission as treating doctors to reduce patients' symptoms, improve quality of life (QoL), and minimize any disability. In the research for this thesis, we used PROMs (patient-reported outcome measurements). There are several reasons for why PROMs are well suited for clinical research. They can provide other information than that assessed by researchers. They reflect patients' own understanding of their response to a given treatment, which is a major benefit as health care personnel often underestimate the side-effects and overestimate the benefits of therapies. However, using a validated scoring system such as Oswestry Disability Index (ODI) can reduce observer bias. Ultimately, PROMs may help clinicians to make well-informed decisions about patients' treatment options.

PRIMARY OUTCOME MEASURES

The primary outcome was change in disease specific functional outcome between baseline and 12 months' follow-up measured with version 2.1 of the Oswestry disability index (54), which has been translated into Norwegian and tested for psychometric properties (55). The Oswestry disability index questionnaire quantifies disability for degenerative conditions of the lumbar spine. It covers intensity of pain, ability to lift, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel. For each topic there are six statements describing potential scenarios, and patients select the one that most closely resembles their situation. The index is scored from 0 to 100. Zero means no disability and 100 reflects maximum disability.

SECONDARY OUTCOME MEASURES

Secondary outcome measures were changes between baseline and 12-months follow-up in generic health-related quality of life, measured with the generic Euro-Qol-5D (EQ-5D) and intensity of back pain and leg pain. The Norwegian version of EQ-5D has shown good psychometric properties (56). Intensity of pain was graded in two separate 0–10 numerical rating scales (NRS) for back pain and leg pain where 0 equals no pain and 10 represents the worst conceivable pain. The NRS pain scales and ODI have shown good validity and are frequently used in research on back pain (55, 56).

Additionally, we compared duration of procedures, length of hospital stays, reoperation at the index level within three months of surgery, and surgical complication rates. Surgeons provided the following complications and adverse events to NORspine: intraoperative hemorrhage blood replacement or postoperative hematoma, unintentional durotomy, cardiovascular complications, respiratory complications, anaphylactic reactions, and wrong level for surgery. Patients reported the following complications if occurring within three months of surgery: wound infection, urinary tract infection, micturition problems, pneumonia, pulmonary embolism, and deep vein thrombosis.

STATISTICAL CONSIDERATIONS

Statistical analyses were performed with SPSS version 23.0 (IBM Corporation, Chicago, IL, USA) and Software R (57). Statistical significance level was defined as $p \leq 0.05$ on the basis of a two-sided hypothesis test with no adjustments made for multiple comparisons. Central tendencies are presented as means when normally distributed and as medians when skewed. We used the Chi square test for categorical variables. Baseline and one-year scores were compared with paired-samples t-test. Mean change scores between the groups were analyzed with independent-samples t-test for complete cases and mixed linear models on all available data in most of the studies.

PROPENSITY MATCHING

To achieve equality, eliminate as many as possible confounding factors and provide best possible balance between the two groups, we generated propensity scores using logistic regression and adjusting for baseline covariates that could influence clinical outcomes, including age, sex, smoking, college/university education, partner, year of operation, BMI, ASA grade >2, relevant comorbidity, emergency operation, duration of sciatica >1year and preoperative ODI score. This was to achieve the closest approximate to a randomized clinical trial.

All covariates were entered into a logistic regression analysis, and we fitted a maximum likelihood model based on these covariates as predictors of private vs public treatment. The coefficients for these predictors of private vs public treatment were used to calculate a propensity score of 0 to 1 for each patient. Based on the calculated propensity scores, two evenly matched groups were formed for private and public treatment using a matching algorithm with the common caliper set at 0.010. This dataset is referred to as the "propensity matched cohort". We analyzed continuous variables using a related sample two tailed t test for data with a normal distribution and continuous data exhibiting a skewed distribution using the Wilcoxon signed rank test for matched pairs. We used the McNemar's test for correlated proportions to compare discrete variables.

MISSING DATA

Missing data is often a challenge in observational studies. In most of the studies (Papers I, III, IV, V) were handled with mixed linear models in most studies. The combination of exposure factor and time was taken as fixed effect and participant ID was specified as random effect. This strategy was in line with studies showing that it is not necessary to handle missing data using multiple imputations before performing a mixed model analyses on longitudinal data (58, 59).

REGRESSION ANALYSES

A multiple linear regression model was applied to assess the relationship between the change in ODI score at one year (dependent variable) and exposure factor, controlling for potential confounders. The selection of predictors included in the final model was based on their clinical importance and association with the dependent variable (60, 61).

ETHICAL APPROVEMENT

All studies were approved by the Regional Committee for Medical Research Ethics in Central Norway (REK midt, ID 2016/840) and all participants provided written informed consent. The registry protocols were approved by the Norwegian Data Protection Authority (Datatilsynet).

USER INVOLVEMENT

The Norwegian Back Pain Association (Ryggforeningen) is represented on the board of NORspine. Ryggforeningen reviewed the study protocol for the research reported in Paper II and provided feedback on the study design and outcome measures.

COMMUNICATION OF RESEARCH

All five studies are published in peer-reviewed medical journals. Study I is published in *JAMA Surgery*, currently the highest-ranking surgical journal in the world, and the study has been mentioned in more than 70 news outlets. The results have been presented at several medical conferences including oral presentations during plenary sessions at the annual meetings for the European Association of Neurological Societes. Study II was recently mentioned on the front page of the Norwegian tabloid *Dagbladet*. The results of Study II have also been presented on the website of the Norwegian Back Pain Association (Ryggforeningen).

SUMMARY OF PAPERS

PAPER I

Surgery for lumbar disc herniation in individuals aged 65 and older: A multicenter observational study

Madsbu MA, Solberg TK, Salvesen Ø, Nygaard ØP, Gulati S. *Jama Surgery 2017*

Background

Lumbar disc herniation (LDH) is a common cause of lower back and radiating leg pain (62). In most patients the natural course is favorable, and the international consensus is that surgical treatment is offered if the radiating pain persists despite a period of conservative treatment (14). Still, the condition is a major contributor to the global burden of disease and the most frequent indication for spinal surgery. Lumbar microdiscectomy is currently the most common surgical treatment for LDH (63), but data on surgical outcomes in the elderly are limited. The aim of this study was to compare patient-reported outcomes (PROM) following lumbar microdiscectomy in patients at least sixty-five years of age with younger patients.

Methods

Data were collected through the Norwegian Registry for Spine Surgery (NORspine), a comprehensive registry for quality control and research (64). Patients were eligible if they had a primary diagnosis of LDH and underwent non-emergency single-level lumbar microdiscectomy between 2007 and 2013. Patients were excluded who had undergone previous lumbar spine surgery or had coexisting spondylolisthesis or scoliosis. The primary outcome was change in disease specific functional outcome between baseline and 12 months' follow-up measured with the Oswestry disability index version 2.0 (ODI) (54). ODI is scored from 0-100, where zero means no disability and 100 reflects maximum disability. Secondary outcome measures were changes in health related quality of life, measured with the Euro-Qol-5D (EQ-5D), changes in low back pain and leg pain measured with numeric rating scales (NRS), surgical complications, and length of hospital stays. Patients completed the questionnaires on admission for surgery and after three and 12 months.

Results

There were 5195 patients <65 years and 381 patients ≥65 years. Baseline characteristics are presented in table 1. Loss to follow-up at one-year was 30.9% for the whole population, and 16.5% (n=63) in patients ≥65 years and 31.9% (n=1658) in patients <65 years (p<0.001). For all patients there was a significant improvement in ODI (difference 31.04 points, 95% CI 30.34, 31.74, p<0.001). Surgical outcomes are presented in table 2. There were no differences between age cohorts in mean changes of ODI (p=0.372), EQ-5D (p=0.929), or leg pain NRS (p=0.162), but elderly patients experienced more improvement in back pain NRS at 12 months (p=0.035). To manage missing data at 12 months, we used mixed linear model analyses and found similar results for all PROMs. At 12 months 84.2% of patients ≥65 years had achieved a minimal clinically important difference (≥10 points improvement in ODI), compared to 83.8% of younger patients (p=0.835). Patients ≥65 years experienced both more perioperative complications (4.2% vs 2.3%, p=0.019) and complications occurring within 3 months of hospital discharge (12.4% vs 5.4%, p<0.001), mainly due to more unintentional durotomies (2.9% vs 1.3%, p=0.015) and urinary tract infections (4.2% vs 1.3%, p<0.001). Younger patients had shorter hospital stays than patients ≥65 years (2.7 vs 1.8 days, p<0.001).

Conclusion

Although the patents 65 years of age or older had more minor complications and longer hospital stays, individuals aged 65 and older experienced improvement after lumbar microdiscectomy that was similar to that of younger individuals. Age alone should not be a contraindication to surgery, as long as the individual is fit for surgery.

PAPER II

Lumbar microdiscectomy for sciatica in adolescents: A multicentre observational registry-based study

Gulati S, Madsbu MA, Solberg TK, Sørlie A, Giannadakis C, Skram MK, Nygaard ØP, Jakola A. *Acta Neurochirurgica 2016*

Background

Lumbar disc herniation (LDH) is rare in the adolescent population. Factors predisposing to LDH in adolescents differ from adults with more cases being related to trauma or structural malformations. Further, there are limited data on patient-reported outcomes after lumbar microdiscectomy in adolescents. Our aim was to compare clinical outcomes at 1 year following single-level lumbar microdiscectomy in adolescents (13–19 years old) compared to younger adults (20–50 years old) with LDH.

Methods

Data were collected through the Norwegian Registry for Spine Surgery. Patients were eligible if they had radiculopathy due to LDH, underwent single-level lumbar microdiscectomy between January 2007 and May 2014, and were between 13 and 50 years old at time of surgery. The primary endpoint was change in Oswestry Disability Index (ODI) 1 year after surgery. Secondary endpoints were generic quality of life (EuroQol five dimensions [EQ-5D]), back pain numerical rating scale (NRS), leg pain NRS and complications.

Results

A total of 3,245 patients were included (97 patients13–19 years old and 3,148 patients 20–50 years old). A significant improvement in ODI was observed for the whole population, but there was no difference between groups (0.6;95% CI, −4.5 to 5.8; p = 0.811). There were no differences between groups concerning EQ-5D (−0.04; 95% CI, −0.15 to 0.07; p = 0.442), back pain NRS (−0.4; 95% CI, −1.2 to 0.4; p = 0.279), leg pain NRS (−0.4; 95% CI, −1.2 to 0.5; p = 0.374) or perioperative complications (1.0% for adolescents, 5.1% for adults, p = 0.072).

Conclusions

The effectiveness and safety of single-level microdiscectomy are similar in adolescents and the adult population at 1-year follow-up.

PAPER III

Surgery for herniated lumbar disc in daily tobacco smokers: A multicenter observational study. Madsbu MA, Salvesen Ø, Werner DAT, Franssen E, Weber C, Nygaard ØP, Gulati S. *World Neurosurgery 2018*

Objective

To compare clinical outcomes at 1 year following single level lumbar microdiscectomy in daily tobacco smokers and nonsmokers.

Methods

Data were collected through the Norwegian Registry for Spine Surgery. The primary endpoint was a change in Oswestry Dissability Index (ODI) at 1 year. Secondary endpoints were change in qulity of life measured with EuroWol 5 dimensions (EQ-5D), leg and back pain measured with a numeric rating scale (NRS), and rates of surgical complications.

Results

A total of 5514 patients were enrolled, including 3907 nonsmokers and 1607 smokers. A significant improvement in ODI was observed for the entire cohort (mean, 31.1 points; 95% confidence interval [CI], 30.4-31.8; *P* <0.001). Nonsmokers experienced a greater improvement in ODI at 1 year compared with smokers (mean, 4.1 points; 95% CI, 2.5-5.7; *P* <0.001). Nonsmokers were more likely to achieve a minimal important change (MIC), defines as an ODI improvement of ≥10 points, compared with smokers (85.5% vs 79.5%; *P* <0.001). Nonsmokers experienced greater improvement in EQ-5D (mean difference, 0.068; 95% CI, 0.04-0.09; *P* <0.001), back pain NRS (mean difference, 0.44; 95% CI, 0.21-0.66; *P* <0.001), and leg pain NRS (mean difference, 0.54; 95% CI, 0.31-0.77; *P* <0.001). There was no difference between smokers and nonsmokers in the overall complication rate (6.2% vs. 6.7%; *P* = 0.512). smoking was identified as a negative predictor for ODI change in a multiple regression analysis (*P*<0.001).

Conclusions

Nonsmokers reported a greater improvement in ODI at 1 year following microdiscectomy, and smokers were less likely to experience a MIC. Nonetheless, significant improvement was also found among smokers.

PAPER IV

Lumbar microdiscectomy in obese patients: A multicenter observational Study. Madsbu MA, Øie LR, Salvesen Ø, Vangen-Lønne V, Nygaard ØP, Solberg TK, Gulati S. *World Neurosurgery 2018*

Objective

To evaluate the association between obesity and outcomes following microdiscectomy for lumbar disc herniation (LDH).

Methods

The primary outcome measure was change in Oswestry disability index (ODI) at one year following surgery. Obesity was defined as body-mass index (BMI) ≥30. Prospective data were retrieved from the Norwegian Registry for Spine Surgery.

Results

We enrolled 4932 patients, 4018 non-obese and 914 obese. For patients with complete one-year follow-up (n=3381) the mean improvement in ODI was 31.2 points (95% CI 30.4 to 31.9, p<0.001). Improvement in ODI was 31.4 points in non-obese and 30.1 points in obese patients (p=0.182). Obese and none-obese patients were as likely to achieve a minimal clinically important difference (84.2 vs 82.7%, p=0.336) in ODI (≥10 points improvement). Obesity was identified as a negative predictor for ODI improvement in a multiple regression analysis (BMI 30-34.99; p<0.001, BMI ≥35; p=0.029). Obese and non-obese patients experienced similar improvement in EQ-5D (0.48 vs 0.49 points, p=0.441) as well as back pain (3.7 vs 3.5 points, p=0.167) and leg pain (4.7 vs 4.8 points, p=0.654) measured by numeric rating scales. Duration of surgery was shorter for non-obese patients (55.7 vs 65.3 minutes, p≤0.001). Non-obese patients experienced less complications compared to obese patients (6.1 vs. 8.3%, p=0.017). Obese patients had slightly longer hospital stays (2.0 vs 1.8 days, p=0.004).

Conclusions

Although they had more minor complications, obese individuals experienced improvement after lumbar microdiscectomy for LDH similar to that of non-obese individuals.

PAPER V

Surgery for herniated lumbar disc in private vs public hospitals: A pragmatic comparative effectiveness study

Madsbu MA, Salvesen Ø, Carlsen SM, Westin S, Onarheim K, Nygaard ØP, Solberg TK, Gulati S

Acta Neurochirurgica 2020

Background

There is limited evidence on the comparative performance of private and public healthcare. Our aim was to compare outcomes following surgery for lumbar disc herniation (LDH) in private vs public hospitals.

Methods

Data were obtained from the Norwegian registry for spine surgery. Primary outcome was change in Oswestry disability index (ODI) one year after surgery. Secondary endpoints were quality of life (EuroQol EQ-5D), back and leg pain, complications, and duration of surgery and hospital stays.

Results

Among 5221 patients, 1728 in the private group and 3493 in the public group, 3624 (69.4%) completed one-year follow-up. In the private group mean improvement in ODI was 28.8 points vs 32.3 points in the public group (mean difference -3.5, 95% CI -5.0 to -1.9; *P* for equivalence <.001). Equivalence was confirmed in a propensity-matched cohort and following mixed linear model analyses. There were differences in mean change between the groups for EQ-5D (mean difference -0.05, 95% CI -0.08 to -0.02; *P*=.002) and back pain (mean difference -0.2, 95% CI -0.2, -0.4 to -0.004; *P*=.046), but after propensity matching the groups did not differ. No difference was found between the two groups for leg pain. Complication rates was lower in the private group (4.5% vs 7.2%; *P*<.001), but after propensity matching there was no difference. Patients operated in private hospitals had shorter duration of surgery (48.4 vs 61.8 minutes) and hospital stay (0.7 vs 2.2 days).

Conclusion

At one year the effectiveness of surgery for LDH was equivalent in private and public hospitals.

DISCUSSION

IMPROVEMENT IN BACK PAIN

Patients with persistent radicular pain are often considered for surgery or conservative treatment for lumbar disc herniation. Many of these patients will also experience concomitant lower back pain (LBP) (65, 66). While the surgeons' main goal is to relief the patient of radicular pain and improve neurological function, residual LBP is a concern for the patient. However, several studies have demonstrated that a significant number of patients also experience improvement in LBP following surgery for LDH. The largest clinical trials have been designed to evaluate the differences between conservative management and surgical management, primarily focusing on relief of radicular pain and change in PROMs. Few studies have evaluated improvement in LBP as a primary endpoint. In a recent study based on data from the Swedish spine registry (Swespine), 60% of patients with significant back pain preoperatively reported a substantial improvement after 1 year follow-up, with a mean change score of 3.2 on the NRS for back pain. However, according to data for all patients with back pain (low and high grade), only 43% reported a minimal clinically important difference (MCID) with a mean change of 2.2 on the NRS for back pain. A separate study based on material from the DaneSpine data base in Denmark, which included 2,399 patients with a preoperative VAS ≥50, patients with LBP also reported significant improvement.

By comparison with the above-mentioned studies, all five of our studies, demonstrated a considerably change in NRS back pain, thus supporting the existing evidence that patients can expect an improvement in LBP as well as radicular pain after surgery.

LDH SURGERY IN THE ELDERLY

The question of whether to offer surgery to elderly patients is often a delicate matter and consideration should be given to their age, comorbidity, and intraoperative and postoperative challenges/risks, as well as the long-term benefits.

In cases of increasing aging population, the numbers of patients with degenerative spinal disorders, such as spinal stenosis and symptomatic LDH, are likely to increase too. Several factors need to be considered before performing surgery on patients, and decisions can often be more complex with regard to elderly patients compared with younger patients. Older patients are more prone to suffer from cardiac, pulmonary, and renal disease. They also have a lower capacity to respond to complications, both perioperative and postoperative, and often take several different types of medications. Therefore, a thorough evaluation before proceeding with surgical management is paramount to avoid unnecessary treatment (67). Furthermore, elderly patients face the risk of developing postoperative complications such as UTI (urinary tract infection), pneumonia and delirium.

Several studies have reported good outcome for elderly patients undergoing surgery for degenerative spinal disorders (68, 69). However, these studies have mainly focused on other degenerative spinal disorders, such as spinal stenosis. Furthermore, considering the relatively high age of patients in the elderly group, they are often excluded from clinical trials and few comparative studies have been done. Among the few existing studies that have evaluated clinical outcomes after LDH surgery in an elderly population, many were done a relatively long time ago and had small patent groups, no prospective design, and no validated primary outcome measures (70-73).

Researchers involved in a recent comparative cohort study based on data from the Swedish spine surgery register (Swespine) concluded that the elderly patients experienced worse outcomes compared with young and middle-aged patients (74). They included 1,250 patients ≥ 65 years of age and compared 1-year results for different PROMs (SF-36, ODI, VAS leg and back pain, EQ-5D, and VAS) (74). Although a substantial improvement was reported in both groups, elderly patients experienced inferior results compared to the younger group for most PROMs. With regard to change in ODI between elderly and younger patients, the difference were not statistically significant, and our findings in Paper I was comparable with them. However, the comparative cohort study was based on multiple factors as a primary end-point, which thus introduced bias.

Ultimately, it is difficult to compare our findings with those of other studies, as few high-quality studies have been published, thus making their results available for comparison. With an aging population, evidence-based medicine for these patients is much needed or even paramount.

LDH SURGERY IN PRIVATE AND PUBLIC HOSPITALS

Public health care is usually provided by the government through national healthcare systems, whereas private health care is often provided as a "for profit" service. Ideological debates on whether countries should strengthen public versus private healthcare services are common. In times of economic recession with constraints on government budgets, disputes between the proponents of private and public health care systems tend to escalate. Discussions about resource allocation between private and public health providers should be evidence-based and focused on clinical effectiveness and costs. Registry-based studies can lead to increased levels of value-driven health care (75). Currently, there is limited and only poor-quality evidence regarding the comparative performance of the two types of health care systems (76).

In Paper II, we present our finding that patients whose operations were done in private clinics reported non-inferior results compared with patients whose operations were done in public hospitals. The study demonstrated that that health care providers in both types of health care systems deliver good quality clinical care.

Considering the equivalence of the surgical results between the two groups of health care providers in our nationwide patient sample, it could be argued that there is widespread access to high quality surgical management of LDH in both private and public health care systems. Thus, the dilemma faced by patients is not about whether the health care will be of sufficiently high quality and effective, but whether they themselves have the economic capacity and possible waiting time for surgery. Furthermore, the role of private health insurance will be under scrutiny in a country where the public health care system is functioning well and providing all emergency treatment and complex in-house medical treatment (77). In sum, our results might not be generalizable to countries other than Norway, which have different health care systems.

LDH SURGERY IN OBESE PATIENTS

Although study IV demonstrates that obese and non-obese patients experienced similar results after surgery for LDH, it should be emphasized that obesity has been recognized as a cause for LDH. Previous studies have indicated that obese patients have a stronger tendency to have LDH (78-80) and an elevated risk of recurrence and revision procedures (81, 82).

The Spine Patient Outcomes Research Trial (SPORT) found that obese patients benefitted less from operative treatment for LDH compared with non-obese patients. In our study, reported in paper IV, a slightly lower change in ODI was observed for obese patients than in the SPORT study (30.1 vs. 35.2). This might be explained by the higher baseline ODI and more strict inclusion criteria in the SPORT study.

In two retrospective studies comparing operative results between obese and non-obese patients, no major differences in surgical outcomes were found (83, 84). However, both studies had a short follow-up period. In order to gain a better understanding of the prognosis in obese patients operated for LDH, longer follow-up periods are warranted, especially for assessing reoperation rates.

Multiple studies have demonstrated that obese patients have inferior outcomes compared with non-obese when it comes to duration of surgical procedures, duration of hospital stays, and minor complications (84-87). Similar results have also been found for other spine-related diagnoses, such as spinal stenosis and spondylolisthesis (61, 88). However, no studies to date linking the effect of preoperative weight loss to surgical outcomes for LDH.

We found that a high ODI score at baseline was associated with the greatest improvement at one year. Previous studies have shown that a history of previous surgery will influence the results of future surgery (89). In order to study the impact of obesity, patients with a history of surgery were excluded from Paper IV. Smoking and comorbidity were stronger predictors for interior outcomes than obesity, a finding that is consistent with findings reported in the literature on spinal surgery (90).

LDH SURGERY IN TOBACCO SMOKERS

Smoking has been identified as a predictor for postoperative infections following spinal surgery (91-93). However, there were few infections in Study III and similar rates among smokers and non-smokers. This finding might reflect the minimally invasive nature of lumbar microdiscectomy, with small incisions and minimal muscle trauma. Similar to Study III, a recent observational study from NORspine found that, compared with non-smokers, smokers experienced less improvement at one year following microsurgical decompression for central lumbar spinal stenosis, and that smokers were less likely to achieve a MIC (90). Nevertheless, considerable improvement was found also among smokers who underwent surgery for lumbar spinal stenosis. However, in two small observational studies it was found that tobacco smoking did not influence PROMs following surgery for LDH (94, 95). Many previous findings pertaining to tobacco smoking and spine surgery cannot be directly associated with patients who have undergone lumbar microdiscectomy. In a retrospective study of 500 patients who underwent lumbar spine surgery, an association was found between smoking and both increased blood loss and the need for intraoperative blood replacement (96). However, intraoperative bleeding is usually limited and rarely a problem when performing lumbar microdiscectomy. The authors of a review of the impact of smoking on neurosurgical outcomes concluded that tobacco smoking is associated with delayed and impaired spinal fusion, as well as pseudoarthrosis following spinal instrumentation (97), yet following lumbar microdiscectomy there is hardly any need for bone healing.

Study III did not establish a definite causal relationship between daily tobacco smoking and lower treatment effects following microdiscectomy for LDH, and we suggest that smoking might have been a marker for other characteristics responsible for the association that were unadjusted for in the regression model. It is known that patient-reported quality of life is lower among smokers than among nonsmokers in a general population, and it is possible that this might affect research results based on disease-specific questionnaires (98). Psychosocial factors are likely to influence outcomes following spinal surgery, but they are difficult to assess in a registry-based study. However, depression and/or anxiety was identified as negative predictors in Study III for change in ODI.

LDH SURGERY IN ADOLESCENTS

Literature on clinical outcomes after surgical treatment for LDH in adolescent populations is mainly limited to retrospective case series (99). Our findings support the retrospective findings that microdiscectomy for LDH is an effective procedure, although as expected in a prospective study using patient-reported outcomes, the success rates are somewhat lower than in the retrospective case series with surgeon-reported outcomes (99). In a recent observational study from SweSpine, Lagerbäck et al. (100) found that adolescents were more satisfied and had fewer spine-related symptoms following surgery compared with adult patients. The primary outcome variable in the Swedish study was a crude self-rating of satisfaction of surgical outcomes. Study II showed that the improvements in ODI and EQ-5D at 1 year were similar in adolescent and adult groups. The study by Lagerbäck et al. was larger with 151 adolescent patients, but the authors did not provide details about the surgical procedure. A related study from SweSpine in the same time period there were 49% open discectomies (101). However, there are no reasons why spine surgeons should choose open procedures in adolescent patients if microdiscectomy offers similar improvement. Our study with 97 adolescent patients who underwent microdiscectomy is the largest prospective study to date to evaluate results after minimally invasive spine surgery in this age group. Based on the two registry-based studies (SweSpine and NORspine), it is not possible to make a direct comparison of open discectomy and microdiscectomy. However, it is interesting that the 86% satisfaction rate reported by Lagerbäck et al. compares well to the 86% of our patients achieving the MIC for ODI. The findings in Study II seems to be consistent with previous studies showing that adolescents have less severe symptoms at baseline and that adolescents are less likely to present with paresis (99, 100). The same trend was observed in the recent SweSpine study. However, in that study EQ-5D scores were higher (i.e., the adolescent patients experienced fewer problems than adults) among adolescents. This is not unexpected since, as the NRS only captures pain intensity, while the ODI and EQ-5D are multi-dimensional and focus on functional status. A clinically relevant age effect per se in EQ-5D is not expected, but spine-related or other comorbidity or other comorbidities may influence results (102). Moreover, adolescents are expected to have fewer degenerative spinal changes at presentation. Finally, based on the literature, it seems that surgical treatment of LDH in the adolescent population is a safe procedure with low operative complications, although open discectomies seem to be the dominating procedure (100, 103). Study II demonstrated safety also after lumbar microdiscectomy with a complication rate of only 1%. The low complication rate might have been related to the young age of included patients and exclusion of individuals who had undergone previous lumbar spine surgery.

REGISTRY BASED SPINE RESEARCH

Surgery for degenerative disorders of the spine is drastically increasing in the general population. The disorders constitute a heterogenous group of conditions, for which diagnostic clarity is lacking. There are large variations in practice for both surgical and non-surgical interventions. In economic terms they represent a substantial burden for society, and therefore research on treatment modalities and documented research is highly warranted. Spinal registries have evolved in recent years, and this in turn has benefitted several high-quality studies (104-107). The registries offer researchers the possibility to acquire data for entire populations, and they are a source of invaluable information on quality control and management, for all stakeholders in health care systems.

Research from the NORspine registry is based on prospectively collected data from PROMs, and such studies can be regarded as observational studies. The unique data protection laws in Norway allow for the spine registry to have an optimized and accurate completeness of data, compared with registries in countries outside Scandinavia (108).

Using registry-based date provides real life clinical data, reflecting daily clinical practice. The results may be as robust and more externally valid than the results from randomized controlled trials (RCTs) (109-112). In comparison with RCTs, conducting research using clinical data from registries is relatively simple and low in cost.

There are several documented challenges with the use of RCTs relating to surgery; patient selection, blinding bias, loss to follow-up, high cost, ethical challenges related to randomization, surgeon preferences and crossover (113). However, RCTs still remain the gold standard for gaining Level I evidence and changing clinical practice.

Data from clinical registries can be used to study different predictors of outcome in subgroups of patients with a probability of favorable or poor outcome. Using data from NORspine we have been able to study predictors such as obesity (Paper IV) and tobacco smoking (Paper III). We found that obese patients had similar results to non-obese patients one year after surgery and that smokers reported inferior results compared to non-smokers (114, 115). Furthermore, it has the potential to examine smaller and rarer patient groups, such as adolescent patients, elderly patients, and patients with extraforaminal lumbar disc herniations (116-118). This claim is supported by a large systematic review of spine registry research published in 2015 (119). The authors, van Hooff et al., also state that registry-based studies can provide valuable information on variations in treatment and outcomes, and they can describe care patterns and appropriateness of care. van Hooff et al. reviewed 34 registry-based studies from several different countries. The studies were evaluated on the basis of several factors. Methodology and risk of bias was given a thorough evaluation, and half of the studies were considered to have a low risk of introducing bias. However, van Hooff et al.'s conclusion is that no studies had a certain impact on the quality of spine care.

Considering the possibilities to address research questions that would otherwise be impossible in randomized clinical trials, registry-based studies can be advantageous to RCTs. Also, due to the strict inclusion and exclusion criteria in RCTs, some patient groups are often excluded,

such as adolescents and elderly patients, thereby ultimately limiting the documented scientific evidence for treatment effects in these patient groups. Therefore, it can be argued that registry-based studies play an important role in supplying much needed information that can be used to answer as yet unanswered research questions, thus complementing RCTs.
To reduce bias in registry-based research, there are several steps that can be made. We have used propensity score matching, blinding of the statistician for patient groups and additional evaluation of radiological examinations.

Missing data is a problem with registry-based studies. Also, loss to follow-up rates vary and could potentially introduce bias. It is uncertain at what rate the results are more likely to be biased, but loss to follow up over 20% has been suggested. Studies have demonstrated that <5% loss to follow up minimizes bias (120). However, Solberg et al.´s study based on data from the NORspine registry showed that there was no differences in outcome between responders and non-responders (121). Their study also found that forgetfulness was the most important reason for a patient to be lost to follow-up. In our study, we handled missing data with linear mixed models (LMMs) and did not perform multiple imputations. This strategy was in line with studies showing that it is not necessary to handle missing data using multiple imputations before performing a mixed model analysis on longitudinal data (58, 117).

CHOICE OF CUT OFF VALUE FOR MIC

Defining significant improvement and success based on PROMs can be a challenge. For our studies, we reported the number of patients achieving a minimal clinical important change (MIC), which is defined as “the smallest difference in score in the domain of interest which patients perceive as beneficial and would mandate, in the absence of troublesome side effects and excessive cost” (122).

For the Oswestry Disability Index score, a MIC is conceptually the minimal change that a patient would consider clinically beneficial, not one that is just statistically significant. It should be emphasized that achieving a MIC is not the same as defining success, which should reflect a substantially larger improvement.

We chose a consensus-based value for our MIC cut off (123). Currently, there is no gold standard for defining a successful outcome. However, two recent studies have suggested other cut off values that might be more suitable to detect a clinical success/clinical difference after treatment for lumbar disc herniation (124, 125).

STRENGTHS AND LIMITATIONS

The major strengths of the five studies reported in the papers on which this thesis is based are our large sample size, pragmatic study designs based on prospective registry data with high external validity, the use of patient-reported outcome measures, and protocol-based statistical analyses with blinded assessment of the main outcome measures. Other strengths include the use of propensity matched groups to minimize confounding factors in Paper II. The main limitation was the lack of randomization. Even though propensity matched patient groups could adjust for known interactions, while unlikely, residual or introduction of confounding cannot be ruled out. Another weakness in the studies was the loss to follow-up rates of participants regarding Oswestry disability index scores at one year. However, a previous study of a similar population from the NORspine registry showed no difference in outcomes between non-responders and responders (126). It is unlikely that the minor differences in baseline characteristics between non-responders and responders at one year would have influenced our results (114, 115, 117, 127). A further consideration is that we lacked data on the exact amounts of costs, payments, and reimbursements, which inhibited us from performing cost-effectiveness analyses.

FUTURE RESEARCH/ FUTURE ASPECTS

It is difficult to quantify the effect on the quality of spinal care based on data from spine registries. There are numerous registries and numerous studies, many with low methodological quality, lack of long-term follow-up, lack of adjustment for covariates and inaccurate descriptions of both patients and interventions that has been done.

Several publications and guidelines have made suggestions to improve registry quality. The STROBE statement (128), the International Consortium for Health Outcome Measurements ICHOM and various publications are useful tools for improving registry-based research (75, 119, 129). Continuous effort is needed in order for spine registries to evolve and to stay relevant.

There are several unanswered questions in the field of spinal surgery. No randomized trials (surgery vs. non-surgical intervention) have addressed the long-term results for patients with prolonged sciatica due to lumbar disc herniation, nor are any ongoing. Also, there has been a clack of research on the long-term outcomes for active physiotherapy.

There is a need for further research in the field of lumbar spine surgery. Knowledge from registry-based research can provide data that are useful for studies of cost-effectiveness, the design of RCTs, and comparative studies between different spine registries.

Our research group is currently conducting studies on persistent opioid use among patients who undergo surgery for degenerative spinal disorders. In addition, we will investigate the number/rates of patients who return to work after surgery.

CONCLUSIONS

PAPER I: Patients aged 65 and older experienced improvement after lumbar microdiscectomy that was similar to that of younger patients.

PAPER II: The effectiveness and safety of single-level microdiscectomy are similar in adolescents and the adult population at 1-year follow-up.

PAPER III: Nonsmokers reported a greater improvement in ODI at 1 year following microdiscectomy, and smokers were less likely to experience a MIC. Nonetheless, significant improvement was also found among smokers.

PAPER IV: Although they had more minor complications, obese individuals experienced improvement after lumbar microdiscectomy for LDH similar to thar of non-obese individuals.

PAPER V: Patients operated in private and public hospital reported equivalent results after surgery for lumbar disc herniation.

REFERENCES

1. Truumees E. A history of lumbar disc herniation from Hippocrates to the 1990s. Clin Orthop Relat R. 2015;473(6):1885-95.
2. Rhee JM, Schaufele M, Abdu WA. Radiculopathy and the Herniated Lumbar Disc: Controversies Regarding Pathophysiology and Management. JBJS. 2006;88(9):2070-80.
3. Porchet F, Wietlisbach V, Burnand B, Daeppen K, Villemure JG, Vader JP. Relationship between severity of lumbar disc disease and disability scores in sciatica patients. Neurosurgery. 2002;50(6):1253-9; discussion 9-60.
4. Dammers R, Koehler PJ. Lumbar disc herniation: level increases with age. Surg Neurol. 2002;58(3-4):209-12; discussion 12-3.
5. Konstantinou K, Dunn KM. Sciatica: review of epidemiological studies and prevalence estimates. Spine (Phila Pa 1976). 2008;33(22):2464-72.
6. Borenstein DG, O'Mara JW, Jr., Boden SD, Lauerman WC, Jacobson A, Platenberg C, et al. The value of magnetic resonance imaging of the lumbar spine to predict low-back pain in asymptomatic subjects : a seven-year follow-up study. J Bone Joint Surg Am. 2001;83(9):1306-11.
7. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med. 1994;331(2):69-73.
8. Weishaupt D, Zanetti M, Hodler J, Boos N. MR imaging of the lumbar spine: prevalence of intervertebral disk extrusion and sequestration, nerve root compression, end plate abnormalities, and osteoarthritis of the facet joints in asymptomatic volunteers. Radiology. 1998;209(3):661-6.
9. Deyo RA, Mirza SK. Herniated Lumbar Intervertebral Disk. New Engl J Med. 2016;374(18):1763-72.
10. van der Windt D, Simons E, Riphagen, II, Ammendolia C, Verhagen AP, Laslett M, et al. Physical examination for lumbar radiculopathy due to disc herniation in patients with low-back pain. Cochrane Database of Systematic Reviews. 2010(2).
11. Majlesi J, Togay H, Unalan H, Toprak S. The sensitivity and specificity of the Slump and the Straight Leg Raising tests in patients with lumbar disc herniation. J Clin Rheumatol. 2008;14(2):87-91.
12. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic Resonance Imaging of the Lumbar Spine in People without Back Pain. New Engl J Med. 1994;331(2):69-73.
13. el Barzouhi A, Vleggeert-Lankamp CLAM, Lycklama à Nijeholt GJ, Van der Kallen BF, van den Hout WB, Koes BW, et al. Influence of low back pain and prognostic value of MRI in sciatica patients in relation to back pain. PloS one. 2014;9(3):e90800-e.
14. Deyo RA, Mirza SK. CLINICAL PRACTICE. Herniated Lumbar Intervertebral Disk. N Engl J Med. 2016;374(18):1763-72.
15. Awad JN, Moskovich R. Lumbar disc herniations: surgical versus nonsurgical treatment. Clin Orthop Relat Res. 2006;443:183-97.
16. Hofstee DJ, Gijtenbeek JM, Hoogland PH, van Houwelingen HC, Kloet A, Lotters F, et al. Westeinde sciatica trial: randomized controlled study of bed rest and physiotherapy for acute sciatica. J Neurosurg. 2002;96(1 Suppl):45-9.
17. Vroomen PC, de Krom MC, Wilmink JT, Kester AD, Knottnerus JA. Lack of effectiveness of bed rest for sciatica. N Engl J Med. 1999;340(6):418-23.

18. Overdevest GM, Vleggeert-Lankamp CL, Jacobs WC, Brand R, Koes BW, Peul WC, et al. Recovery of motor deficit accompanying sciatica--subgroup analysis of a randomized controlled trial. Spine J. 2014;14(9):1817-24.
19. Lewis RA, Williams NH, Sutton AJ, Burton K, Din NU, Matar HE, et al. Comparative clinical effectiveness of management strategies for sciatica: systematic review and network meta-analyses. Spine J. 2015;15(6):1461-77.
20. Luijsterburg PA, Verhagen AP, Ostelo RW, van Os TA, Peul WC, Koes BW. Effectiveness of conservative treatments for the lumbosacral radicular syndrome: a systematic review. Eur Spine J. 2007;16(7):881-99.
21. Valat JP, Genevay S, Marty M, Rozenberg S, Koes B. Sciatica. Best Pract Res Clin Rheumatol. 2010;24(2):241-52.
22. Jordan J, Konstantinou K, O'Dowd J. Herniated lumbar disc. BMJ Clin Evid. 2009;2009.
23. Wilby MJ, Best A, Wood E, Burnside G, Bedson E, Short H, et al. Microdiscectomy compared with transforaminal epidural steroid injection for persistent radicular pain caused by prolapsed intervertebral disc: the NERVES RCT. Health Technol Assess. 2021;25(24):1-86.
24. Bernstein IA, Malik Q, Carville S, Ward S. Low back pain and sciatica: summary of NICE guidance. BMJ. 2017;356:i6748.
25. Qaseem A, Wilt TJ, McLean RM, Forciea MA, Clinical Guidelines Committee of the American College of P, Denberg TD, et al. Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med. 2017;166(7):514-30.
26. Stochkendahl MJ, Kjaer P, Hartvigsen J, Kongsted A, Aaboe J, Andersen M, et al. National Clinical Guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy. Eur Spine J. 2018;27(1):60-75.
27. Traeger A, Buchbinder R, Harris I, Maher C. Diagnosis and management of low-back pain in primary care. CMAJ. 2017;189(45):E1386-E95.
28. Luijsterburg PA, Verhagen AP, Ostelo RW, van den Hoogen HJ, Peul WC, Avezaat CJ, et al. Physical therapy plus general practitioners' care versus general practitioners' care alone for sciatica: a randomised clinical trial with a 12-month follow-up. Eur Spine J. 2008;17(4):509-17.
29. Fritz JM, Lane E, McFadden M, Brennan G, Magel JS, Thackeray A, et al. Physical Therapy Referral From Primary Care for Acute Back Pain With Sciatica : A Randomized Controlled Trial. Ann Intern Med. 2021;174(1):8-17.
30. MIXTER WJ, BARR JS. Rupture of the Intervertebral Disc with Involvement of the Spinal Canal. New Engl J Med. 1934;211(5):210-5.
31. Yasargil MG, editor Microsurgical Operation of Herniated Lumbar Disc1977; Berlin, Heidelberg: Springer Berlin Heidelberg.
32. Caspar W, Campbell B, Barbier DD, Kretschmmer R, Gotfried Y. The Caspar microsurgical discectomy and comparison with a conventional standard lumbar disc procedure. Neurosurgery. 1991;28(1):78-86; discussion -7.
33. Williams RW. Microlumbar discectomy: a conservative surgical approach to the virgin herniated lumbar disc. Spine (Phila Pa 1976). 1978;3(2):175-82.
34. Foley KT. Microendoscopic discectomy. Techniques in Neurosurgery. 1997;3:301-7.
35. Jacobs WCH, Arts MP, van Tulder MW, Rubinstein SM, van Middelkoop M, Ostelo RW, et al. Surgical techniques for sciatica due to herniated disc, a systematic review. European Spine Journal. 2012;21(11):2232-51.

36. Arts MP, Brand R, van den Akker ME, Koes BW, Bartels RHMA, Peul WC, et al. Tubular Diskectomy vs Conventional Microdiskectomy for Sciatica: A Randomized Controlled Trial. JAMA. 2009;302(2):149-58.
37. Chang X, Chen B, Li H-y, Han X-b, Zhou Y, Li C-q. The safety and efficacy of minimally invasive discectomy: a meta-analysis of prospective randomised controlled trials. International Orthopaedics. 2014;38(6):1225-34.
38. Lurie JD, Tosteson TD, Tosteson ANA, Zhao W, Morgan TS, Abdu WA, et al. Surgical versus nonoperative treatment for lumbar disc herniation: eight-year results for the spine patient outcomes research trial. Spine. 2014;39(1):3-16.
39. Osterman H, Seitsalo S, Karppinen J, Malmivaara A. Effectiveness of microdiscectomy for lumbar disc herniation: a randomized controlled trial with 2 years of follow-up. Spine (Phila Pa 1976). 2006;31(21):2409-14.
40. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JAH, Tans JTJ, et al. Surgery versus Prolonged Conservative Treatment for Sciatica. New Engl J Med. 2007;356(22):2245-56.
41. Peul WC, van den Hout WB, Brand R, Thomeer RT, Koes BW, Leiden-The Hague Spine Intervention Prognostic Study G. Prolonged conservative care versus early surgery in patients with sciatica caused by lumbar disc herniation: two year results of a randomised controlled trial. BMJ. 2008;336(7657):1355-8.
42. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JA, Tans JT, et al. Surgery versus prolonged conservative treatment for sciatica. N Engl J Med. 2007;356(22):2245-56.
43. Weber H. Lumbar disc herniation. A controlled, prospective study with ten years of observation. Spine (Phila Pa 1976). 1983;8(2):131-40.
44. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study. Spine (Phila Pa 1976). 2005;30(8):927-35.
45. Buttermann GR. Treatment of lumbar disc herniation: epidural steroid injection compared with discectomy. A prospective, randomized study. J Bone Joint Surg Am. 2004;86(4):670-9.
46. Weinstein JN, Lurie JD, Tosteson TD, Tosteson AN, Blood EA, Abdu WA, et al. Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT). Spine (Phila Pa 1976). 2008;33(25):2789-800.
47. Schoenfeld AJ, Bono CM. Does surgical timing influence functional recovery after lumbar discectomy? A systematic review. Clin Orthop Relat Res. 2015;473(6):1963-70.
48. Rihn JA, Hilibrand AS, Radcliff K, Kurd M, Lurie J, Blood E, et al. Duration of symptoms resulting from lumbar disc herniation: effect on treatment outcomes: analysis of the Spine Patient Outcomes Research Trial (SPORT). J Bone Joint Surg Am. 2011;93(20):1906-14.
49. Bailey CS, Rasoulinejad P, Taylor D, Sequeira K, Miller T, Watson J, et al. Surgery versus Conservative Care for Persistent Sciatica Lasting 4 to 12 Months. New Engl J Med. 2020;382(12):1093-102.
50. van den Hout WB, Peul WC, Koes BW, Brand R, Kievit J, Thomeer RT, et al. Prolonged conservative care versus early surgery in patients with sciatica from lumbar disc herniation: cost utility analysis alongside a randomised controlled trial. BMJ. 2008;336(7657):1351-4.
51. Tosteson AN, Skinner JS, Tosteson TD, Lurie JD, Andersson GB, Berven S, et al. The cost effectiveness of surgical versus nonoperative treatment for lumbar disc herniation over

two years: evidence from the Spine Patient Outcomes Research Trial (SPORT). Spine (Phila Pa 1976). 2008;33(19):2108-15.
52. Oosterhuis T, Costa LO, Maher CG, de Vet HC, van Tulder MW, Ostelo RW. Rehabilitation after lumbar disc surgery. Cochrane Database Syst Rev. 2014(3):CD003007.
53. Oosterhuis T, Ostelo RW, van Dongen JM, Peul WC, de Boer MR, Bosmans JE, et al. Early rehabilitation after lumbar disc surgery is not effective or cost-effective compared to no referral: a randomised trial and economic evaluation. J Physiother. 2017;63(3):144-53.
54. Fairbank JC, Couper J, Davies JB, O'Brien JP. The Oswestry low back pain disability questionnaire. Physiotherapy. 1980;66(8):271-3.
55. Grotle M, Brox JI, Vollestad NK. Cross-cultural adaptation of the Norwegian versions of the Roland-Morris Disability Questionnaire and the Oswestry Disability Index. J Rehabil Med. 2003;35(5):241-7.
56. Solberg TK, Olsen JA, Ingebrigtsen T, Hofoss D, Nygaard OP. Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. Eur Spine J. 2005;14(10):1000-7.
57. Team. RDC. R A language and environment for statistical computing. R Foundation for Statistical Computing 2007.
58. Twisk J, de Boer M, de Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. J Clin Epidemiol. 2013;66(9):1022-8.
59. Madsbu MA, Solberg TK, Salvesen O, Nygaard OP, Gulati S. Surgery for Herniated Lumbar Disk in Individuals 65 Years of Age or Older: A Multicenter Observational Study. JAMA Surg. 2017.
60. Nerland US, Jakola AS, Giannadakis C, Solheim O, Weber C, Nygaard OP, et al. The Risk of Getting Worse: Predictors of Deterioration After Decompressive Surgery for Lumbar Spinal Stenosis: A Multicenter Observational Study. World Neurosurg. 2015;84(4):1095-102.
61. Giannadakis C, Nerland US, Solheim O, Jakola AS, Gulati M, Weber C, et al. Does Obesity Affect Outcomes After Decompressive Surgery for Lumbar Spinal Stenosis? A Multicenter, Observational, Registry-Based Study. World Neurosurg. 2015;84(5):1227-34.
62. Ropper AH, Zafonte RD. Sciatica. The New England journal of medicine. 2015;372(13):1240-8.
63. Arts MP, Brand R, van den Akker ME, Koes BW, Bartels RH, Peul WC. Tubular diskectomy vs conventional microdiskectomy for sciatica: a randomized controlled trial. JAMA : the journal of the American Medical Association. 2009;302(2):149-58.
64. Nerland US, Jakola AS, Solheim O, Weber C, Rao V, Lonne G, et al. Minimally invasive decompression versus open laminectomy for central stenosis of the lumbar spine: pragmatic comparative effectiveness study. BMJ (Clinical research ed). 2015;350:h1603.
65. Hakkinen A, Ylinen J, Kautiainen H, Airaksinen O, Herno A, Tarvainen U, et al. Pain, trunk muscle strength, spine mobility and disability following lumbar disc surgery. J Rehabil Med. 2003;35(5):236-40.
66. Stromqvist F, Stromqvist B, Jonsson B, Karlsson MK. Surgical treatment of lumbar disc herniation in different ages-evaluation of 11,237 patients. Spine J. 2017;17(11):1577-85.
67. Epstein NE. Spine surgery in geriatric patients: Sometimes unnecessary, too much, or too little. Surg Neurol Int. 2011;2:188-.
68. Jakola AS, Sorlie A, Gulati S, Nygaard OP, Lydersen S, Solberg T. Clinical outcomes and safety assessment in elderly patients undergoing decompressive laminectomy for lumbar spinal stenosis: a prospective study. BMC Surg. 2010;10:34.

69. Tacconi L, Giordan E, Baldo S, Serra G, Signorelli F. Percutaneous endoscopic lumbar discectomy in the elderly: An effective treatment for prolapsed disc: Consideration on 75 case. Interdisciplinary Neurosurgery. 2020;20:100655.
70. Di Silvestre M, Greggi T, Rulli E, Paderni S, Palumbi P, Parisini P. Lumbar disc herniation in the elderly patient. Chir Organi Mov. 2001;86(3):223-30.
71. Barr JS, Riseborough EJ. Treatment of low back and sciatic pain in patients over 60 years of age. A study of 100 patients. Clin Orthop Relat Res. 1963;26:12-8.
72. An HS, Vaccaro A, Simeone FA, Balderston RA, O'Neill D. Herniated Lumbar Disc in Patients Over the Age of Fifty. Clinical Spine Surgery. 1990;3(2).
73. Pérez-Prieto D, Lozano-Álvarez C, Saló G, Molina A, Lladó A, Puig-Verdié L, et al. Should age be a contraindication for degenerative lumbar surgery? European Spine Journal. 2014;23(5):1007-12.
74. Strömqvist F, Strömqvist B, Jönsson B, Karlsson MK. The outcome of lumbar disc herniation surgery is worse in old adults than in young adults. Acta Orthop. 2016;87(5):516-21.
75. McGirt MJ, Parker SL, Asher AL, Norvell D, Sherry N, Devin CJ. Role of prospective registries in defining the value and effectiveness of spine care. Spine (Phila Pa 1976). 2014;39(22 Suppl 1):S117-28.
76. Basu S, Andrews J, Kishore S, Panjabi R, Stuckler D. Comparative performance of private and public healthcare systems in low- and middle-income countries: a systematic review. PLoS Med. 2012;9(6):e1001244.
77. Gulati S, Solheim O, Carlsen SM, Oie LR, Jensberg H, Gulati AM, et al. Risk of intracranial hemorrhage (RICH) in users of oral antithrombotic drugs: Nationwide pharmacoepidemiological study. PLoS One. 2018;13(8):e0202575.
78. Xu X, Li X, Wu W. Association Between Overweight or Obesity and Lumbar Disk Diseases: A Meta-Analysis. J Spinal Disord Tech. 2015;28(10):370-6.
79. Heliovaara M. Body height, obesity, and risk of herniated lumbar intervertebral disc. Spine (Phila Pa 1976). 1987;12(5):469-72.
80. Rodriguez-Martinez NG, Perez-Orribo L, Kalb S, Reyes PM, Newcomb AG, Hughes J, et al. The role of obesity in the biomechanics and radiological changes of the spine: an in vitro study. J Neurosurg Spine. 2016;24(4):615-23.
81. Bohl DD, Ahn J, Mayo BC, Massel DH, Tabaraee E, Sershon RA, et al. Does Greater Body Mass Index Increase the Risk for Revision Procedures Following a Single-Level Minimally Invasive Lumbar Discectomy? Spine (Phila Pa 1976). 2016;41(9):816-21.
82. Meredith DS, Huang RC, Nguyen J, Lyman S. Obesity increases the risk of recurrent herniated nucleus pulposus after lumbar microdiscectomy. Spine J. 2010;10(7):575-80.
83. Tomasino A, Parikh K, Steinberger J, Knopman J, Boockvar J, Hartl R. Tubular microsurgery for lumbar discectomies and laminectomies in obese patients: operative results and outcome. Spine (Phila Pa 1976). 2009;34(18):E664-72.
84. Yoo MW, Hyun SJ, Kim KJ, Jahng TA, Kim HJ. Does obesity make an influence on surgical outcomes following lumbar microdiscectomy? Korean J Spine. 2014;11(2):68-73.
85. McGuire KJ, Khaleel MA, Rihn JA, Lurie JD, Zhao W, Weinstein JN. The effect of high obesity on outcomes of treatment for lumbar spinal conditions: subgroup analysis of the spine patient outcomes research trial. Spine (Phila Pa 1976). 2014;39(23):1975-80.
86. Buerba RA, Fu MC, Gruskay JA, Long WD, 3rd, Grauer JN. Obese Class III patients at significantly greater risk of multiple complications after lumbar surgery: an analysis of 10,387 patients in the ACS NSQIP database. Spine J. 2014;14(9):2008-18.

87. Rihn JA, Kurd M, Hilibrand AS, Lurie J, Zhao W, Albert T, et al. The influence of obesity on the outcome of treatment of lumbar disc herniation: analysis of the Spine Patient Outcomes Research Trial (SPORT). J Bone Joint Surg Am. 2013;95(1):1-8.
88. Onyekwelu I, Glassman SD, Asher AL, Shaffrey CI, Mummaneni PV, Carreon LY. Impact of obesity on complications and outcomes: a comparison of fusion and nonfusion lumbar spine surgery. J Neurosurg Spine. 2017;26(2):158-62.
89. Abdu RW, Abdu WA, Pearson AM, Zhao W, Lurie JD, Weinstein JN. Reoperation for Recurrent Intervertebral Disc Herniation in the Spine Patient Outcomes Research Trial: Analysis of Rate, Risk Factors, and Outcome. Spine (Phila Pa 1976). 2017;42(14):1106-14.
90. Gulati S, Nordseth T, Nerland US, Gulati M, Weber C, Giannadakis C, et al. Does daily tobacco smoking affect outcomes after microdecompression for degenerative central lumbar spinal stenosis? - A multicenter observational registry-based study. Acta Neurochir (Wien). 2015;157(7):1157-64.
91. Fang A, Hu SS, Endres N, Bradford DS. Risk factors for infection after spinal surgery. Spine (Phila Pa 1976). 2005;30(12):1460-5.
92. Tang H, Zhu J, Ji F, Wang S, Xie Y, Fei H. Risk factors for postoperative complication after spinal fusion and instrumentation in degenerative lumbar scoliosis patients. J Orthop Surg Res. 2014;9(1):15.
93. Kong L, Liu Z, Meng F, Shen Y. Smoking and Risk of Surgical Site Infection after Spinal Surgery: A Systematic Review and Meta-Analysis. Surg Infect (Larchmt). 2016.
94. Stienen MN, Joswig H, Smoll NR, Tessitore E, Schaller K, Hildebrandt G, et al. Short- and long-term effects of smoking on pain and health-related quality of life after non-instrumented lumbar spine surgery. Clin Neurol Neurosurg. 2016;142:87-92.
95. Lee JC, Kim MS, Shin BJ. An analysis of the prognostic factors affecing the clinical outcomes of conventional lumbar open discectomy : clinical and radiological prognostic factors. Asian Spine J. 2010;4(1):23-31.
96. Dean C, Glenn W, Ahn U, Cassinelli E, Hart D, Bohlman H, et al. Smoking Increases Blood Loss and Transfusion Requirements Following Lumbar Spine Surgery. Spine J. 2006;Volume 6(Issue 5, Supplement):26S-7S.
97. Lau D, Berger MS, Khullar D, Maa J. The impact of smoking on neurosurgical outcomes. J Neurosurg. 2013;119(5):1323-30.
98. Vogl M, Wenig CM, Leidl R, Pokhrel S. Smoking and health-related quality of life in English general population: implications for economic evaluations. BMC Public Health. 2012;12:203.
99. Dang L, Liu Z. A review of current treatment for lumbar disc herniation in children and adolescents. Eur Spine J. 2010;19(2):205-14.
100. Lagerback T, Elkan P, Moller H, Grauers A, Diarbakerli E, Gerdhem P. An observational study on the outcome after surgery for lumbar disc herniation in adolescents compared with adults based on the Swedish Spine Register. Spine J. 2015;15(6):1241-7.
101. Stromqvist F, Stromqvist B, Jonsson B, Gerdhem P, Karlsson MK. Lumbar disc herniation surgery in children: outcome and gender differences. Eur Spine J. 2016;25(2):657-63.
102. Burstrom K, Johannesson M, Diderichsen F. Swedish population health-related quality of life results using the EQ-5D. Qual Life Res. 2001;10(7):621-35.
103. Cahill KS, Dunn I, Gunnarsson T, Proctor MR. Lumbar microdiscectomy in pediatric patients: a large single-institution series. J Neurosurg Spine. 2010;12(2):165-70.

104. Forsth P, Michaelsson K, Sanden B. Does fusion improve the outcome after decompressive surgery for lumbar spinal stenosis? A TWO-YEAR FOLLOW-UP STUDY INVOLVING 5390 PATIENTS. Bone Joint J. 2013;95b(7):960-5.
105. Knutsson B, Michaelsson K, Sanden B. Obesity Is Associated With Inferior Results After Surgery for Lumbar Spinal Stenosis. Spine. 2013;38(5):435-41.
106. Nerland US, Jakola AS, Solheim O, Weber C, Rao V, Lonne G, et al. Minimally invasive decompression versus open laminectomy for central stenosis of the lumbar spine: pragmatic comparative effectiveness study. Bmj-Brit Med J. 2015;350.
107. Solberg T, Johnsen LG, Nygaard OP, Grotle M. Can we define success criteria for lumbar disc surgery? Estimates for a substantial amount of improvement in core outcome measures. Acta Orthop. 2013;84(2):196-201.
108. Meyer B, Shiban E, Albers LE, Krieg SM. Completeness and accuracy of data in spine registries: an independent audit-based study. Eur Spine J. 2020;29(6):1453-61.
109. Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. New Engl J Med. 2000;342(25):1878-86.
110. Colditz GA. Overview of the Epidemiology Methods and Applications: Strengths and Limitations of Observational Study Designs. Crit Rev Food Sci. 2010;50:10-2.
111. Concato J, Shah N, Horwitz RI. Observational studies and randomized trials. New Engl J Med. 2000;343(16):1197-+.
112. Jacobs WCH, Kruyt MC, Verbout AJ, Oner FC. Spine surgery research: on and beyond current strategies. Spine Journal. 2012;12(8):706-13.
113. Jacobs WCH, Kruyt MC, Verbout AJ, Oner FC. Effect of methodological quality measures in spinal surgery research: a metaepidemiological study. Spine Journal. 2012;12(4):339-48.
114. Madsbu MA, Oie LR, Salvesen O, Vangen-Lonne V, Nygaard OP, Solberg TK, et al. Lumbar Microdiscectomy in Obese Patients: A Multicenter Observational Study. World Neurosurg. 2018;110:e1004-e10.
115. Madsbu MA, Salvesen O, Werner DAT, Franssen E, Weber C, Nygaard OP, et al. Surgery for Herniated Lumbar Disc in Daily Tobacco Smokers: A Multicenter Observational Study. World Neurosurg. 2018;109:e581-e7.
116. Gulati S, Madsbu MA, Solberg TK, Sorlie A, Giannadakis C, Skram MK, et al. Lumbar microdiscectomy for sciatica in adolescents: a multicentre observational registry-based study. Acta Neurochir (Wien). 2017;159(3):509-16.
117. Madsbu MA, Solberg TK, Salvesen O, Nygaard OP, Gulati S. Surgery for Herniated Lumbar Disk in Individuals 65 Years of Age or Older: A Multicenter Observational Study. JAMA Surg. 2017;152(5):503-6.
118. Polak SB, Madsbu MA, Vangen-Lonne V, Salvesen O, Nygaard O, Solberg TK, et al. Surgery for extraforaminal lumbar disc herniation: a single center comparative observational study. Acta Neurochir (Wien). 2020;162(6):1409-15.
119. van Hooff ML, Jacobs WC, Willems PC, Wouters MW, de Kleuver M, Peul WC, et al. Evidence and practice in spine registries. Acta Orthop. 2015;86(5):534-44.
120. Schulz KF, Grimes DA. Sample size slippages in randomised trials: exclusions and the lost and wayward. Lancet. 2002;359(9308):781-5.
121. Solberg TK, Sorlie A, Sjaavik K, Nygaard OP, Ingebrigtsen T. Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? Acta Orthop. 2011;82(1):56-63.

122. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. Control Clin Trials. 1989;10(4):407-15.
123. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976). 2008;33(1):90-4.
124. Solberg T, Johnsen LG, Nygaard ØP, Grotle M. Can we define success criteria for lumbar disc surgery? : estimates for a substantial amount of improvement in core outcome measures. Acta Orthop. 2013;84(2):196-201.
125. Werner DAT, Grotle M, Gulati S, Austevoll IM, Madsbu MA, Lønne G, et al. Can a Successful Outcome After Surgery for Lumbar Disc Herniation Be Defined by the Oswestry Disability Index Raw Score? Global Spine Journal. 2019;10(1):47-54.
126. Solberg TK, Sorlie A, Sjaavik K, Nygaard OP, Ingebrigtsen T. Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? Acta Orthop. 2011;82(1):56-63.
127. Giannadakis C, Solheim O, Jakola AS, Nordseth T, Gulati AM, Nerland US, et al. Surgery for Lumbar Spinal Stenosis in Individuals Aged 80 and Older: A Multicenter Observational Study. J Am Geriatr Soc. 2016;64(10):2011-8.
128. Cuschieri S. The STROBE guidelines. Saudi J Anaesth. 2019;13(Suppl 1):S31-S4.
129. von Elm E, Altman DG, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Bmj-Brit Med J. 2007;335(7624):806-8.

PAPERS

PAPER I

Letters

RESEARCH LETTER

Surgery for Herniated Lumbar Disk in Individuals 65 Years of Age or Older: A Multicenter Observational Study

For most patients, the natural course of a herniated lumbar disk is favorable, and the consensus is that surgical treatment is offered if the pain in the lower back and radiating down the legs persists despite a period of conservative treatment.[1] Lumbar microdiskectomy is the most common surgical treatment,[2] but data on surgical outcomes among elderly patients are limited. The aim of this study was to compare patient-reported outcomes following lumbar microdiskectomy among patients at least 65 years of age vs younger patients.

Methods | Data were collected through the Norwegian Registry for Spine Surgery (NORspine), a comprehensive registry for quality control and research.[3] Approximately 65% of all patients who undergo lumbar spine surgery in Norway are included in NORspine. The regional committee for medical research approved this study, and all participants provided written informed consent. Patients were eligible if they had a primary diagnosis of lumbar disk herniation and underwent a nonemergency single-level lumbar microdiskectomy between 2007 and 2013. Patients who had undergone previous lumbar spine surgery or had a coexisting spinal deformity were excluded.

On admission, the patients completed the baseline questionnaire, including patient-reported outcomes, demographics, and lifestyle issues. The primary outcome was change in disease-specific functional outcome between baseline and 12

Table 1. Demographic Characteristics, Coexisting Illnesses, and Measures of Health Status for Both Groups of Patients

Variable	Patients, No. (%) <65 y	Patients, No. (%) ≥65 y	*P* Value
Total No. (%)	5195 (93.2)	381 (6.8)	
Age, median (range), y	42.1 (18-64)	70.9 (65-89)	<.001
Female sex	2097 (40.4)	176 (46.2)	.03
Married or partner	3906 (75.2)	286 (75.1)	.94
Attended college	2014 (38.8)	126 (33.1)	.02
Body mass index, mean	26.6	25.7	<.001
Current smoker	1530 (29.5)	77 (20.2)	<.001
Coexisting spinal stenosis in operated level	541 (10.4)	128 (33.6)	<.001
Comorbidity	959 (18.5)	201 (52.8)	<.001
Cardiovascular disease	121 (2.3)	78 (20.5)	
Cerebrovascular disease	10 (0.2)	11 (2.9)	
Vascular claudication	3 (0.1)	2 (0.5)	
Diabetes mellitus	103 (2.0)	31 (8.1)	
Chronic lung disease	86 (1.7)	22 (5.8)	
Hypertension	194 (3.7)	72 (18.9)	
Osteoporosis	4 (0.1)	4 (1.0)	
Knee and/or hip osteoarthritis	22 (0.4)	25 (6.6)	
Chronic neurologic disease	29 (0.6)	1 (0.3)	
Chronic musculoskeletal pain	79 (1.5)	10 (2.6)	
Cancer	24 (0.5)	8 (2.1)	
Rheumatoid arthritis	15 (0.3)	6 (1.6)	
Ankylosing spondylitis	8 (0.2)	0 (0)	
Other rheumatic diseases	41 (0.8)	9 (2.4)	
ASA grade >2	144 (2.8)	80 (21.0)	<.001
Preoperative mean ODI	45	49.8	<.001
Preoperative mean EQ-5D	0.28	0.24	.02
Preoperative diagnostic imaging			
MRI	5053 (97.3)	365 (95.8)	.10
CT	244 (4.7)	24 (6.3)	.16

Abbreviations: ASA, American Society of Anesthesiologists; CT, computed tomography; MRI, magnetic resonance imaging; ODI, Oswestry Disability Index.

Table 2. Outcomes at 1 Year for Patients Who Underwent Surgery for a Single-Level Herniated Lumbar Disk

Variable	Mean Value						Difference in Mean Change (95% CI)	*P* Value
	Age <65 y (n = 3537)			Age ≥65 y (n = 318)				
	Baseline	1 y	Mean Change	Baseline	1 y	Mean Change		
Complete case analyses (n = 3855)								
ODI	45.3	14.3	−30.9	50	17.8	−32.1	−1.2 (−3.7 to 1.4)	.37
EQ-5D	0.28	0.77	0.48	0.25	0.73	0.48	−0.002 (−0.06 to 0.05)	.93
Numeric rating scale								
Back pain	6.1	2.6	−3.4	6.7	2.9	−3.8	−0.4 (−0.8 to −0.03)	.04
Leg pain	6.8	2.1	−4.8	7.3	2.8	−4.5	0.3 (−0.7 to 0.1)	.16
Variable	Age <65 y (n = 5195)			Age ≥65 y (n = 381)			Difference in Mean Change (95% CI)	*P* Value
	Baseline	1 y	Mean Change	Baseline	1 y	Mean Change		
Mixed linear model analyses (n = 5572)								
ODI	45	14.5	−30.5	49.8	18.3	−31.5	−0.96 (−3.2 to 1.3)	.40
EQ-5D	0.28	0.76	0.48	0.24	0.72	0.49	0.01 (−0.04 to 0.05)	.71
Numeric rating scale								
Back pain	6.1	2.7	−3.4	6.7	2.9	−3.9	−0.4 (−0.8 to −0.1)	.01
Leg pain	6.8	2.1	−4.7	7.2	2.7	−4.5	−0.3 (−0.6 to 0.1)	.11
Variable	Patients, No./Total No. (%)						Difference (95% CI)	*P* Value
	Age <65 y			Age ≥65 y				
Surgical treatments, complications, and events								
Mean operation time, min	57.0			70.8			−13.8 (−16.8 to −10.9)	<.001
Hospital stay, mean, d	1.8			2.7			−0.9 (−1.1 to −0.7)	<.001
Patients with complications	306/5195 (5.9)			51/381 (13.4)				<.001
Perioperative complications	119/5195 (2.3)			16/381 (4.2)				.02
Unintentional durotomy	70/5195 (1.3)			11/381 (2.9)				.02
Nerve injury	11/5195 (0.2)			2/381 (0.5)				.22
Blood replacement or postoperative hematoma	17/5195 (0.3)			1/381 (0.3)				.83
Cardiovascular	4/5195 (0.1)			1/381 (0.3)				.24
Respiratory	2/5195 (<0.1)			0/381 (0.0)				.70
Anaphylactic reaction	6/5195 (0.1)			0/381 (0.0)				.51
Wrong level of surgery	9/5195 (0.2)			0/381 (0.0)				.42
Patient-reported complications within 3 mo	193/3551 (5.4)			38/306 (12.4)				<.001
Wound infection	96/3551 (2.7)			11/306 (3.6)				.36
UTI	46/3551 (1.3)			13/306 (4.2)				<.001
Pneumonia	12/3551 (0.3)			4/306 (1.3)				.01
PE	0/3551 (0.0)			1/306 (0.3)				.001
DVT	2/3551 (0.1)			0/306 (0.0)				.68
Micturition problems	50/3551 (1.4)			13/306 (4.2)				<.001

Abbreviations: DVT, deep vein thrombosis; ODI, Oswestry Disability Index; PE, pulmonary embolism; UTI, urinary tract infection.

months' follow-up measured with the Oswestry Disability Index (ODI) version 2.0. The ODI is scored using a scale from 0 to 100, with increasing values reflecting more disability. A minimal clinically important change for the ODI is approximately 10 points.[4] Secondary outcome measures were changes in health-related quality of life, measured with the EQ-5D, a standardized instrument for use as a measure of health outcome from the EuroQol Research Foundation; changes in low back pain and leg pain measured with numeric rating scales; complications; and length of hospital stays.

Missing data were handled with mixed linear models. This strategy was in line with a study[5] showing that multiple imputations are not necessary before performing a mixed-model analysis on longitudinal data. Surgeons recorded comorbidity and perioperative complications. Microdiskectomy was performed by ipsilateral paravertebral muscle retraction and removal of the disk herniation by a unilateral transflaval approach. Patient questionnaires for 3- and 12-month follow-up were distributed and collected by NORspine. Patients reported complications within 3 months of hospital discharge. For statistical comparison tests, we defined the significance level as $P \leq .05$.

Results | There were 5195 patients younger than 65 years of age and 381 patients 65 years of age or older. Baseline characteristics are presented in **Table 1**. Sixty-three of 381 patients 65 years of age or older (16.5%) and 1658 of 5195 patients younger than 65 years of age (31.9%) were lost to follow-up ($P < .001$). For all patients, there was a significant improvement in the ODI (−31.04 points [95% CI, −30.34 to −31.74 points]; $P < .001$). Surgical outcomes are presented in **Table 2**. There were no differences between age cohorts in mean changes of the ODI, the EQ-5D, or leg pain, but elderly patients experienced more improvement in low back pain.

Mixed linear model analyses showed similar results for all patient-reported outcomes. Among patients with complete 12-month follow-up, 268 of 318 patients 65 years of age or older (84.3%) and 2964 of 3537 patients younger than 65 years of age (83.8%) had achieved a minimal clinically important change in the ODI ($P = .83$). Compared with the patients younger than 65 years of age, the patients 65 years of age or older experienced more perioperative complications (16 of 381 [4.2%] vs 119 of 5195 [2.3%]; $P = .02$) and more complications occurring within 3 months of hospital discharge (38 of 306 [12.4%] vs 193 of 3551 [5.4%]; $P < .001$), mainly because they had more urinary tract infections, micturition problems, and unintentional durotomies. The patients younger than 65 years of age had shorter hospital stays than did the patients 65 years of age or older (2.7 vs 1.8 days; $P < .001$).

Discussion | Although the patients 65 years of age or older had more minor complications and longer hospital stays, they experienced improvements in their conditions after a lumbar microdiskectomy that were similar to those of the patients younger than 65 years of age. Age alone should not be a contraindication to surgery, as long as the individual is fit for surgery.

The strengths of this study were the use of prospective registry data with high external validity and the large sample size. Still, the 2 cohorts of patients were not balanced for all baseline and treatment factors because spinal degeneration and comorbidity increase with age. Loss to follow-up at 1 year is a concern, but at a rate of only 16.5% in the patients 65 years of age or older, we demonstrate that older age should not be an exclusion criterion in surgical outcomes research. A previous study from NORspine showed no difference in outcomes between responders and nonresponders.[6]

Mattis A. Madsbu, MS
Tore K. Solberg, MD, PhD
Øyvind Salvesen, MSc, PhD
Øystein P. Nygaard, MD, PhD
Sasha Gulati, MD, PhD

Author Affiliations: Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway (Madsbu); Department of Clinical Medicine, University Hospital of Northern Norway, Tromsø, Norway (Solberg); Department of Public Health and General Practice, Norwegian University of Science and Technology, Trondheim, Norway (Salvesen); National Advisory Unit on Spinal Surgery, Center for Spinal Disorders, St Olavs University Hospital, Trondheim, Norway (Nygaard); Department of Neurosurgery, St Olavs University Hospital, Trondheim, Norway (Gulati).

Corresponding Author: Sasha Gulati, MD, PhD, Department of Neurosurgery, St Olavs University Hospital, 7006 Trondheim, Sør-Trøndelag, Norway (sashagulati@hotmail.com).

Published Online: February 22, 2017. doi:10.1001/jamasurg.2016.5557

Author Contributions: Dr Gulati had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Madsbu, Solberg, Gulati.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Madsbu, Solberg, Gulati.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Madsbu, Salvesen, Gulati.
Obtained funding: Gulati.
Administrative, technical, or material support: Madsbu, Nygaard.
Study supervision: Madsbu, Solberg, Nygaard, Gulati.

Conflict of Interest Disclosures: None reported.

Additional Information: The Norwegian Registry for Spine Surgery receives funding from the University of Northern Norway and Norwegian health authorities.

Additional Contributions: We thank NORspine. We also thank all the patients and spine surgeons who participate in the NORspine registration.

1. Deyo RA, Mirza SK. Clinical practice: herniated lumbar intervertebral disk. *N Engl J Med*. 2016;374(18):1763-1772.

2. Arts MP, Brand R, van den Akker ME, Koes BW, Bartels RH, Peul WC; Leiden-The Hague Spine Intervention Prognostic Study Group (SIPS). Tubular diskectomy vs conventional microdiskectomy for sciatica: a randomized controlled trial. *JAMA*. 2009;302(2):149-158.

3. Nerland US, Jakola AS, Solheim O, et al. Minimally invasive decompression versus open laminectomy for central stenosis of the lumbar spine: pragmatic comparative effectiveness study. *BMJ*. 2015;350:h1603.

4. Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine (Phila Pa 1976)*. 2008;33(1):90-94.

5. Twisk J, de Boer M, de Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. *J Clin Epidemiol*. 2013;66(9):1022-1028.

6. Solberg TK, Sørlie A, Sjaavik K, Nygaard ØP, Ingebrigtsen T. Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? *Acta Orthop*. 2011;82(1):56-63.

PAPER II

Acta Neurochir
DOI 10.1007/s00701-017-3077-4

ORIGINAL ARTICLE - SPINE

Lumbar microdiscectomy for sciatica in adolescents: a multicentre observational registry-based study

Sasha Gulati[1,2,3] · **Mattis A. Madsbu**[1] · **Tore K. Solberg**[4,5] · **Andreas Sørlie**[4,5] · **Charalampis Giannadakis**[2,6] · **Marius K. Skram**[7] · **Øystein P. Nygaard**[1,2,3,5] · **Asgeir S. Jakola**[1,8,9]

Received: 22 November 2016 / Accepted: 4 January 2017

Abstract

Background Lumbar disc herniation (LDH) is rare in the adolescent population. Factors predisposing to LDH in adolescents differ from adults with more cases being related to trauma or structural malformations. Further, there are limited data on patient-reported outcomes after lumbar microdiscectomy in adolescents. Our aim was to compare clinical outcomes at 1 year following single-level lumbar microdiscectomy in adolescents (13–19 years old) compared to younger adults (20–50 years old) with LDH.

Methods Data were collected through the Norwegian Registry for Spine Surgery. Patients were eligible if they had radiculopathy due to LDH, underwent single-level lumbar microdiscectomy between January 2007 and May 2014, and were between 13 and 50 years old at time of surgery. The primary endpoint was change in Oswestry Disability Index (ODI) 1 year after surgery. Secondary endpoints were generic quality of life (EuroQol five dimensions [EQ-5D]), back pain numerical rating scale (NRS), leg pain NRS and complications.

Results A total of 3,245 patients were included (97 patients 13–19 years old and 3,148 patients 20–50 years old). A significant improvement in ODI was observed for the whole population, but there was no difference between groups (0.6; 95% CI, −4.5 to 5.8; $p = 0.811$). There were no differences between groups concerning EQ-5D (−0.04; 95% CI, −0.15 to 0.07; $p = 0.442$), back pain NRS (−0.4; 95% CI, −1.2 to 0.4; $p = 0.279$), leg pain NRS (−0.4; 95% CI, −1.2 to 0.5; $p = 0.374$) or perioperative complications (1.0% for adolescents, 5.1% for adults, $p = 0.072$).

Conclusions The effectiveness and safety of single-level microdiscectomy are similar in adolescents and the adult population at 1-year follow-up.

Keywords Adolescent · Disc herniation · Microdiscectomy · Spine

✉ Asgeir S. Jakola
legepost@gmail.com

1 Department of Neurosurgery, St. Olavs University Hospital, Trondheim, Norway

2 Department of Neuroscience, Norwegian University of Science and Technology (NTNU), Trondheim, Norway

3 National Advisory Unit on Spinal Surgery, St. Olavs University Hospital, Trondheim, Norway

4 Department of Neurosurgery, University Hospital of Northern Norway (UNN), Tromsø, Norway

5 The Norwegian National Registry for Spine Surgery, University Hospital of Northern Norway (UNN), Tromsø, Norway

6 Department of Medicine, Ålesund Hospital, Ålesund, Norway

7 Department of Paediatrics, Rikshospitalet, Oslo University Hospital, Oslo, Norway

8 Department of Neurosurgery, Sahlgrenska University Hospital, Blå Stråket 5, vån 3, 413 45 Göteborg, Sweden

9 Institute of Neuroscience and Physiology, Sahlgrenska Academy, Gothenburg, Sweden

Introduction

The lumbosacral radicular syndrome, also known as sciatica, is commonly caused by a herniated disc [11]. In the majority of patients the natural course of sciatica is favourable [21]. The international consensus is that surgical treatment is offered if the radiating leg pain persists despite a period of conservative management [1]. In the adolescent population lumbar disc herniation (LDH) is rare, but when present it generally

Published online: 16 January 2017

causes symptoms similar to those in the adult population [6]. In adults the outcome after surgical treatment of lumbar disc herniation with lumbar microdiscectomy is well established and favourable [15, 16, 20], but treatment and outcome are less well defined in adolescents [6].

There seems to be different predisposing factors in the adolescent populations with LDH compared to the adult population. Dang et al. [5] reported recently that spinal malformations were more common in the adolescents, but outcome was not improved by fusion. Another factor causing LDH seen more often in adolescents is trauma [6] and, since adolescents have less widespread degeneration, the outcome may be better than in adults, as recently reported [12]. In adolescents the growing spine may also have an impact on outcome, and adolescents may have different demands and expectations with respect to outcome compared to their peers and compared to the adult population. Consequently, outcome studies with implementation of patient reported data in adolescent LDH patients are needed.

There are limited data on patient-reported outcomes after lumbar microdiscectomy in adolescents, and the literature consist largely of small, retrospective series [6]. To achieve adequate patient numbers to study rare entities and subgroups, such as adolescents, LDH spine registries are invaluable.

In fact, a recent study from the Swedish Spine Registry (SweSpine) demonstrated that adolescents were more satisfied and had fewer spine-related symptoms following surgery than adult patients [12]. The SweSpine study included patients that were operated on with both open discectomies and microdiscectomies [12, 19]. As there is only one prospective study on surgical management of LDH in the adolescent population, there is a need to validate the results in another population to establish the effectiveness of treatment with high external validity [12]. As microdiscectomy is more common than open discectomies in the adolescent population, a more focused study is necessary to evaluate effectiveness of this particular procedure.

Due to the differences in aetiology and the sparse patient reported outcome data in the adolescent LDH population, further data are needed to assess treatment effectiveness in terms of patient reported outcomes and safety. We hypothesised that outcome in adolescents would be better compared to adults due to the more focal disease; thus, surgery, being a focal treatment, would be more targeted.

The primary aim of this registry-based study was to compare functional results at 1 year after single-level lumbar microdiscectomy in adolescents (13–19 years old) and younger adults (20–50 years old) with LDH using data from the Norwegian Registry for Spine Surgery (NORspine).

Patients and methods

Study population

Data for this observational study were collected through NORspine, a comprehensive registry for quality control and research. In total, 36 of 40 centres performing lumbar spine surgery in Norway report to NORspine. NORspine is linked to the National Registry and Statistics Norway, which contain information concerning everyone who either is or has been a resident in Norway. According to the Norwegian Directorate of Health, approximately 65% of all patients who undergo lumbar spine surgery in Norway are included in NORspine [13]. Participation in the registration by providers or patients was not mandatory, nor was participation required as a necessary condition for a patient to gain access to healthcare or for a provider to be eligible for payment. Follow-up time from the date of the operation was 1 year. Follow-up time from the date of the operation (baseline) was 1 year.

Inclusion criteria

1. Diagnosis of sciatica due to LDH
2. Scheduled operation (i.e. non-emergency surgery) with single-level lumbar microdiscectomy between January 2007 and May 2014
3. Included in the NORspine registry
4. Age at time of surgery between 13 and 50 years old

Exclusion criteria

1. History of lumbar spine surgery
2. Extraforaminal LDH
3. Spondylolisthesis and/or scoliosis
4. Fusion surgery

Ethical approval

The study was approved by the regional committee for medical research in Central-Norway (2016/840) and all participants provided written informed consent. The Norwegian Data Protection Authority approved the registry protocol.

Primary outcome measure

We used version 2.0 of the Oswestry Disability Index (ODI) [8] as the primary endpoint. ODI is a widely accepted outcome measure in surgery for degenerative lumbar spine disorders, including surgery for LDH [2, 22]. This version is translated into Norwegian and has been validated for psychometric properties [9, 17]. The ODI questionnaire is used to quantify disability for degenerative conditions of the lumbar spine and covers intensity of pain, ability to lift, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality and ability to travel. For each topic there are six statements describing potential scenarios, and patients select the one that most closely resembles their situation. The index is scored from 0 to 100. Zero means no disability and 100 reflects maximum disability. The minimal important change (MIC) in ODI score is considered to be approximately 10 points [14].

Secondary outcome measure

Changes in generic health-related quality of life were measured with the generic EuroQol five dimensions (EQ-5D) instrument between baseline and 1-year follow-up. Intensity of pain was graded in two separate 0–10 numerical rating scales (NRSs) for back pain and leg pain, where 0 equals no pain and 10 represents the worst imaginable or ever experienced pain by the patient [10]. The NRS pain scales and ODI have shown good validity and are frequently used in research on back pain [9]. Complications were registered as described in the paragraph below. We also compared duration of procedures, length of hospital stays, and repeated surgery at the index level within 3 months of surgery between groups.

Data collection and registration by the NORspine registry protocol

On admission for surgery, the patients completed the baseline questionnaire, which included questions about demographics and lifestyle issues in addition to the primary and secondary outcome measure. Information about marital status, educational level, body-mass index (BMI) and tobacco smoking was available in the NORspine registry. During the hospital stay, using a standard registration form, the surgeon recorded data concerning diagnosis, previous lumbar spine surgery, comorbidity, American Society of Anesthesiologists (ASA) grade, treatment and image findings. The surgeons provided the following complications and adverse events to the NORspine registry: intraoperative haemorrhage requiring blood replacement, postoperative haematoma requiring repeated surgery, unintentional durotomy, nerve injury, cardiovascular complications, respiratory complications, anaphylactic reactions and wrong level surgery. Patients reported the following complications if they occurred within 3 months of surgery: wound infection, urinary tract infection, pneumonia, pulmonary embolism and deep vein thrombosis. A questionnaire was distributed to all patients at 3 months and 1 year after surgery. The patients who did not respond received one reminder with a new copy of the questionnaire. The patients completed preoperative questionnaire data and postal follow-up questionnaires without any assistance from the treating surgeon.

Surgical procedures

All patients underwent single-level lumbar microdiscectomy. Since this is a multicentre observational study, small variations in the surgical management may occur and the surgical procedures can only be described in general terms and in accordance with the data collected in the NORspine registry. The microsurgical discectomy involves preoperative fluoroscopy for detection of the target level, paramedian or median incision of about 3–6 cm, straight or curved opening of the paravertebral muscular fascia, subperiosteal release of the paravertebral musculature from the spinous process and basal lamina above and below the target disc-level. Self-retaining retractors (typically Caspar retractors) and a microscope or loupes are introduced. Often a flavectomy and arcotomy of the lamina above the disc-level are done. This is followed by careful mobilisation of the dural sac and the nerve-root medially, before evacuating the herniated disc. This might involve entering the disc space, or just removing a free sequestrated disc fragment (sequestrectomy).

Statistical analysis

Statistical analyses were performed with SPSS version 21 (IBM Corporation, Chicago, IL, USA). Statistical significance level was defined as $p \leq 0.05$ on the basis of a two-sided hypothesis test with no adjustments made for multiple comparisons. Central tendencies are presented as means when normally distributed and as medians when skewed. We used the chi-squared test for categorical variables. Baseline and 1-year scores were compared with paired-samples *t*-test. Mean change scores between the groups were analysed with independent-samples *t*-test. A multiple linear regression model was applied to assess the relationship between the difference in ODI score at 12-months (dependent variable) and age group (adolescence versus young adults), controlling for potential confounders. The multiple linear regression analysis included BMI (linear), adolescence (yes/no), sex, smoking (yes/no), and preoperative ODI (linear).

Missing data

For missing data we chose to exclude cases pairwise in the complete case analyses. This method excluded patients only if they were missing the data required for the specific analysis. They were still included in any of the analyses for which they had the necessary information. This strategy was based on a study on an equivalent patient population from NORspine that showed no difference in outcomes between responders and non-responders [18]. To minimise the number of missing data points, additional "last observation carried forward" analyses were also performed. In patients where the ODI score at 1 year after surgery was missing, we used the value registered at 3 months assuming little difference between these two time points.

Results

Study population

A total of 3,245 patients were enrolled out of 7,158 screened patients (Fig. 1). Among the 7,158 patients screened for inclusion, 752 underwent open discectomy and were excluded from the study. There were 97 adolescents and 3,148 adults. The mean age at baseline was 37.0 (±8.3) years and 40.7% were females. Baseline characteristics are presented in Table 1.

Oswestry Disability Index

Complete 1-year follow-up for ODI was achieved in 63.8% of patients ($n = 2{,}071$) with no differences between adolescents and adult patients (59.8% vs 63.9%, $p = 0.402$). For the whole study population there was an improvement of 27.2 points in ODI at 1 year (95% CI, 26.3–28.0; $p < 0.001$). In a complete case analysis ($n = 2{,}071$) there was no difference in mean ODI change between age cohorts at 1-year follow-up (mean difference, 0.6; 95% CI, −4.5 to 5.8; $p = 0.811$). Among the 2071 patients with complete 1-year follow-up, 82.7% ($n = 1{,}711$) achieved a MIC predefined as an improvement of ≥10 points in ODI score from baseline. At 1 year, 86.2% of adolescents had achieved a MIC, compared to 82.6% of adult patients ($p = 0.474$). Changes in ODI score are presented in Table 2.

Secondary outcomes

Changes in EQ-5D, back pain NRS and leg pain NRS after 1-year follow-up for both age groups are presented in Table 2. No differences between the two age groups were found for any of the secondary patient-reported outcomes. Details regarding surgical treatment, duration of procedure, hospitalisation period and complications are presented in Table 3. There were no differences between groups in duration of surgery. Adolescents had slightly longer hospital stays (mean difference, 0.4 days; $p < 0.042$). Further, there were no differences in the rate of repeated surgery for any cause within 3 months between adolescents and adults (0% vs 1.2%, $p = 0.270$). The proportion of patients experiencing one or more complications within 3 months of surgery (both surgeon and patient-reported) was 5.0% ($n = 160$). There were no differences between groups in perioperative complications

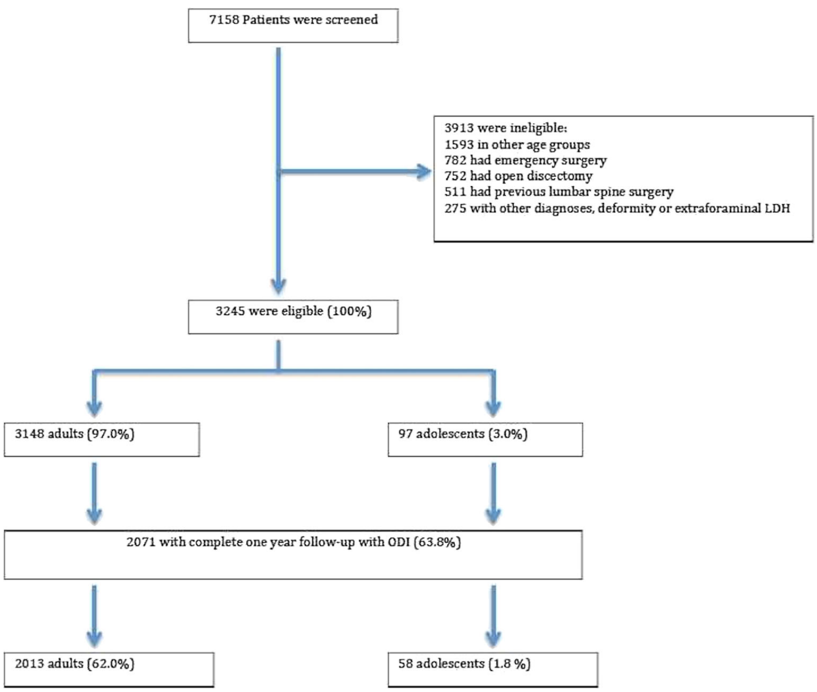

Fig. 1 Study enrollment and follow-up

Table 1 Demographic characteristics, coexisting illnesses and measures of health status for both groups ($n = 3{,}245$)

Variable	Adolescents (age <20), $n = 97$	Adults (age 20–50), $n = 3{,}148$	p value
Mean age, years ± SD	17.5 ± 1.6	37.6 ± 7.7	<0.001
Female sex, no. (%)	48 (49.5)	1271 (40.4)	0.072
BMI ± SD[a]	24.4 ± 4.1	26.5 ± 4.4	<0.001
Daily tobacco smoking, no. (%)	13 (13.4)	955 (30.7)	<0.001
ASA grade >2[b]	0 (0)	47 (1.5)	0.224
Preoperative ODI ± SD[c]	33.9 ± 13.0	41.3 ± 16.6	<0.001
Preoperative EQ-5D ± SD	0.38 ± 0.34	0.34 ± 0.34	0.265
Preoperative leg pain (NRS) ± SD	6.3 ± 2.2	6.5 ± 2.2	0.525
Preoperative back pain (NRS) ± SD	5.6 ± 2.5	5.8 ± 2.3	0.333
Preoperative paresis, no. (%)	2 (2.1)	342 (10.9)	0.006
Duration of leg pain >1 year, no. (%)	28 (29.5)	720 (24.0)	0.221

[a] The bodymass index (*BMI*) is the weight in kilograms divided by the square of the height in metres

[b] The American Society of Anesthesiologists (*ASA*) grade ranges from I to V; grade V is the worst, indicating life-threating condition

[c] Oswestry Disability Index (*ODI*) ranges from 0 to 100; lower scores indicating less severe symptoms

(i.e. during hospital admission) or complications occurring within 3 months of surgery.

Multiple regression analysis

A multiple regression analysis was performed with difference in ODI score at 1 year as the dependent variable (Table 4). Smoking ($p < 0.001$), ASA grade >2 ($p = 0.003$), female sex ($p = 0.010$), BMI ($p = 0.011$) and preoperative ODI ($p < 0.001$) were associated with statistically significant ODI change at 1 year, whereas no association was found for adolescence ($p = 0.103$).

Discussion

This multicentre observational study from NORspine shows similar effectiveness and safety of single-level lumbar microdiscectomy in adolescents and adults at 1 year. A MIC was achieved in 86% of adolescents following microdiscectomy for LDH, similar to the adult population.

Clinical outcomes after surgical treatment for LDH in the adolescent population are mostly limited to retrospective case series [6]. Our findings support the retrospective findings that this is an effective procedure, although as expected in a prospective study using patient reported outcomes, the success rates are somewhat lower than in the retrospective case series with surgeon reported outcomes [6]. In a recent observational study from SweSpine, Lagerbäck et al. [12] found that adolescents were more satisfied and had fewer spine related symptoms following surgery than adult patients. The primary outcome variable in the Swedish study was a crude self-rating of satisfaction of surgical outcomes. Our study shows that the improvements in ODI and EQ-5D at 1 year were similar in adolescents compared to the adult group. The study by Lagerbäck et al. was larger with 151 adolescent patients, but did not provide details about the surgical procedure. In a related study from SweSpine in the same time period there were 49% open discectomies [19]. However, we think that there are no reasons why spine surgeons should choose open procedures in adolescent patients if microdiscectomy offers similar improvement. Our series with 97 adolescent patients

Table 2 Primary and secondary patient reported outcomes at 1 year

Complete case analysis								
	Adolescents ($n = 59$)			Adults ($n = 2{,}013$)			Difference in mean change between groups (95% CI)	p value
	Baseline	1 year	Mean change	Baseline	1 year	Mean change		
ODI	35.0	8.5	26.5	41.3	14.1	27.2	0.6 (−4.5, 5.8)	0.811
EQ-5D	0.36	0.83	0.48	0.34	0.78	0.43	−0.04 (−0.15, 0.07)	0.442
Back pain NRS	5.7	2.2	3.5	5.7	2.7	3.1	−0.4 (−1.2, 0.4)	0.279
Leg pain NRS	6.3	1.4	4.9	6.5	2.0	4.5	−0.4 (−1.2, 0.5)	0.374
Last value carried forward analysis								
	Adolescents ($n = 77$)			Adults ($n = 2{,}470$)			Difference in mean change between groups (95% CI)	P-value
	Baseline	1 year	Mean change	Baseline	1 year	Mean change		
ODI	33.7	8.3	25.4	41.2	14.6	26.6	1.2 (−3.3, 5.8)	0.593
EQ-5D	0.38	0.85	0.47	0.34	0.77	0.43	−0.04 (−0.13, 0.05)	0.386
Back pain NRS	5.5	2.0	3.5	5.8	2.7	3.1	−0.4 (−1.1, 0.3)	0.261
Leg pain NRS	6.4	1.3	5.0	6.5	2.0	4.5	−0.5 (−1.2, 0.2)	0.173

Table 3 Surgical treatments, complications and events

Variable	Adolescents ($n = 97$)	Adults, 20–50 years ($n = 3{,}148$)	*p* value
Level operated, no. (%)			
- L2/L3	1 (1.0)	18 (0.6%)	0.559
- L3/L4	2 (2.1)	83 (2.6)	0.727
- L4/L5	55 (56.7)	1,235 (39.2)	0.001
- L5/S1	39 (40.2)	1,812 (57.6)	0.001
Operation time (minutes)	56.6	54.7	0.488
Days in hospital, no.	1.9	1.5	0.042
Any complication, no. (%)	1 (1.0)	159 (5.1)	0.072
Perioperative complications, no. (%)	0 (0.0)	63 (2.0)	0.159
- Dural tear or spinal fluid leak	0 (0)	35 (1.1)	0.296
- Nerve injury	0 (0)	6 (0.2)	0.667
- Blood replacement or postoperative haematoma	0 (0)	11 (0.3)	0.560
- Cardiovascular complications	0 (0)	1 (0.0)	0.861
- Respiratory complications	0 (0)	1 (0.0)	0.861
- Anaphylactic reaction	0 (0)	4 (0.1)	0.725
- Wrong level surgery	0 (0)	4 (0.1)	0.725
Complications within 3 months, no. (%)	1 (1.5)	100 (4.9)	0.214
- Wound infection	0 (0)	57 (2.8)	0.173
- Urinary tract infection	0 (0)	20 (1.0)	0.424
- Pneumonia	0 (0)	7 (0.3)	0.637
- Pulmonary embolism	0 (0)	0 (0)	–
- Deep vein thrombosis	0 (0)	0 (0)	–
- Micturition problems	1 (1.5)	24 (1.2)	0.787

undergoing microdiscectomy is the largest prospective study to date evaluating results after minimally invasive spine surgery in this age group. Based on these two registry-based studies, it is not possible to directly compare open discectomy with microdiscectomy; however, it is interesting that the 86% satisfaction rate reported by Lagerbäck et al. compares well to the 86% of our patients achieving the MIC for ODI.

Our study seems to be consistent with previous studies showing that adolescents have less severe symptoms at baseline and that adolescents are less likely to present with paresis [6, 12]. The same trend was observed in the recent SweSpine study; however, in their study EQ-5D scores were higher (i.e. experiencing less problems) among adolescents. This is not unexpected since NRS captures pain intensity only, while the ODI and EQ-5D are multi-dimensional and focus on functional status. A clinical relevant age effect per se in EQ-5D is not expected, but spine-related or other co-morbidity may influence results [3]. Moreover, adolescents are expected to have less spinal degenerative changes at presentation.

Finally, based on the literature, it seems that surgical treatment of LDH in the adolescent population is a safe procedure with low operative complications, although open discectomies seem to be the dominating procedure [4, 12]. Our study demonstrates safety also after lumbar microdiscectomy with a complication rate of only 1%. The low complication rate in our study might be related to the young age of included patients and exclusion of individuals who had undergone previous lumbar spine surgery.

Table 4 Multiple regression analysis with change in ODI at 1 year as the dependent variable

Variable	Parameter estimate	95% confidence interval	*p* value
Adolescent	3.4	−4.5, 4.6	0.103
Oswestry score, pre-surgery	0.9	0.8, 0.9	<0.001
Smoking	−5.7	−7.2, −4.3	<0.001
ASA grade >2	−8.7	−14.5, −2.9	0.003
Female sex	−1.8	−3.1, −0.4	0.010
BMI	−0.2	−0.4, −0.05	0.011

A negative score means a worsening of ODI score 1 year after surgery

Study strengths and limitations

The results in the present study were strengthened by the use of specific inclusion and exclusion criteria, prospective data collection and the large sample size. One of the main advantages of using data from spine registries such as NORspine is the use of widely accepted and validated outcome measures such as ODI, EQ-5D, back pain NRS and leg pain NRS. The preoperative baseline values of our outcome measures reflect indications for surgery. Further, the use of prospectively collected outcomes make future comparisons across clinical studies much more feasible. Moreover, patient-reported outcomes in neurosurgical research are often lacking and may provide a better understanding of the effectiveness and safety of surgical procedures [7]. The main limitation of the present study is that the loss to follow-up was relatively high. However, in a study on an equivalent patient population with 22% non-responders, no difference in outcomes between responders and non-responders was found at long-term follow-up [18].

Also, ideally we would have a control group undergoing conservative management. However, based on the symptom duration, it is unlikely that adolescents are fast-tracked to surgery, and faster recovery and surgical treatment is reserved for acute or intolerable pain, or when conservative treatment fails. Similar to SweSpine, the NORspine registry covers degenerative spine surgery as a whole and consequently no validated adolescent outcome measures were used [12]. Although we found no difference at 1 year, a longer follow-up may be warranted to investigate surgery rates for disc reherniation and detect progression of symptoms and back-pain-related disability.

Conclusions

At 1 year, the effectiveness and safety of one level microdiscectomy are similar in adolescents and the adult population.

Acknowledgements The authors would like to thank the Norwegian Registry for Spine Surgery (NORspine). The NORspine registry receives funding from the University of Northern Norway and Norwegian health authorities. We thank all patients and surgeons participating in NORspine registration.

Authors' contributions All authors read and approved the final manuscript. S.G.: study design, collection of data, statistics and writing; A.S.J.: study design and drafting of the manuscript; M.A.M. and C.H.: statistics and writing; A.S., Ø.P.N. and T.K.S.: collection of data and writing.

Compliance with ethical standards

Conflicts of interest All authors certify that they have no affiliations with or involvement in any organisation or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Funding No funding was received for this research.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Andersson GB, Brown MD, Dvorak J, Herzog RJ, Kambin P, Malter A, McCulloch JA, Saal JA, Spratt KF, Weinstein JN (1996) Consensus summary of the diagnosis and treatment of lumbar disc herniation. Spine 21:75S–78S
2. Arden NK, Price C, Reading I, Stubbing J, Hazelgrove J, Dunne C, Michel M, Rogers P, Cooper C (2005) A multicentre randomized controlled trial of epidural corticosteroid injections for sciatica: the WEST study. Rheumatology (Oxford) 44:1399–1406
3. Burstrom K, Johannesson M, Diderichsen F (2001) Swedish population health-related quality of life results using the EQ-5D. Qual Life Res 10:621–635
4. Cahill KS, Dunn I, Gunnarsson T, Proctor MR (2010) Lumbar microdiscectomy in pediatric patients: a large single-institution series. J Neurosurg Spine 12:165–170
5. Dang L, Chen Z, Liu X, Guo Z, Qi Q, Li W, Zeng Y, Jiang L, Wei F, Sun C, Liu Z (2015) Lumbar disk herniation in children and adolescents: the significance of configurations of the lumbar spine. Neurosurgery 77:954–959, discussion 959
6. Dang L, Liu Z (2010) A review of current treatment for lumbar disc herniation in children and adolescents. Eur Spine J 19:205–214
7. Drewes C, Sagberg LM, Jakola AS, Gulati S, Solheim O (2015) Morbidity after intracranial tumor surgery: sensitivity and specificity of retrospective review of medical records compared with patient-reported outcomes at 30 days. J Neurosurg 123:972–977
8. Fairbank JC, Couper J, Davies JB, O'Brien JP (1980) The Oswestry low back pain disability questionnaire. Physiotherapy 66:271–273
9. Grotle M, Brox JI, Vollestad NK (2003) Cross-cultural adaptation of the Norwegian versions of the Roland-Morris disability questionnaire and the Oswestry disability index. J Rehabil Med 35:241–247
10. Jensen MP, Karoly P (1992) Self-report scales and procedures for assessing pain in adults. In: Truk DC, Melzack R (eds) Handbook of pain assessment. Guilford Press, New York, pp 135–151

11. Koes BW, van Tulder MW, Peul WC (2007) Diagnosis and treatment of sciatica. BMJ 334:1313–1317
12. Lagerback T, Elkan P, Moller H, Grauers A, Diarbakerli E, Gerdhem P (2015) An observational study on the outcome after surgery for lumbar disc herniation in adolescents compared with adults based on the Swedish Spine Register. Spine J 15:1241–1247
13. Nerland US, Jakola AS, Solheim O, Weber C, Rao V, Lonne G, Solberg TK, Salvesen O, Carlsen SM, Nygaard OP, Gulati S (2015) Minimally invasive decompression versus open laminectomy for central stenosis of the lumbar spine: pragmatic comparative effectiveness study. BMJ 350:h1603
14. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, Bouter LM, de Vet HC (2008) Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine 33:90–94
15. Peul WC, van den Hout WB, Brand R, Thomeer RT, Koes BW (2008) Prolonged conservative care versus early surgery in patients with sciatica caused by lumbar disc herniation: two year results of a randomised controlled trial. BMJ 336:1355–1358
16. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JA, Tans JT, Thomeer RT, Koes BW (2007) Surgery versus prolonged conservative treatment for sciatica. N Engl J Med 356: 2245–2256
17. Solberg TK, Olsen JA, Ingebrigtsen T, Hofoss D, Nygaard OP (2005) Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. Eur Spine J 14:1000–1007
18. Solberg TK, Sorlie A, Sjaavik K, Nygaard OP, Ingebrigtsen T (2011) Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? Acta Orthop 82:56–63
19. Stromqvist F, Stromqvist B, Jonsson B, Gerdhem P, Karlsson MK (2016) Lumbar disc herniation surgery in children: outcome and gender differences. Eur Spine J 25:657–663
20. van den Hout WB, Peul WC, Koes BW, Brand R, Kievit J, Thomeer RT (2008) Prolonged conservative care versus early surgery in patients with sciatica from lumbar disc herniation: cost utility analysis alongside a randomised controlled trial. BMJ 336: 1351–1354
21. Vroomen PC, de Krom MC, Wilmink JT, Kester AD, Knottnerus JA (1999) Lack of effectiveness of bed rest for sciatica. N Engl J Med 340:418–423
22. Weinstein JN, Lurie JD, Tosteson TD, Skinner JS, Hanscom B, Tosteson AN, Herkowitz H, Fischgrund J, Cammisa FP, Albert T, Deyo RA (2006) Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT) observational cohort. JAMA 296:2451–2459

PAPER III

Surgery for Herniated Lumbar Disc in Daily Tobacco Smokers: A Multicenter Observational Study

Mattis A. Madsbu[1,2], Øyvind Salvesen[3], David A.T. Werner[4,5], Eric Franssen[6], Clemens Weber[7], Øystein P. Nygaard[1,2,8,9], Tore K. Solberg[4,5,9], Sasha Gulati[1,2,8]

■ OBJECTIVE: **To compare clinical outcomes at 1 year following single-level lumbar microdiscectomy in daily tobacco smokers and nonsmokers.**

■ METHODS: **Data were collected through the Norwegian Registry for Spine Surgery. The primary endpoint was a change in the Oswestry Disability Index (ODI) at 1 year. Secondary endpoints were change in quality of life measured with EuroQol 5 Dimensions (EQ-5D), leg and back pain measured with a numerical rating scale (NRS), and rates of surgical complications.**

■ RESULTS: **A total of 5514 patients were enrolled, including 3907 nonsmokers and 1607 smokers. A significant improvement in ODI was observed for the entire cohort (mean, 31.1 points; 95% confidence interval [CI], 30.4–31.8; $P < 0.001$). Nonsmokers experienced a greater improvement in ODI at 1 year compared with smokers (mean, 4.1 points; 95% CI, 2.5–5.7; $P < 0.001$). Nonsmokers were more likely to achieve a minimal important change (MIC), defined as an ODI improvement of ≥10 points, compared with smokers (85.5% vs. 79.5%; $P < 0.001$). Nonsmokers experienced greater improvements in EQ-5D (mean difference, 0.068; 95% CI, 0.04–0.09; $P < 0.001$), back pain NRS (mean difference, 0.44; 95% CI, 0.21–0.66; $P < 0.001$), and leg pain NRS (mean difference, 0.54; 95% CI, 0.31–0.77; $P < 0.001$). There was no difference between smokers and nonsmokers in the overall complication rate (6.2% vs. 6.7%; $P = 0.512$). Smoking was identified as a negative predictor for ODI change in a multiple regression analysis ($P < 0.001$).**

■ CONCLUSIONS: **Nonsmokers reported a greater improvement in ODI at 1 year following microdiscectomy, and smokers were less likely to experience an MIC. Nonetheless, significant improvement was also found among smokers.**

INTRODUCTION

Daily tobacco smoking can have adverse effects on the spinal column,[1] and tobacco smokers are more prone to develop degenerative changes of the spinal column, including lumbar disc herniation (LDH).[2-8] Lumbar microdiscectomy is currently the most common surgical procedure for symptomatic LDH,[9] but data are limited on the impact of smoking on patient-reported outcome measures (PROMs) following lumbar microdiscectomy. Daily tobacco smoking has been identified as a risk factor for LDH requiring surgical treatment,[10] and a recent meta-analysis identified smoking as the strongest predictor of recurrent LDH following primary discectomy.[11,12]

The primary aim of the present registry-based study was to compare clinical outcomes at 1 year after single-level lumbar

Key words
- Discectomy
- Lifestyle
- Microdiscectomy
- Patient-reported outcome
- Quality of life
- Sciatica
- Tobacco

Abbreviations and Acronyms
EQ-5D: EuroQol 5 Dimensions
LDH: Lumbar disc herniation
MIC: Minimal important change
NORspine: Norwegian Registry for Spine Surgery
NRS: Numerical rating scale
ODI: Oswestry Disability Index
PROM: Patient-reported outcome measure

From the [1]Department of Neurosurgery, St. Olavs University Hospital, Trondheim; [2]Department of Neuroscience, Norwegian University of Science and Technology, Trondheim; [3]Department of Public Health and General Practice, Norwegian University of Science and Technology, Trondheim; [4]Department of Neurosurgery, University Hospital of Northern Norway, Tromsø; [5]Department of Clinical Medicine, University of Tromsø, Tromsø; Departments of [6]Orthopedic Surgery and [7]Neurosurgery, Stavanger University Hospital, Stavanger; [8]National Advisory Unit on Spinal Surgery, St. Olavs University Hospital, Trondheim; and [9]Norwegian National Registry for Spine Surgery, University Hospital of Northern Norway, Tromsø, Norway

To whom correspondence should be addressed: Mattis A. Madsbu, M.S. [E-mail: mattis.madsbu@gmail.com]

Citation: World Neurosurg. (2017). https://doi.org/10.1016/j.wneu.2017.10.024

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

microdiscectomy in smokers and nonsmokers with LDH using data from the Norwegian Registry for Spine Surgery (NORspine).

MATERIALS AND METHODS

Study Population

Data were collected through NORspine, a comprehensive registry for quality control and research.[13] Thirty-six of the 40 centers performing lumbar spine surgery in Norway report to NORspine. According to the Norwegian Directorate of Health, approximately 63% of all patients who underwent lumbar spine surgery in Norway during the study period were included in NORspine.[13] Microdiscectomy was performed by ipsilateral paravertebral muscle retraction and removal of the disc herniation via a unilateral transflaval approach. Participation in the registration by providers or patients was not mandated, and participation was not a necessary condition for a patient to gain access to health care or for a provider to be eligible for payment. Follow-up from the date of the operation was 1 year.

Criteria for inclusion into the study were a diagnosis of symptomatic LDH, scheduled operation (i.e., nonemergency surgery) with single-level lumbar microdiscectomy between January 2007 and May 2014, and inclusion in the NORspine registry. Exclusion criteria were a history of lumbar spine surgery, extraforaminal LDH, coexisting degenerative spondylolisthesis and/or scoliosis, and fusion surgery.

The study was evaluated and approved by the Regional Committee for Medical Research and Health Research Ethics in Central Norway (2016/840), and all participants provided written informed consent. The Data Inspectorate of Norway approved the registry protocol.

Primary Outcome Measure

The NORspine registry uses version 2.0 of the Oswestry Disability Index (ODI).[14] This version has been translated into Norwegian and tested for psychometric properties.[15,16] The ODI contains 10 questions on limitations of activities of daily living. Each variable is rated on a scale of 0 to 5 points, summarized, and converted into a percentage score. Scores range from 0 to 100, with a lower score indicating less severe pain and disability. In this patient population, the minimal clinically important difference for change in the mean ODI score is considered to be approximately 10 points.[17] Because a minimal important change (MIC) value of 10 might not be sufficient to indicate that a patient has experienced a clinically important change,[18] we also determined the proportion of patients with minimal disability at 1 year.

Secondary Outcome Measure

Changes in generic health-related quality of life were measured with the generic EuroQol 5 Dimensions (EQ-5D) instrument between baseline and the 1-year follow-up. The EQ-5D questionnaire evaluates the generic quality of life with 1 question for each of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The intensity of pain was graded on 2 separate numerical rating scales (NRSs) of 0–10 for back pain and leg pain, with 0 representing no pain and 10 representing the worst pain imaginable or ever experienced by the patient.[19] The NRSs for pain and the ODI have shown good validity and are frequently used in research on back pain.[15] We also evaluated the duration of procedures, length of hospital stay, repeated surgery at the index level within 3 months of the initial surgery, and surgical complication rates.

Table 1. Demographic Characteristics, Coexisting Illnesses, and Measures of Health Status for the 2 Groups

Variable	Nonsmokers	Smokers	*P* Value
Number of patients (%)	3907 (70.9)	1607 (29.1)	
Age (years), median (range)	44.1 (18–89)	43.7 (18–83)	0.011
Female sex, number (%)	1518 (27.5)	732 (13.3)	<0.001
Married or partner, number (%)	3059 (55.9)	1099 (20.1)	<0.001
Attended college, number (%)	1751 (31.8)	377 (6.8)	<0.001
Body mass index (kg/m^2), mean	26.7	26.3	0.002
Current smoker, number (%)	3907 (70.9)	1607 (29.1)	<0.001
Coexisting spinal stenosis at the operated level, number (%)	468 (12.0)	194 (12.1)	0.923
Comorbidity, number (%)	769 (19.7)	372 (23.1)	0.004
Cardiovascular disease	140 (3.6)	56 (3.5)	-
Cerebrovascular disease	15 (0.4)	6 (0.4)	-
Vascular claudication	3 (0.1)	2 (0.1)	-
Diabetes mellitus	96 (2.5)	36 (2.2)	-
Osteoporosis	5 (0.1)	3 (0.2)	-
Knee and/or hip osteoarthritis	38 (1)	7 (0.4)	-
Chronic neurologic disease	22 (0.6)	8 (0.5)	-
Chronic musculoskeletal pain	54 (1.4)	33 (2.1)	-
Cancer	22 (0.6)	10 (0.6)	-
Rheumatoid arthritis	17 (0.4)	4 (0.2)	-
Ankylosing spondylitis	14 (0.4)	4 (0.2)	-
Other rheumatic diseases	31 (0.8)	18 (0.1)	-
Depression and/or anxiety	34 (0.9)	48 (3.0)	-
American Society of Anesthesiologists grade >2, number (%)	150 (3.9)	71 (4.5)	0.320
Mean preoperative ODI	44.8	46.6	0.002
Mean preoperative EQ-5D	0.29	0.26	0.013
Preoperative diagnostic imaging, number (%)			
Magnetic resonance imaging	3808 (97.5)	1551 (96.5)	0.052
Computed tomography	168 (4.3)	94 (5.8)	0.014
Level of surgery, number (%)			
L2/L3	46 (0.8)	21 (0.4)	0.690
L3/L4	227 (4.1)	72 (1.3)	0.048
L4/L5	1699 (30.8)	695 (12.6)	0.871
L5/S1	1935 (35.1)	819 (14.9)	0.332

Data Collection and Registration with the NORspine Registry Protocol

On admission for surgery, the patients completed the baseline questionnaire, which included questions about demographic details and lifestyle issues in addition to the primary outcome measure. During the hospital stay, using a standard registration form, the surgeon recorded data on the diagnosis, previous lumbar spine surgery, comorbidity, American Society of Anesthesiologists grade, imaging findings, and surgical approach and procedure. The surgeons provided data on the following possible complications and adverse events to the NORspine registry: intraoperative hemorrhage requiring blood replacement, postoperative hematoma requiring repeated surgery, unintentional durotomy, nerve injury, cardiovascular complications, respiratory complications, anaphylactic reactions, and wrong-level surgery. Patients reported the following complications occurring within 3 months of surgery: wound infection, urinary tract infection, pneumonia, pulmonary embolism, and deep venous thrombosis. A questionnaire was distributed to patients by regular mail at 3 months and 1 year after surgery, completed at home by the patients, and returned in the same way. The patients who did not respond received a reminder with a new copy of the questionnaire. The patients completed the preoperative and follow-up questionnaires without any assistance from the surgeon or other staff at the treating hospital.

Statistical Analysis

All statistical analyses were performed with SPSS version 23.0 (IBM, Armonk, New York, USA). Statistical significance was defined as $P \leq 0.05$ on the basis of a 2-sided hypothesis test, with no adjustments made for multiple comparisons. Central tendencies are presented as means when normally distributed and as medians when skewed. The χ^2 test was used for categorical variables. Baseline and 1-year scores were compared using the paired-samples *t* test. Mean change scores between the groups were analyzed with the independent-samples *t* test.

A multiple linear regression model was applied to assess the relationship between the difference in ODI score at 1 year (dependent variable) and smoking, controlling for potential confounders. The selection of predictors included in the final model

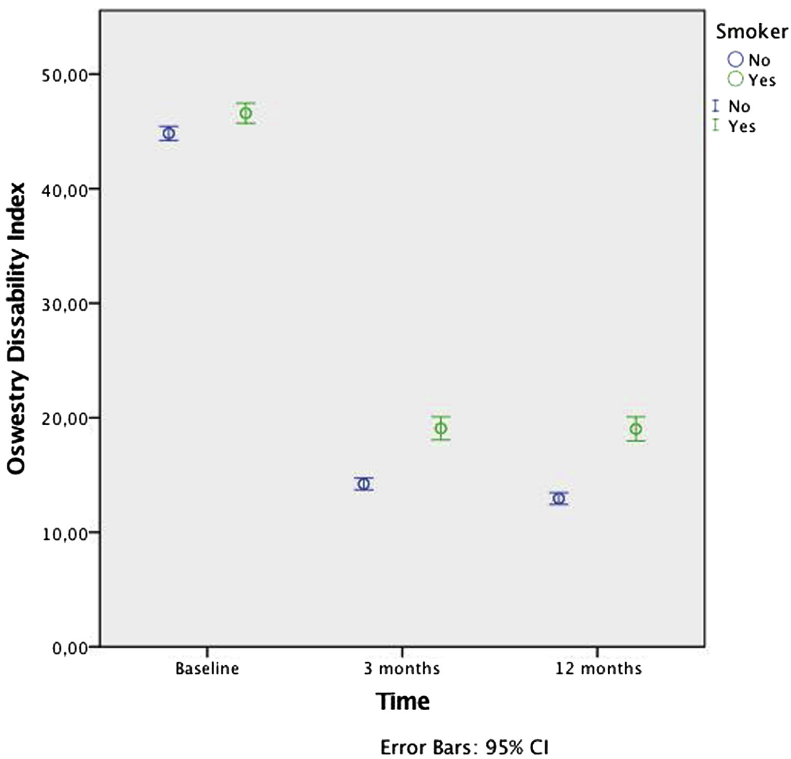

Figure 1. Oswestry disability index scores in patients undergoing microdiscectomy for lumbar disc herniation at baseline, 3 months, and 12 months. Error bars represent 95% confidence intervals (CIs).

was based on their clinical importance and association with the dependent variable.[20,21] The multiple linear regression analysis included variables that might affect clinical outcomes, including age, sex, body mass index, preoperative ODI, depression and/or anxiety, and smoking.[20-24] In the final regression model, patients were categorized according to body mass index as normal (<25 kg/m^2; reference), overweight (25–29.9 kg/m^2), class I obesity (30–34.9 kg/m^2) or class II–III obesity (>35 kg/m^2) (i.e., as "dummy" variables). Owing to a strong nonlinear relationship between preoperative ODI and the dependent variable, patients were categorized according to the preoperative ODI score as minimal disability, ODI 0–20 (reference value); moderate disability, ODI 21–40; severe disability, ODI 41–60; crippled, ODI 61–80; or bed-bound, ODI 81–100 (bed-bound) (i.e., as dummy variables).

Missing Data

Missing data were handled with mixed linear models. This strategy was in line with studies showing that it is not necessary to handle missing data using multiple imputations before performing a mixed-model analyses on longitudinal data.[24,25]

RESULTS

Study Population

The 5514 patients enrolled in this study included 3907 nonsmokers and 1607 smokers. A total of 3814 patients (69.2%) completed the 12-month follow-up with the ODI, including 2797 nonsmokers (71.6%) and 1017 smokers (63.3%) ($P < 0.001$). Baseline characteristics, surgical treatments, and comorbidities are summarized in Table 1. The mean patient age at baseline was 44.0 ± 9.9 years, and the cohort was 40.8% female. In the entire cohort, there was a significant difference between mean preoperative ODI and mean ODI at the 1-year follow-up (31.1 points; 95% confidence interval [CI], 30.4–31.8; $P < 0.001$). There was a significant difference in ODI change at 1 year between nonsmokers and smokers (4.1 points; 95% CI, 2.48–5.66; $P < 0.001$) as shown in Figure 1. At 1 year, 85.5% of nonsmokers had achieved an MIC (≥10-point ODI improvement), compared with 79.5% of smokers ($P < 0.001$). In patients with complete one-year follow-up, smokers were less likely to report minimal disability (ODI <20) at one year compared to non-smokers (62.6% vs. 77.3%, $P < 0.001$).

Out of the 3814 patients with a complete one year ODI follow up, there were 2800 (73.4%) that had an ODI score of 20 or less at 12 months. Within non-smokers and smokers there was 2163 (77.3%) and 637 (62.6%) respectively with an ODI score ≤20 after 1 year ($P < 0.001$).

Changes in EQ-5D, back pain NRS, and leg pain NRS at one year for both age groups are presented in Table 2. There was a small but statistically significant difference between the two groups in favor of non-smokers for EQ-5D (0.068, 95% CI, 0.04 to 0.09; $P = <0.001$), back pain NRS (0.44; 95% CI, 0.21 to 0.66, $P < 0.001$) and leg pain NRS (0.54, 95% CI, 0.31 to 0.77, $P < 0.001$). Mixed linear model analyses for missing data showed similar results for all PROMs. As shown in Table 3, there was no difference between smokers and non-smokers in the overall complication rate (6.2% vs. 6.7%, $P = 0.512$).

Multiple Regression Analysis

A multiple regression analysis with change in ODI at one year as the dependent variable was performed. A positive value in the outcome corresponds to less low back pain related disability. The effect estimates are presented in Table 4 (1700 observations deleted due to missing data [30.8%]). Preoperative ODI score was the strongest outcome predictor with increasing values were strongly associated with improvement at 1 year. Smoking, American Society of Anesthesiologists grade >2, female sex, age ≥65 years, depression and/or anxiety, overweight and obesity

Table 2. Outcomes at 1 Year in Patients Undergoing Surgery for Single-Level LDH

Variable	Nonsmokers			Smokers			Difference in Mean Change Between Groups (95% CI)	*P* Value
	Baseline	1 Year	Mean Change	Baseline	1 Year	Mean Change		
Complete case analyses for ODI (n = 3814)								
ODI	45.1	12.9	−32.2	47.1	19.0	−28.1	4.1 (2.5–5.7)	<0.001
EQ-5D	0.29	0.79	0.50	0.27	0.70	0.43	0.07 (0.04–0.09)	<0.001
Back pain NRS	6.0	2.4	−3.6	6.4	3.3	−3.2	0.4 (0.2–0.7)	<0.001
Leg pain NRS	6.8	1.9	−4.9	7.1	2.7	−4.4	0.5 (0.3–0.8)	<0.001
Mixed linear model analyses (n = 5510)								
ODI	44.8	13.1	−31.7	46.6	19.2	−27.4	4.4 (3.1–5.7)	<0.001
EQ-5D	0.29	0.78	0.49	0.26	0.69	0.43	0.06 (0.04–0.09)	<0.001
Back pain NRS	6.0	2.4	−3.6	6.4	3.3	−3.1	0.5 (0.3–0.7)	<0.001
Leg pain NRS	6.8	1.9	−4.9	7.0	2.7	−4.3	0.6 (0.4–0.8)	<0.001

LDH, lumbar disc herniation; CI, confidence interval; ODI, Oswestry Disability Index; EQ-5D, EuroQol 5 Dimensions: NRS, numerical rating scale.

Table 3. Operation Time, Days in the Hospital, and Complications in Patients Undergoing Surgery for Single-Level LDH

Variable	Nonsmokers	Smokers	Difference (95% CI)	*P* Value
Operation time (minutes), mean	57.5	58.9	−1.5 (−3.16 to 0.232)	0.091
Days in hospital, number, mean	1.8	1.9	−0.151 (−0.273 to −0.28)	0.016
Toral complications, number (%)	244 (6.2)	108 (6.7)	—	0.512
Perioperative complications, number (%)	86 (2.2)	48 (3.0)	—	0.085
Unintentional durotomy	50 (1.3)	31 (1.9)	—	0.069
Nerve injury	6 (0.2)	7 (0.4)	—	0.050
Blood replacement or postoperative hematoma	11 (0.3)	6 (0.4)	—	0.576
Cardiovascular complications	3 (0.1)	2 (0.1)	—	0.593
Respiratory complications	0 (0)	2 (0.1)	—	0.027
Anaphylactic reaction	4 (0.1)	2 (0.1)	—	0.821
Wrong level surgery	7 (0.2)	2 (0.1)	—	0.647
Patient-reported complications within 3 months, number (%)	164 (5.9)	63 (6.2)	—	0.744
Wound infection	82 (2.9)	23 (2.2)	—	0.249
Urinary tract infection	44 (1.6)	14 (1.4)	—	0.642
Pneumonia	11 (0.4)	4 (0.4)	—	0.989
Pulmonary embolism	1 (0)	0 (0)	—	0.545
Deep vein thrombosis	0 (0)	2 (0.2)	—	0.019
Micturition problems	36 (1.3)	27 (2.6)	—	0.004
Reoperation within 90 days	39 (1.0)	26 (1.6)	—	0.053

LDH, lumbar disc herniation; CI, confidence interval.

Table 4. Multiple Regression Analysis with Change in ODI at 1 Year as the Dependent Variable

Variable	Parameter Estimate	95% CI	*P* Value
Smoker	−4.9	−6.1 to −3.8	<0.001
ODI score 21—40 presurgery	13.2	11.3—15.2	<0.001
ODI score 41—60 presurgery	29.3	27.3—31.3	<0.001
ODI score 61—80 presurgery	46.4	44.2—48.6	<0.001
ODI score >81 presurgery	67.2	64.3—70.1	<0.001
Age >65 years	−2.5	−4.5 to −0.6	0.010
Depression and/or anxiety	−8.9	−13.1 to −4.8	<0.001
American Society of Anesthesiologists grade >2	−5.3	−8.0 to −2.6	<0.001
Female sex	−2.7	−3.8 to −1.6	<0.001
BMI 25—29.99 kg/m^2	−2.1	−3.3 to −1.0	<0.001
BMI 30—34.99 kg/m^2	−3.7	−5.3 to −2.1	<0.001
BMI ≥35 kg/m^2	−3.0	−5.8 to −0.2	0.039

A positive value in the outcome corresponds to less low back pain related disability.
ODI, Oswestry Disability Index; CI, confidence interval; BMI, body mass index.

were all identified as negative predictors for ODI change in the multivariate analysis.

DISCUSSION

This multicenter observational registry-based study shows that nonsmokers experienced greater improvement at 1 year after lumbar microdiscectomy compared with daily tobacco smokers. Furthermore, smokers were less likely to achieve an MIC as measured by the ODI. Although patient-reported outcomes of microdiscectomy were inferior for daily tobacco smokers, it should be emphasized that considerable improvement in ODI also was found in this group. Our study supports the increasing body of evidence indicating that smoking has a negative impact on surgical outcomes, and that smokers do not improve as much as nonsmokers after lumbar discectomy.[26]

Smoking has been identified as a predictor for postoperative infections following spinal surgery,[27-29] yet there were few infections in our series, and similar rates in smokers and nonsmokers. This could possibly reflect the minimally invasive nature of lumbar microdiscectomy with small incisions and minimal muscle trauma. Similar to the present study, a recent observational study from NORspine showed that smokers experienced less improvement at 1 year following microsurgical decompression for central lumbar spinal stenosis compared with nonsmokers, and were less likely to achieve an MIC.[22] Nonetheless, considerable improvement was also found among smokers undergoing surgery for lumbar spinal stenosis. However, in 2 small observational studies, tobacco smoking had no influence on PROMs following surgery for LDH.[12,30] Many previous findings pertaining to tobacco smoking and spine surgery cannot be directly applied to patients undergoing lumbar microdiscectomy. A retrospective study of 500 patients who underwent lumbar spine surgery identified an association between smoking and increased blood loss and the need for intraoperative blood replacement.[31] However, intraoperative bleeding is usually limited and rarely a problem in lumbar microdiscectomy. A recent review concluded that tobacco smoking is associated with delayed and impaired spinal fusion as well as with pseudoarthrosis following spinal instrumentation,[26] but there is little need for bone healing after lumbar microdiscectomy.

In the present study, we could not establish a definite causal relationship between daily tobacco smoking and poorer outcomes following microdiscectomy for LDH. Smoking may be a marker for other characteristics responsible for the association that are unadjusted for in the regression model. Patient-reported quality of life is known to be lower among smokers in the general population, and it is possible that this may be true for disease-specific questionnaires as well.[32] Psychosocial factors are likely to influence outcomes following spinal surgery, but these are difficult to assess in a registry-based study. Nonetheless, depression and anxiety were identified as negative predictors of ODI change in our study.

Study Strengths and Limitations

Our present results are strengthened by our specific inclusion and exclusion criteria, prospective data collection, and large sample size. The main limitation of the study is that the relatively high loss to follow-up. However, a study of an equivalent patient population with 22% nonresponders found no difference in outcomes between responders and nonresponders on long-term follow-up.[33]

Furthermore, there may be interactions between variables in the regression model, such as education, sex, age, and smoking. We did not have information on daily tobacco consumption (i.e., number of cigarettes per day or pack-years), making it difficult to establish a dose-response relationship between tobacco smoking and PROMs. Furthermore, our study did not consider the duration of symptoms before operation. Given that this factor is known to have some influence on outcomes of LDH, it would be preferable to include it in future studies.[34] Oral tobacco products (i.e., snus, small bags of moist tobacco placed under the lip) are also used in Norway, and data on the use of these products were not available in the NORspine database during the study period. Future studies should evaluate the effect of smoking cessation on treatment outcomes and explore the duration of cessation necessary to observe a potential benefit.

CONCLUSION

This observational multicenter study shows that nonsmokers experienced a greater improvement after surgery for LDH compared with daily tobacco smokers. Furthermore, smokers were less likely to achieve what is considered an MIC and more likely to report moderate or worse disability at 1 year. Smokers did not experience more complications than nonsmokers, possibly reflecting the minimally invasive nature of lumbar microdiscectomy.

ACKNOWLEDGMENTS

We thank the Norwegian Registry for Spine Surgery (NORspine), and all of the patients and surgeons participating in NORspine registration. The NORspine Registry receives funding from the University of Northern Norway and Norwegian health authorities.

REFERENCES

1. Hadley MN, Reddy SV. Smoking and the human vertebral column: a review of the impact of cigarette use on vertebral bone metabolism and spinal fusion. *Neurosurgery*. 1997;41:116-124.

2. Huang W, Qian Y, Zheng K, Yu L, Yu X. Is smoking a risk factor for lumbar disc herniation? *Eur Spine J*. 2016;25:168-176.

3. An HS, Silveri CP, Simpson JM, File P, Simmons C, Simeone FA, et al. Comparison of smoking habits between patients with surgically confirmed herniated lumbar and cervical disc disease and controls. *J Spinal Disord*. 1994;7:369-373.

4. Battié MC, Bigos SJ, Fisher LD, Hansson TH, Nachemson AL, Spengler DM, et al. A prospective study of the role of cardiovascular risk factors and fitness in industrial back pain complaints. *Spine (Phila Pa 1976)*. 1989;14:141-147.

5. Biering-Sørensen F, Thomsen C. Medical, social and occupational history as risk indicators for low-back trouble in a general population. *Spine (Phila Pa 1976)*. 1986;11:720-725.

6. Boshuizen HC, Verbeek JH, Broersen JP, Weel AN. Do smokers get more back pain? *Spine (Phila Pa 1976)*. 1993;18:35-40.

7. Deyo RA, Bass JE. Lifestyle and low-back pain. The influence of smoking and obesity. *Spine (Phila Pa 1976)*. 1989;14:501-506.

8. Frymoyer JW, Pope MH, Clements JH, Wilder DG, MacPherson B, Ashikaga T. Risk factors in low-back pain. An epidemiological survey. *J Bone Joint Surg Am*. 1983;65:213-218.

9. Arts MP, Brand R, van den Akker ME, Koes BW, Bartels RH, Peul WC. Tubular diskectomy vs conventional microdiskectomy for sciatica: a randomized controlled trial. *JAMA*. 2009;302:149-158.

10. Mattila VM, Saarni L, Parkkari J, Koivusilta L, Rimpelä A. Early risk factors for lumbar discectomy: an 11-year follow-up of 57,408 adolescents. *Eur Spine J*. 2008;17:1317-1323.

11. Huang W, Han Z, Liu J, Yu L, Yu X. Risk factors for recurrent lumbar disc herniation: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2016;95:e2378.

12. Stienen MN, Joswig H, Smoll NR, Tessitore E, Schaller K, Hildebrandt G, et al. Short- and long-term effects of smoking on pain and health-related quality of life after non-instrumented lumbar spine surgery. *Clin Neurol Neurosurg*. 2016;142:87-92.

13. Nerland US, Jakola AS, Solheim O, Weber C, Rao V, Lønne G, et al. Minimally invasive decompression versus open laminectomy for central stenosis of the lumbar spine: pragmatic comparative effectiveness study. *BMJ*. 2015;350:h1603.

14. Fairbank JC, Couper J, Davies JB, O'Brien JP. The Oswestry low back pain disability questionnaire. *Physiotherapy*. 1980;66:271-273.

15. Grotle M, Brox JI, Vøllestad NK. Cross-cultural adaptation of the Norwegian versions of the Roland-Morris Disability Questionnaire and the Oswestry Disability Index. *J Rehabil Med*. 2003;35:241-247.

16. Solberg TK, Olsen JA, Ingebrigtsen T, Hofoss D, Nygaard OP. Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. *Eur Spine J*. 2005;14:1000-1007.

17. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine (Phila Pa 1976)*. 2008;33:90-94.

18. van Hooff ML, Mannion AF, Staub LP, Ostelo RW, Fairbank JC. Determination of the Oswestry Disability Index score equivalent to a "satisfactory symptom state" in patients undergoing surgery for degenerative disorders of the lumbar spine—a Spine Tango registry-based study. *Spine J*. 2016;16:1221-1230.

19. Jensen MP, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Turk DC, Melzack R, eds. *Handbook of Pain Assessment*. New York, NY: Guilford Press; 2011:19-41.

20. Nerland US, Jakola AS, Giannadakis C, Solheim O, Weber C, Nygaard ØP, et al. The risk of getting worse: predictors of deterioration after decompressive surgery for lumbar spinal stenosis: a multicenter observational study. *World Neurosurg*. 2015;84:1095-1102.

21. Giannadakis C, Nerland US, Solheim O, Jakola AS, Gulati M, Weber C, et al. Does obesity affect outcomes after decompressive surgery for lumbar spinal stenosis? A multicenter, observational, registry-based study. *World Neurosurg*. 2015; 84:1227-1234.

22. Gulati S, Nordseth T, Nerland US, Gulati M, Weber C, Giannadakis C, et al. Does daily tobacco smoking affect outcomes after microdecompression for degenerative central lumbar spinal stenosis? A multicenter observational registry-based study. *Acta Neurochir (Wien)*. 2015; 157:1157-1164.

23. Giannadakis C, Solheim O, Jakola AS, Nordseth T, Gulati AM, Nerland US, et al. Surgery for lumbar spinal stenosis in individuals aged 80 and older: a multicenter observational study. *J Am Geriatr Soc*. 2016;64:2011-2018.

24. Madsbu MA, Solberg TK, Salvesen Ø, Nygaard ØP, Gulati S. Surgery for herniated lumbar disk in individuals 65 years of age or older: a multicenter observational study. *JAMA Surg*. 2017;152:503-506.

25. Twisk J, de Boer M, de Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. *J Clin Epidemiol*. 2013;66:1022-1028.

26. Lau D, Berger MS, Khullar D, Maa J. The impact of smoking on neurosurgical outcomes. *J Neurosurg*. 2013;119:1323-1330.

27. Fang A, Hu SS, Endres N, Bradford DS. Risk factors for infection after spinal surgery. *Spine (Phila Pa 1976)*. 2005;30:1460-1465.

28. Tang H, Zhu J, Ji F, Wang S, Xie Y, Fei H. Risk factors for postoperative complication after spinal fusion and instrumentation in degenerative lumbar scoliosis patients. *J Orthop Surg Res*. 2014;9:15.

29. Kong L, Liu Z, Meng F, Shen Y. Smoking and risk of surgical site infection after spinal surgery: a systematic review and meta-analysis. *Surg Infect (Larchmt)*. 2017;18:206-214.

30. Lee JC, Kim MS, Shin BJ. An analysis of the prognostic factors affecing the clinical outcomes of conventional lumbar open discectomy: clinical and radiological prognostic factors. *Asian Spine J*. 2010;4:23-31.

31. Dean C, Glenn W, Ahn U, Cassinelli E, Hart D, Bohlman H, et al. Smoking increases blood loss and transfusion requirements following lumbar spine surgery. *Spine J*. 2006;6(Suppl):26S-27S.

32. Vogl M, Wenig CM, Leidl R, Pokhrel S. Smoking and health-related quality of life in English general population: implications for economic evaluations. *BMC Public Health*. 2012;12:203.

33. Solberg TK, Sørlie A, Sjaavik K, Nygaard ØP, Ingebrigtsen T. Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? *Acta Orthop*. 2011;82:56-63.

34. Rihn JA, Hilibrand AS, Radcliff K, Kurd M, Lurie J, Blood E, et al. Duration of symptoms resulting from lumbar disc herniation: effect on treatment outcomes: analysis of the Spine Patient Outcomes Research Trial (SPORT). *J Bone Joint Surg Am*. 2011;93:1906-1914.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 14 July 2017; accepted 6 October 2017

Citation: World Neurosurg. (2017). https://doi.org/10.1016/j.wneu.2017.10.024

Journal homepage: ***www.WORLDNEUROSURGERY.org***

Available online: ***www.sciencedirect.com***

PAPER IV

Lumbar Microdiscectomy in Obese Patients: A Multicenter Observational Study

Mattis A. Madsbu[1,4], Lise R. Øie[2,4], Øyvind Salvesen[5], Vetle Vangen-Lønne[4], Øystein P. Nygaard[1,3,4,6], Tore K. Solberg[6,7], Sasha Gulati[1,3,4]

■ OBJECTIVE: **To evaluate the association between obesity and outcomes after microdiscectomy for lumbar disc herniation.**

■ METHODS: **The primary outcome measure was change in Oswestry Disability Index (ODI) at 1 year after surgery. Obesity was defined as body mass index (BMI) ≥30. Prospective data were retrieved from the Norwegian Registry for Spine Surgery.**

■ RESULTS: **We enrolled 4932 patients, 4018 nonobese and 914 obese. For patients with complete 1-year follow-up ($n = 3381$) the mean improvement in ODI was 31.2 points (95% confidence interval 30.4–31.9, $P < 0.001$). Improvement in ODI was 31.4 points in nonobese and 30.1 points in obese patients ($P = 0.182$). Obese and nonobese patients were as likely to achieve a minimal clinically important difference (84.2 vs. 82.7%, $P = 0.336$) in ODI (≥10 points improvement). Obesity was identified as a negative predictor for ODI improvement in a multiple regression analysis (BMI 30–34.99; $P < 0.001$, BMI ≥35; $P = 0.029$). Obese and nonobese patients experienced similar improvement in Euro-Qol-5 scores (0.48 vs. 0.49 points, $P = 0.441$) as well as back pain (3.7 vs. 3.5 points, $P = 0.167$) and leg pain (4.7 vs. 4.8 points, $P = 0.654$), as measured by the Numeric Rating Scale. Duration of surgery was shorter for nonobese patients (55.7 vs. 65.3 minutes, $P \leq 0.001$). Nonobese patients experienced fewer complications compared with obese patients (6.1% vs. 8.3%, $P = 0.017$). Obese patients had slightly longer hospital stays (2.0 vs. 1.8 days, $P = 0.004$).**

■ CONCLUSIONS: **Although they had more minor complications, obese individuals experienced improvement after lumbar microdiscectomy for lumbar disc herniation similar to that of nonobese individuals.**

INTRODUCTION

The health consequences of the growing obesity epidemic include increased risk of serious chronic conditions that reduce the overall quality of life and premature death.[1-4] Several studies have demonstrated previously that obesity also has a negative influence on surgical outcomes.[4-6] In spine surgery, it has been reported that obese patients have a greater risk of wound infection, a greater amount of blood loss, and longer operation time.[7-9] For the most common spinal surgical procedure, namely lumbar microdiscectomy for lumbar disc herniation (LDH), data on surgical outcomes among obese patients are limited. Moreover, the few existing studies investigating the impact of obesity on outcomes after LDH have shown conflicting results.[9,10] The aim of this study was to evaluate the association between obesity and patient-reported outcomes after microdiscectomy for LDH.

MATERIALS AND METHODS

Study Population

Data were collected through the Norwegian Registry for Spine Surgery (NORspine), a comprehensive registry for quality control and research.[11] In total, 36 of 40 centers performing lumbar spine

Key words
- Lumbar disc herniation
- Neurosurgical procedures
- Obesity
- Quality of life
- Sciatica

Abbreviations and Acronyms
BMI: Body mass index
CI: Confidence interval
EQ-5D: Euro-Qol-5
LDH: Lumbar disc herniation
NORspine: Norwegian Registry for Spine Surgery
NRS: Numerical Rating Scale
ODI: Oswestry Disability Index

From the [1]Department of Neurosurgery, [2]Department of Neurology and [3]National Advisory Unit on Spinal Surgery, St. Olavs University Hospital, Trondheim; Departments of [4]Neuroscience, and [5]Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim; and [6]The Norwegian National Registry for Spine Surgery and [7]Department of Neurosurgery, University Hospital of Northern Norway (UNN), Tromsø, Norway

To whom correspondence should be addressed: Mattis A. Madsbu, M.S. [E-mail: mattis.madsbu@gmail.com]

Citation: World Neurosurg. (2018) 110:e1004-e1010. https://doi.org/10.1016/j.wneu.2017.11.156

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

surgery in Norway reported to NORspine during the study period. According to the Norwegian Directorate of Health, approximately 63% of all patients who underwent lumbar spine surgery in Norway during the study period were included in NORspine.[11] Microdiscectomy was performed by ipsilateral paravertebral muscle retraction and removal of the disc herniation by a unilateral transflaval approach. Participation in the NORspine register was not mandatory for providers or patients, and it was not required for a patient to gain access to health care or for a provider to be eligible for payment. Follow-up time from the date of the operation was 1 year.

Inclusion Criteria

Inclusion criteria were 1) a diagnosis of symptomatic LDH; 2) scheduled (i.e., nonemergency surgery) single-level lumbar microdiscectomy between January 2007 and May 2014; and 3) inclusion in the NORspine registry.

Exclusion Criteria

Inclusion criteria were 1) a history of lumbar spine surgery; 2) extraforaminal LDH; 3) coexisting degenerative spondylolisthesis and/or scoliosis; and 4) fusion surgery.

Primary Outcome Measure

NORspine uses version 2.0 of the Oswestry Disability Index (ODI).[12] This version has been translated into Norwegian and tested for psychometric properties.[13,14] The ODI contains 10 questions on limitations of activities of daily living. Each variable is rated on a 0- to 5-point scale, summarized, and converted into a percentage score. Scores range from 0 (no disability) to 100 (bedridden). For this patient population, the minimal clinical important difference for change in the mean ODI score is considered to be approximately 10 points.[15]

Secondary Outcome Measure

Changes in generic health-related quality of life were measured with the generic Euro-Qol-5D (EQ-5D) instrument. The EQ-5D questionnaire evaluates the generic quality of life with 1 question for each of the 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Intensity of pain was graded in 2 separate 0–10 numerical rating scales (NRS) for back pain and leg pain, where 0 equals no pain and 10 represents the worst conceivable pain.[16] The NRS pain scales and ODI have shown good validity and are frequently used in research on back pain.[13] We also compared duration of procedures, length of hospital stays, repeated surgery at the index level within 3 months of surgery, and surgical complication rates.

Data Collection and Registration by the NORspine Registry Protocol

On admission for surgery, the patients completed the baseline questionnaire, which included questions about demographics and lifestyle issues in addition to the outcome measures. During the hospital stay, using a standard registration form, the surgeon recorded data concerning diagnosis, previous lumbar spine surgery, comorbidity, American Society of Anesthesiologists grade, image findings, and surgical approach and procedure. The surgeons provided data on the following possible complications and adverse events to the NORspine registry: intraoperative hemorrhage requiring blood replacement, postoperative hematoma requiring repeated surgery, unintentional durotomy, nerve injury, cardiovascular complications, respiratory complications, anaphylactic reactions, and wrong-level surgery. Patients reported

Table 1. Demographic Characteristics, Coexisting Illnesses, and Measures of Health Status for Both Groups

Variable	Nonobese	Obese	*P* Value
n (%)	4018 (81.5)	914 (18.5)	
Age, years, median (range)	44.1 (18–89)	43.2 (18–79)	0.061
Female sex, *n* (%)	1629 (40.5)	364 (39.8)	0.690
Married or partner, *n* (%)	3050 (76.5)	673 (73.9)	0.089
Attended college, *n* (%)	1601 (39.8)	291 (31.8)	<0.001
Mean body mass index	25.1	33.3	<0.001
Current smoker, *n* (%)	1165 (29.3)	237 (26.2)	0.065
Coexisting spinal stenosis in the operated level	499 (12.4)	125 (13.7)	0.302
Comorbidity, *n* (%)	754 (18.8)	282 (30.9)	<0.001
Cardiovascular disease	131 (3.3)	44 (4.8)	—
Cerebrovascular disease	16 (0.4)	3 (0.3)	—
Vascular claudication	3 (0.1)	1 (0.1)	—
Diabetes mellitus	70 (1.7)	48 (5.3)	—
Osteoporosis	8 (0.2)	0 (0.0)	—
Knee and/or hip osteoarthritis	33 (0.8)	10 (1.1)	—
Chronic neurologic disease	23 (0.6)	5 (0.5)	—
Chronic musculoskeletal pain	56 (1.4)	25 (2.7)	—
Cancer	22 (0.5)	6 (0.7)	—
Rheumatoid arthritis	17 (0.4)	4 (0.4)	—
Ankylosing spondylitis	17 (0.3)	1 (0.0)	—
Other rheumatic diseases	34 (0.8)	9 (1.0)	—
Depression and/or anxiety	61 (1.5)	15 (1.6)	—
ASA grade >2	122 (3.1)	60 (6.7)	<0.001
Mean preoperative ODI	45	46.2	0.080
Mean preoperative EQ-5D	0.29	0.27	0.250
Preoperative diagnostic imaging			
Preoperative MRI, *n* (%)	3914 (97.4)	886 (96.9)	0.422
Preoperative CT, *n* (%)	162 (4)	47 (5.1)	0.133
Level of surgery, *n* (%)			
L2–L3	44 (0.9)	14 (0.3)	0.269
L3–L4	206 (4.2)	62 (1.3)	0.046
L4–L5	1721 (34.9)	412 (8.4)	0.216
L5–S1	2047 (41.5)	426 (8.6)	0.018

ASA, American Society of Anesthesiologists; ODI, Oswestry Disability Index; EQ-5D, Euro-Qol-5D; MRI, magnetic resonance imaging; CT, computed tomography.

the following complications if they occurred within 3 months of surgery: wound infection, urinary tract infection, pneumonia, pulmonary embolism, and deep venous thrombosis. A questionnaire was distributed to patients by regular mail at 3 months and 1 year after surgery, completed at home by the patients, and returned in the same way. The patients who did not respond received one reminder with a new copy of the questionnaire. The patients completed preoperative questionnaire data and postal follow-up questionnaires without any assistance from the surgeon or other staff from the treating hospital.

Statistical Analysis

Statistical analyses were performed with SPSS, version 23.0 (IBM Corp., Armonk, New York, USA). Statistical significance level was defined as $P \leq 0.05$ on the basis of a 2-sided hypothesis test with no adjustments made for multiple comparisons. Central tendencies are presented as means when normally distributed and as medians when skewed. We used the χ^2 test for categorical variables. Baseline and 1-year scores were compared with paired-samples t test. Mean change scores between the groups were analyzed with independent-samples t test for complete cases and mixed linear models on all available data. For mixed linear models, the combination of obesity and time was taken as fixed effect and participant ID was specified as random effect. A multiple linear regression model was applied to assess the relationship between the change in ODI score at 1 year (dependent variable) and obesity, controlling for potential confounders. The selection of predictors included in the final model was based on their clinical importance and association with the dependent variable.[17-19] In the regression model, patients were categorized according to their body mass index (BMI) as normal (<25 kg/m^2, reference), overweight (25–29.9 kg/m^2), class I obesity (30–34.9 kg/m^2), or class II-III obesity (>35 kg/m^2) (i.e., as "dummy variables"). To further investigate how preoperative ODI scores affected the, patients were categorized according to the preoperative ODI score: ODI 0–20 (minimal disability, reference value), ODI 21–40 (moderate disability), ODI 41–60 (severe disability), ODI 61–80 (crippled), or ODI 81–100 (bed-bound) (i.e., as "dummy variables").

Missing Data

Missing data for ODI, EQ-5D, and NRS back and leg pain were handled with mixed linear models. This strategy was in line with studies showing that it is not necessary to handle missing data using multiple imputations before performing a mixed model analyses on longitudinal data.[20,21]

RESULTS

Study Population

A total of 4932 patients with LDH were included, and among these, 914 patients (18.5%) were obese. The average BMI was 25.1 ± 2.7 for nonobese and 33.3 ± 3.4 for obese patients. In total, 3381 (68.7%) completed the 12-month follow-up with ODI. A total of 82.2% (n = 2780) of these patients were nonobese, and 17.8% (n = 601) were obese ($P = 0.044$). Baseline characteristics, surgical treatments, and comorbidities are presented in Table 1. The mean age at baseline was 44.0 (±12.8) years, and 40.4% were women.

For the whole patient population, there was a significant improvement in ODI at 1 year (31.2 points, 95% confidence interval [CI] 30.4–31.9, $P < 0.001$). At 1 year, there was not a statistical significant difference in change in ODI between nonobese and obese patients (1.3 points, 95% CI −0.62 to 3.31, $P = 0.182$). Obese patients were just as likely to achieve a minimal clinically important difference in ODI (defined as ≥10 points improvement) compared with nonobese patients (84.2 vs. 82.7%, $P = 0.336$). Change in ODI are illustrated in Figure 1 showing baseline, 3 months and 12 months data.

Changes in EQ-5D, back pain NRS, and leg pain NRS at 1 year for both age groups are presented in Table 2. There was no statistically significant difference between nonobese and obese patients for EQ-5D (0.01; 95% CI −0.02 to 0.05; $P = 0.441$), back pain NRS (0.4; 95% CI 0.2–0.7, $P = 0.167$), and leg pain NRS (0.07; 95% CI −0.2 to 0.4, $P = 0.654$). Mixed linear model analyses for missing data showed similar results for all patient-reported outcomes. As shown in Table 3, obese patients had a small but significant greater rate of overall complications (8.3% vs. 6.1, $P = 0.017$).

Multiple Regression Analysis

A multiple regression analysis was performed with change in ODI at 1 year as the dependent variable. A positive value in the outcome corresponds to less low back pain related disability. The effect estimates are presented in Table 4 (1700 patients excluded due to missing data [30.8%]). Preoperative ODI score was the strongest predictor of outcome, with increasing values associated with better outcomes. Smoking, American Society of Anesthesiologists grade >2, female sex, age ≥65 years, depression and/or anxiety, overweight, and obesity were all identified as negative predictors for ODI change in the multivariate analysis.

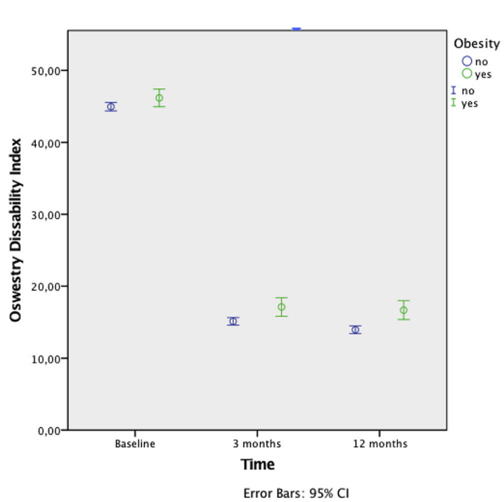

Figure 1. Oswestry Disability Index score in patients undergoing microdiscectomy for lumbar disc herniation at baseline, 3 months, and 12 months. *Error bars* represent 95% confidence intervals (CI).

Table 2. Outcomes at 1 Year in Patients Operated for Single-Level Lumbar Disc Herniation

Variable	Nonobese Baseline	Nonobese 1 year	Nonobese Mean Change	Obese Baseline	Obese 1 year	Obese Mean Change	Difference in Mean Change Between Groups (95% CI)	*P* Value
Complete case analyses for ODI (*N* = 3381)								
ODI	45.4	14.0	−31.4	46.8	16.7	−30.1	1.3 (−0.6, 3.3)	0.182
EQ-5D	0.28	0.78	0.49	0.27	0.74	0.48	0.01 (−0.02, 0.05)	0.441
Back pain NRS	6.0	2.6	−3.5	6.5	2.9	−3.7	0.4 (0.2, 0.7)	0.167
Leg pain NRS	6.8	2.1	−4.8	7.0	2.3	−4.7	0.07 (−0.2, 0.4)	0.654
Mixed linear model analyses (*N* = 4932)								
ODI	45.0	13.9	−31.1	46.2	16.6	−29.6	1.47 (−0.4, 3.3)	0.117
EQ-5D	0.29	0.77	0.48	0.27	0.74	0.47	−0.02 (−0.1, 0.02)	0.367
Back pain NRS	6.0	2.6	−3.4	6.5	2.8	−3.7	−0.13 (−0.4, 0,1)	0.321
Leg pain NRS	6.8	1.9	−4.9	7.0	2.7	−4.3	0.15 (−0.1, 0.4)	0.264

CI, confidence interval; ODI, Oswestry Disability Index; EQ-5D, Euro-Qol-5D; NRS, Numerical Rating Scale.

DISCUSSION

This multicenter, observational, registry-based study shows that obese patients with LDH experienced similar effects from microdiscectomy as nonobese patients. However, obese patients experienced more minor complications and had longer hospital stays compared with the nonobese group. Still, obesity alone should not be a contradiction to surgery, given that the individual is fit for surgery.

Even though our study demonstrates that obese and nonobese patients experienced similar results after surgery for LDH, it should be emphasized that obesity has been recognized as a cause for LDH. Previous studies have suggested that obese patients have a stronger tendency to have an LDH[22-24] and further an elevated risk of recurrence and revision procedures.[25,26]

The Spine Patient Outcomes Research Trial (SPORT) found that obese patients benefit less from operative treatment for LDH. In our study, a slightly lower ODI change was observed than in the SPORT study for the obese patients (30.1 vs. 35.2). This might be explained by the greater baseline ODI and more strict inclusion criteria in the SPORT study.

In 2 retrospective studies comparing operative results between obese and nonobese patients, there were no major differences in surgical outcomes.[10,27] However, both of these studies had a short follow-up period. To establish a more certain understanding of the prognosis in obese patients operated for LDH, longer follow-up periods are warranted, especially for assessing reoperation rates.

Multiple studies have demonstrated that obese patients have inferior outcomes compared with nonobese when it comes to duration of surgical procedures, duration of hospital stays, and minor complications.[9,10,28,29] Similar results also have been found for other spine-related diagnoses, such as spinal stenosis and spondylolisthesis.[18,30]

Preoperative weight loss has not been examined for disc herniation surgery. To our knowledge, there are no studies examining preoperative weight loss before decompressive surgery for LDH. Still, considering the profound effects obesity has on the spinal column, it could be possible that substantial preoperative weight loss could influence postoperative results and overall quality of life. However, weight loss might be difficult to achieve when experiencing sciatica.

We found that a high ODI score at baseline was associated with the largest improvement at 1 year. Previous studies have shown that a history of previous surgery will influence the results of future surgery.[31] To study the impact of obesity, patients with a history of surgery were excluded in the present study. Smoking and comorbidity were the stronger predictors for interior outcomes than obesity, consistent with previous literature on spinal surgery.[32,33]

Study Strengths and Limitations

The major strength of our study is the use of specific inclusion and exclusion criteria, prospective data collection, and the large sample size. Also, the use of widely accepted and validated outcome measures such as ODI, EQ-5D, and back pain NRS and leg pain NRS, strengthen our results.

The main limitation is the relatively high number of patients lost to follow-up. However, a previous study on a similar population from the NORspine registry showed no difference in outcomes between responders and nonresponders.[34] A behavioral attitude toward worse self-rated health has been described among obese individuals.[3] Our study cannot establish a definite causal relationship between obesity and treatment effects after lumbar microdiscectomy for LDH, and obesity may be a marker for other, unobserved confounders responsible for this association. Psychosocial factors are likely to influence outcomes after spinal surgery but are difficult to assess in a registry-based

Table 3. Operation Time, Days in Hospital, and Complications for Patients Operated for Single-Level Lumbar Disc Herniation

Variable	Nonobese	Obese	Difference (95% CI)	*P* Value
Operation time, minutes	55.7	65.3	−9.6 (−11.7, −7.57)	<0.001
Days in hospital, *n*	1.8	2.04	−0.22 (−0.375, −0.070)	0.004
Patients with complications, *n* (%)	247 (6.1)	76 (8.3)	—	0.017
Perioperative complications, *n* (%)	96 (2.4)	24 (2.6)	—	0.675
Unintentional durotomy	61 (1.5)	14 (1.5)	—	0.976
Nerve injury	7 (0.2)	4 (0.4)	—	0.128
Blood replacement or postoperative hematoma	10 (0.2)	1 (0.1)	—	0.420
Cardiovascular complications	5 (0.1)	0 (—)	—	0.286
Respiratory complications	2 (—)	0 (—)	—	0.500
Anaphylactic reaction	4 (0.1)	1 (0.1)	—	0.933
Wrong-level surgery	6 (0.1)	3 (0.1)	—	0.253
Patient-reported complications within 3 months, *n* (%)	156 (5.6)	53 (8.7)	—	0.004
Wound infection	77 (2.8)	18 (3.0)	—	0.793
Urinary tract infection	41 (1.5)	13 (2.1)	—	0.235
Pneumonia	9 (0.3)	4 (0.7)	—	0.227
Pulmonary embolism	1 (—)	0 (—)	—	0.640
Deep vein thrombosis	2 (0.1)	0 (—)	—	0.509
Micturition problems	35 (1.3)	24 (3.9)	—	<0.001
Reoperated within 90 days	43 (1.1)	9 (1.0)	—	0.819

CI, confidence interval.

Table 4. Multiple Regression Analysis with Change in ODI at 1 Year as the Dependent Variable

Variable	Parameter Estimate	95% Confidence Interval	*P* Value
Smoker	−4.9	−6.1, −3.8	<0.001
ODI score 21—40, presurgery	13.2	11.3—15.2	<0.001
ODI score 41—60, presurgery	29.3	27.3—31.3	<0.001
ODI score 61—80, presurgery	46.4	44.2—48.6	<0.001
ODI score >81, presurgery	67.2	64.3—70.1	<0.001
Elderly (>65 years)	−2.5	−4.5, 0.6	0.010
ASA grade >2	−5.3	−8.0, −2.6	<0.001
Depression and/or anxiety	−8.9	−13.1, −4.8	<0.001
Female sex	−2.7	−3.8, −1.6	<0.001
Body mass index 25—29.99 kg/m^2	−2.1	−3.3, −1.0	<0.001
Body mass index 30—34.99 kg/m^2	−3.7	−5.3, −2.1	<0.001
Body mass index ≥35 kg/m^2	−3.0	−5.8, −0.15	0.039

A positive value in the outcome corresponds to less low back pain-related disability.
ODI, Oswestry Disability Index; ASA, American Society of Anesthesiologists.

study. Still, depression and/or anxiety was identified as negative predictors for ODI change in our study. Evaluating conservative treatment to surgical treatment was not the purpose of our study, as this topic has been thoroughly investigated.[35-38] All patients were operated with conventional lumbar microdiscectomy, and the surgical procedure is described in the Materials and Methods section. Patients operated on via endoscopic procedures or microscope-assisted percutaneous nucleotomy were excluded.

Another study weakness is our follow-up period of only 12 months compared with the SPORT study's 3-year follow-up period. However, the SPORT study found similar results throughout the study period for both groups.[9] We did not have data on BMI beyond preoperative measurements. There are several studies demonstrating that spinal surgery has little influence on postoperative weight change in obese patients.[39-41] Future studies could investigate the long-term results between conservative and surgical treatment with reassessment of BMI at specific post-operative time points as well as residual disc herniation.

CONCLUSIONS

Although they had more minor complications and longer hospital stays, obese individuals experienced improvement after lumbar microdiscectomy for LDH that was similar to that of nonobese individuals.

ACKNOWLEDGMENTS

The authors thank the Norwegian Registry for Spine Surgery (NORspine). The NORspine registry receives funding from the University of Northern Norway and Norwegian health authorities. We thank all patients and surgeons participating in NORspine registration.

REFERENCES

1. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med*. 2003;48:1625-1638.

2. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation*. 1983;67:968-977.

3. Prosper MH, Moczulski VL, Qureshi A. Obesity as a predictor of self-rated health. *Am J Health Behav*. 2009;33:319-329.

4. Vincent HK, Horodyski M, Gearen P, Vlasak R, Seay AN, Conrad BP, et al. Obesity and long term functional outcomes following elective total hip replacement. *J Orthop Surg Res*. 2012;7:16.

5. Baker P, Petheram T, Jameson S, Reed M, Gregg P, Deehan D. The association between body mass index and the outcomes of total knee arthroplasty. *J Bone Joint Surg Am*. 2012;94:1501-1508.

6. Li X, Williams PN, Nguyen JT, Craig EV, Warren RF, Gulotta LV. Functional outcomes after total shoulder arthroplasty in obese patients. *J Bone Joint Surg Am*. 2013;95:e160.

7. Abdallah DY, Jadaan MM, McCabe JP. Body mass index and risk of surgical site infection following spine surgery: a meta-analysis. *Eur Spine J*. 2013;22:2800-2809.

8. Jiang J, Teng Y, Fan Z, Khan S, Xia Y. Does obesity affect the surgical outcome and complication rates of spinal surgery? A meta-analysis. *Clin Orthop Rel Res*. 2014;472:968-975.

9. Rihn JA, Kurd M, Hilibrand AS, Lurie J, Zhao W, Albert T, et al. The influence of obesity on the outcome of treatment of lumbar disc herniation: analysis of the Spine Patient Outcomes Research Trial (SPORT). *J Bone Joint Surg Am*. 2013;95:1-8.

10. Yoo MW, Hyun SJ, Kim KJ, Jahng TA, Kim HJ. Does obesity make an influence on surgical outcomes following lumbar microdiscectomy? *Korean J Spine*. 2014;11:68-73.

11. Nerland US, Jakola AS, Solheim O, Weber C, Rao V, Lønne G, et al. Minimally invasive decompression versus open laminectomy for central stenosis of the lumbar spine: pragmatic comparative effectiveness study. *BMJ*. 2015;350:h1603.

12. Fairbank JC, Couper J, Davies JB, O'Brien JP. The Oswestry low back pain disability questionnaire. *Physiotherapy*. 1980;66:271-273.

13. Grotle M, Brox JI, Vollestad NK. Cross-cultural adaptation of the Norwegian versions of the Roland-Morris Disability Questionnaire and the Oswestry Disability Index. *J Rehabil Med*. 2003;35:241-247.

14. Solberg TK, Olsen JA, Ingebrigtsen T, Hofoss D, Nygaard OP. Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. *Eur Spine J*. 2005;14:1000-1007.

15. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine (Phila Pa 1976)*. 2008;33:90-94.

16. Jensen MP, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Truk DC, Melzack R, eds. *Handbook of Pain Assessment*. New York: Guilford Press; 1992:135-151.

17. Nerland US, Jakola AS, Giannadakis C, Solheim O, Weber C, Nygaard ØP, et al. The risk of getting worse: predictors of deterioration after decompressive surgery for lumbar spinal stenosis: a multicenter observational study. *World Neurosurg*. 2015;84:1095-1102.

18. Giannadakis C, Nerland US, Solheim O, Jakola AS, Gulati M, Weber C, et al. Does obesity affect outcomes after decompressive surgery for lumbar spinal stenosis? A multicenter, observational, registry-based study. *World Neurosurg*. 2015;84:1227-1234.

19. Gulati S, Madsbu MA, Solberg TK, Sørlie A, Giannadakis C, Skram MK, et al. Lumbar microdiscectomy for sciatica in adolescents: a multicentre observational registry-based study. *Acta Neurochir (Wien)*. 2017;159:509-516.

20. Twisk J, de Boer M, de Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. *J Clin Epidemiol*. 2013;66:1022-1028.

21. Madsbu MA, Solberg TK, Salvesen Ø, Nygaard ØP, Gulati S. Surgery for herniated lumbar disk in individuals 65 years of age or older: a multicenter observational study. *JAMA Surg*. 2017;152:503-506.

22. Xu X, Li X, Wu W. Association between overweight or obesity and lumbar disk diseases: a meta-analysis. *J Spinal Disord Tech*. 2015;28:370-376.

23. Heliovaara M. Body height, obesity, and risk of herniated lumbar intervertebral disc. *Spine (Phila Pa 1976)*. 1987;12:469-472.

24. Rodriguez-Martinez NG, Perez-Orribo L, Kalb S, Reyes PM, Newcomb AG, Hughes J, et al. The role of obesity in the biomechanics and radiological changes of the spine: an in vitro study. *J Neurosurg Spine*. 2016;24:615-623.

25. Bohl DD, Ahn J, Mayo BC, Massel DH, Tabaraee E, Sershon RA, et al. Does greater body mass index increase the risk for revision procedures following a single-level minimally invasive lumbar discectomy? *Spine (Phila Pa 1976)*. 2016;41:816-821.

26. Meredith DS, Huang RC, Nguyen J, Lyman S. Obesity increases the risk of recurrent herniated nucleus pulposus after lumbar microdiscectomy. *Spine J*. 2010;10:575-580.

27. Tomasino A, Parikh K, Steinberger J, Knopman J, Boockvar J, Härtl R. Tubular microsurgery for lumbar discectomies and laminectomies in obese patients: operative results and outcome. *Spine (Phila Pa 1976)*. 2009;34:E664-E672.

28. McGuire KJ, Khaleel MA, Rihn JA, Lurie JD, Zhao W, Weinstein JN. The effect of high obesity on outcomes of treatment for lumbar spinal conditions: subgroup analysis of the spine patient outcomes research trial. *Spine (Phila Pa 1976)*. 2014;39:1975-1980.

29. Buerba RA, Fu MC, Gruskay JA, Long WD 3rd, Grauer JN. Obese Class III patients at significantly greater risk of multiple complications after lumbar surgery: an analysis of 10,387 patients in the ACS NSQIP database. *Spine J*. 2014;14:2008-2018.

30. Onyekwelu I, Glassman SD, Asher AL, Shaffrey CI, Mummaneni PV, Carreon LY. Impact of obesity on complications and outcomes: a comparison of fusion and nonfusion lumbar spine surgery. *J Neurosurg Spine*. 2017;26:158-162.

31. Abdu RW, Abdu WA, Pearson AM, Zhao W, Lurie JD, Weinstein JN. Reoperation for recurrent intervertebral disc herniation in the spine patient outcomes research trial: analysis of rate, risk factors, and outcome. *Spine (Phila Pa 1976)*. 2017;42:1106-1114.

32. Gulati S, Nordseth T, Nerland US, Gulati M, Weber C, Giannadakis C, et al. Does daily tobacco smoking affect outcomes after microdecompression for degenerative central lumbar spinal stenosis? A multicenter observational registry-based study. *Acta Neurochir (Wien)*. 2015;157:1157-1164.

33. Madsbu MA, Salvesen Ø, Werner DAT, Franssen E, Weber C, Nygaard ØP, et al. Surgery for herniated lumbar disc in daily tobacco smokers: a multicenter observational study. *World Neurosurg*. 2018;109:e581-e587.

34. Solberg TK, Sørlie A, Sjaavik K, Nygaard ØP, Ingebrigtsen T. Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? *Acta Orthop*. 2011;82:56-63.

35. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JA, Tans JT, et al. Surgery versus prolonged conservative treatment for sciatica. *N Engl J Med*. 2007;356:2245-2256.

36. Lequin MB, Verbaan D, Jacobs WC, Brand R, Bouma GJ, Vandertop WP, et al. Surgery versus prolonged conservative treatment for sciatica:5-year results of a randomised controlled trial. *BMJ Open*. 2013;3. https://doi.org/10.1136/bmjopen-2012- 002534.

37. van den Hout WB, Peul WC, Koes BW, Brand R, Kievit J, Thomeer RT, Leiden-The Hague Spine Intervention Prognostic Study Group. Prolonged conservative care versus early surgery in patients with sciatica from lumbar disc herniation: cost utility analysis alongside a randomised controlled trial. *BMJ*. 2008;336:1351-1354.

38. Jacobs WC, van Tulder M, Arts M, Rubinstein SM, van Middelkoop M, Ostelo R, et al. Surgery versus conservative management of sciatica due to a lumbar herniated disc: a systematic review. *Eur Spine J*. 2011;20:513-522.

39. Garcia RM, Messerschmitt PJ, Furey CG, Bohlman HH, Cassinelli EH. Weight loss in overweight and obese patients following successful lumbar decompression. *J Bone Joint Surg Am*. 2008;90:742-747.

40. Vaidya R, Carp J, Bartol S, Ouellette N, Lee S, Sethi A. Lumbar spine fusion in obese and morbidly obese patients. *Spine (Phila Pa 1976)*. 2009;34:495-500.

41. Anderson PA, Dettori JR, Hermsmeyer JT. Does lumbar decompression in overweight patients assist in postoperative weight loss? *Evid Based Spine Care J*. 2010;1:34-38.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 3 October 2017; accepted 27 November 2017

Citation: World Neurosurg. (2018) 110:e1004-e1010.
https://doi.org/10.1016/j.wneu.2017.11.156

Journal homepage: ***www.WORLDNEUROSURGERY.org***

Available online: ***www.sciencedirect.com***

PAPER V

Acta Neurochirurgica (2020) 162:703–711
https://doi.org/10.1007/s00701-019-04195-7

ORIGINAL ARTICLE - SPINE DEGENERATIVE

Surgery for herniated lumbar disc in private vs public hospitals: A pragmatic comparative effectiveness study

Mattis A. Madsbu[1,2] · Øyvind Salvesen[3] · Sven M. Carlsen[4,5] · Steinar Westin[3] · Kristian Onarheim[6] · Øystein P. Nygaard[1,2,7] · Tore K. Solberg[8,9,10] · Sasha Gulati[1,2,7]

Received: 14 November 2019 / Accepted: 20 December 2019 / Published online: 4 January 2020

Abstract

Background There is limited evidence on the comparative performance of private and public healthcare. Our aim was to compare outcomes following surgery for lumbar disc herniation (LDH) in private versus public hospitals.

Methods Data were obtained from the Norwegian registry for spine surgery. Primary outcome was change in Oswestry disability index (ODI) 1 year after surgery. Secondary endpoints were quality of life (EuroQol EQ-5D), back and leg pain, complications, and duration of surgery and hospital stays.

Results Among 5221 patients, 1728 in the private group and 3493 in the public group, 3624 (69.4%) completed 1-year follow-up. In the private group, mean improvement in ODI was 28.8 points vs 32.3 points in the public group (mean difference − 3.5, 95% CI − 5.0 to − 1.9; P for equivalence < 0.001). Equivalence was confirmed in a propensity-matched cohort and following mixed linear model analyses. There were differences in mean change between the groups for EQ-5D (mean difference − 0.05, 95% CI − 0.08 to − 0.02; $P = 0.002$) and back pain (mean difference − 0.2, 95% CI − 0.2, − 0.4 to − 0.004; $P = 0.046$), but after propensity matching, the groups did not differ. No difference was found between the two groups for leg pain. Complication rates was lower in the private group (4.5% vs 7.2%; $P < 0.001$), but after propensity matching, there was no difference. Patients operated in private clinics had shorter duration of surgery (48.4 vs 61.8 min) and hospital stay (0.7 vs 2.2 days).

Conclusion At 1 year, the effectiveness of surgery for LDH was equivalent in private and public hospitals.

Keywords Intervertebral disc displacement · Neurosurgery · Orthopedics · Public health · Sciatica

Introduction

Public health care is usually provided by the government through national healthcare systems, whereas private health care is often provided as "for profit" services. Ideological debates whether countries should strengthen public versus private healthcare services are common. In times of economic recession with constraints on government budgets, disputes between the proponents of private and public health care systems tend to escalate. Discussions about resource allocation between private and public health providers should be evidence based, and focused on clinical effectiveness and costs.

This article is part of the Topical Collection on *Spine degenerative*

✉ Mattis A. Madsbu
mattis.madsbu@gmail.com

Øyvind Salvesen
oyvind.salvesen@ntnu.no

Sven M. Carlsen
sven.carlsen@ntnu.no

Steinar Westin
steinar.westin@ntnu.no

Kristian Onarheim
kristian.onarheim@helse-midt.no

Øystein P. Nygaard
oystein.nygaard@ntnu.no

Tore K. Solberg
tore.solberg@unn.no

Sasha Gulati
sasha.gulati@ntnu.no

Extended author information available on the last page of the article

There is currently limited and only poor-quality evidence regarding the comparative performance of the two health care systems [2]. In order to achieve a more informed policy, there is an urgent need for robust evidence by comparing the quality and effectiveness of the health care provided through both systems. Degenerative lumbar spine disorders are a leading cause of activity limitation and work absence throughout much of the world, and places an enormous economic burden on the whole society ranging from individuals, families, communities, industry, and all the way to governments. The most common reason for spine surgery is persisting or intolerable pain due to sciatica caused by lumbar disc herniation [4, 19]. In many countries, surgical management of degenerative lumbar spine disorders is provided by both public and private hospitals, providing a unique opportunity to compare the two health care provider systems. The aim of this study was to compare patient-reported outcomes following surgery for lumbar disc herniation (LDH) because of sciatica in public versus private hospitals.

Methods

Reporting is consistent with the strengthening the reporting of observational studies in epidemiology (STROBE) statement. [25]

Ethical approval

This study was approved by the regional committee for medical research in central Norway (ID2016/840) and all participants provided written informed consent. The Data Inspectorate of Norway approved the registry protocol.

Study population

Norway has a public healthcare system with equal distribution of resources and uniform training and licensing of healthcare staff. The population is relatively homogenous and stable. Patients utilizing the public healthcare system are usually treated at the hospital serving their residential address, limiting referral bias. Surgery for LDH is provided free of cost to patients in the public healthcare system. In private hospitals, expenses of surgery (approximately USD 5400 for single-level lumbar microdiscectomy) are covered by the patients themselves or their insurance providers. Many of the patients treated at private hospitals have private health insurance paid for by their employers. During the study period, some of the private hospitals had government funding through contracts with the public regional health authorities.

We collected data through the Norwegian Registry for Spine Surgery (NORspine), a comprehensive registry for quality control and research [17]. In total, 37 of 40 centers performing lumbar spine surgery in Norway reported to NORspine during the study period. According to the Norwegian Directorate of Health, approximately 63% of all patients who underwent lumbar spine surgery in Norway during the study period were included in NORspine [17]. In general, the departments that participated in this study had the same preferred surgical strategy for LDH without radiological instability. Surgery was performed by ipsilateral paravertebral muscle retraction and removal of the disc herniation under microscope magnification by a unilateral transflaval approach [1]. Participation in the NORspine register was not mandatory for providers or patients, and it was not required for a patient to gain access to health care or for a provider to be eligible for payment. Follow-up time from the date of the operation was 1 year. Patients included in the study were treated at hospitals reporting at least 50 patients to NORspine during the study period.

We screened patients who underwent surgery between January 2007 and May 2014 for eligibility. Follow-up time from the date of the operation was 1 year.

We considered patients eligible for the study if they had a diagnosis of symptomatic paramedian lumbar disc herniation, surgery was performed as a single-level lumbar microdiscectomy, and their data were included in the NORspine registry. Patients were excluded who had undergone previous surgery of the lumbar spine, undergone fusion and/or open laminectomy as a surgical approach, or had associated spinal conditions (degenerative spondylolisthesis and/or scoliosis).

User involvement

The Norwegian Back Pain Association (Ryggforeningen) reviewed the study protocol and provided feedback concerning study design and outcome measures.

Outcome measures

The primary outcome was change in disease-specific functional outcome between baseline and 12-month-follow-up measured with version 2.1 of the Oswestry disability index [5], which has been translated into Norwegian and tested for psychometric properties [8]. The Oswestry disability index questionnaire quantifies disability for degenerative conditions of the lumbar spine. It covers intensity of pain, ability to lift, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel. For each topic, there are six statements describing potential scenarios, and patients select the one that most closely resembles their situation. The index is scored from 0 to 100. Zero means no disability and 100 reflects maximum disability.

Secondary outcome measures were changes between baseline and 12-month follow-up in generic health-related quality of life, measured with the generic Euro-Qol-5D (EQ-5D), and intensity of back pain and leg pain. The Norwegian version of EQ-5D has shown good psychometric properties [20]. Intensity of pain was graded in two separate 0–10 numerical rating scales (NRS) for back pain and leg pain where 0 equals no pain and 10 represents the worst conceivable pain. The NRS pain scales and ODI have shown good validity and are frequently used in research on back pain [8, 20]. We also compared duration of procedures, length of hospital stays, reoperation at the index level within 3 months of surgery, and surgical complication rates. Surgeons provided the following complications and adverse events to NORspine: intraoperative hemorrhage blood replacement or postoperative hematoma, unintentional durotomy, cardiovascular complications, respiratory complications, anaphylactic reactions, and wrong level for surgery. Patients reported the following complications if occurring within 3 months of surgery: wound infection, urinary tract infection, micturition problems, pneumonia, pulmonary embolism, and deep vein thrombosis.

Data collection by NORspine

On admission for surgery, the patients completed the baseline questionnaire, which included questions about demographics and lifestyle issues in addition to the outcome measures. During the hospital stay, using a standard registration form, the surgeon recorded data concerning diagnosis, previous lumbar spine surgery, comorbidity, American Society of Anesthesiologists (ASA) grade, image findings, and surgical approach and procedure. A questionnaire was distributed to patients by regular mail at 3 months and 1 year after surgery, completed at home by the patients, and returned in the same way. The patients who did not respond received one reminder with a new copy of the questionnaire. The patients completed baseline questionnaire data and postal follow-up questionnaires without any assistance from the surgeon or other staff from the treating hospital.

Statistical analysis

Statistical analyses were performed with SPSS version 23.0 (IBM Corporation, Chicago, IL, USA) and Software R [23]. The size of the study was based on a null hypothesis on non-equivalence and an alternative hypothesis of equivalence. If the population effect of treatment on changes in ODI was eight points or less, treatments were considered equivalent for effectiveness [3, 12, 18]. The sample size calculation relates to a two one-sided test for equivalence, with a significance level of 2.5%. We computed the P values for equivalence as 1 minus the maximum confidence level at which the confidence interval is contained in (− 8 to 8) divided by 2 giving the P values of the two one-sided test for equivalence. This applied to both the complete case analysis and the mixed linear model analysis in both the aggregate cohort and the propensity-matched cohort. Assuming a correlation of 0.5 between baseline and follow-up measurements and a standard deviation of 18 for the individual measurements, this study has a 90% power, with 340 patients in each group.

For statistical comparison tests, we defined the significance level defined as $P \leq 0.05$ on the basis of a two-sided hypothesis test with no adjustments made for multiple comparisons. For the primary outcome and one secondary outcome (EQ-5D), a statistician (ØS) blinded to treatment provider performed both a complete case analysis and a full information analysis using mixed linear models. Central tendencies are presented as means when normally distributed and as medians when skewed. We used the Chi square test for categorical variables. Baseline- and 1-year scores were compared with paired-samples t test. Mean change scores between the groups were analyzed with independent-samples t test for complete cases and mixed linear models on all available data. For mixed linear models, the combination of patients operated in private or public clinics and time was taken as fixed effect and participant ID specified as random effect. A multiple linear regression model was applied to assess the relationship between the change in ODI score at 1 year (dependent variable) and private or public treatment, controlling for potential confounders. The selection of predictors included was based on their clinical importance and association with the dependent variable [6, 10, 16].

To achieve equality, we eliminate as many as possible confounding factors and provide best possible balance between the two groups; we generated propensity scores using logistic regression and adjusting for baseline covariates that could influence clinical outcomes, including age, sex, smoking, college education, partner, year of operation, BMI, ASA grade > 2, relevant comorbidity, emergency operation, duration of sciatica > 1 year, and preoperative ODI score. This was to achieve the closest approximate to a randomized clinical trial.

All covariates were entered into a logistic regression analysis, and we fitted a maximum likelihood model based on these covariates as predictors of private versus public treatment. The coefficients for these predictors of private versus public treatment was used to calculate a propensity score of 0 to 1 for each patient. Based on the calculated propensity scores, two evenly matched groups were formed for private and public treatment using a matching algorithm with the common caliper set at 0.010. This dataset is referred to as the “propensity-matched cohort”. We have analyzed continuous variables using a related sample two-tailed t test for data with a normal distribution and continuous data exhibiting a skewed distribution using the Wilcoxon signed rank test for matched pairs. We used the McNemar’s test for correlated proportions to compare discrete variables. We handled missing data with mixed linear models and did not perform multiple imputations. This strategy was in line with studies showing that it is not necessary to handle missing data using multiple imputations before performing a mixed model analysis on longitudinal data [15, 24].

Results

Baseline characteristics

A total of 5221 patients were included, 1728 operated in private hospitals and 3493 in public hospitals. Participants underwent surgery at 24 orthopedic or neurosurgical departments in 22 hospitals in Norway, 14 public and 8 private. Baseline characteristics were stratified by type of treatment center and matching (Table 1). In the aggregate cohort, there were significant differences between the two groups for baseline characteristics including age, sex, educational level, body mass index, tobacco use, comorbidity, American Society of Anesthesiologists grade, mean baseline Oswestry disability index score, mean baseline EQ-5D, mean NRS back and leg pain, and number of emergency surgery procedures. After propensity score matching (1281 pairs), these differences in baseline characteristics disappeared. The loss to follow-up rate in the aggregate cohort at 1 year was 30.9% ($n = 533$) in the private group and 30.5% ($n = 1064$) in the public group ($P = 0.77$). In the propensity-matched cohort, the loss to follow-up rate in the private group was 32.5% ($n = 416$) and 31.2% ($n = 400$) for the public group ($P = 0.52$). There were no differences between non-responders and responders at 1 year for preoperative ODI, preoperative back pain, preoperative leg pain, preoperative EQ-5D, comorbidity, or ASA grade. However, there were differences between non-responders and responders in age (40.2 vs 45.6; $P < 0.001$), BMI (27.0 vs 26.5; $P = 0.05$), female sex (36.9% vs 42.5%; $P < 0.001$), college education (33.8% vs 41.4%; $P < 0.001$), and tobacco smoking (34.6% vs 26.4%; $P < 0.001$).

Primary outcome

Complete case analyses and mixed linear model analyses for outcomes in both the aggregate and propensity-matched cohorts at 1 year are presented in Table 2. Figures 1 and 2 show the primary outcomes in the aggregate and propensity-matched cohorts during 1 year of follow-up. For the private and public group combined, the mean improvement in ODI was 31.1 (95% CI 30.4 to 31.9; $P < 0.001$) in the aggregate cohort and 28.4 (95% CI 27.5 to 29.3; $P < 0.001$) in the propensity-matched cohort. For the private group in the aggregate cohort, the improvement in ODI was 28.8 points vs 32.3 in the public group (mean difference 95% CI − 5.0 to − 1.9; P for equivalence < 0.001). Equivalence was confirmed in the propensity-matched cohort (mean difference 2.0, 95% CI − 0.25 to 4.3; $P < 0.001$ for equivalence).

Secondary outcomes

There was a small difference in mean change between the groups in the aggregate cohort in favor of the public group for EQ-5D (0.25 vs 0.50, mean difference − 0.05, 95% CI − 0.08 to − 0.02; $P = 0.002$) and back pain (3.3 vs 3.5, mean difference − 0.2, 95% CI − 0.22, − 0.44 to − 0.004; $P = 0.046$). After propensity matching, the groups did not differ

Table 1 Personal characteristics, coexisting illnesses, and measures of health status for both treatment groups in aggregate and propensity-matched cohorts. Values are numbers (percentages) unless stated otherwise

Variables	Aggregate cohort		*P* value	Propensity-matched cohort		*P* value
	Private hospitals (*n* = 1728)	Public hospitals (*n* = 3493)		Private hospitals (*n* = 1281)	Public hospitals (*n* = 1281)	
Age (years)	43.3	44.3	0.01	42.9	42.9	0.96
Female sex	622 (36%)	1506 (4.1%)	< 0.001	253 (31.8%)	255 (32%)	0.97
Life partner/married	1313 (76.5%)	2605 (75.3%)	0.17	228 (75.7%)	225 (75.5%)	0.93
Attended college	783 (45.7%)	1243 (35.8%)	< 0.001	200 (26.8%)v	198 (26.6%)	0.96
Body mass index (BMI)	26.3	26.7	0.001	26.4	26.4	0.84
Current smoker	443 (25.9%)	1050 (30.4%)	0.001	228 (24.2%)	219 (23.4%)	0.71
Comorbidity	247 (14.3%)	823 (23.6%)	< 0.001	134 (12.5%)	146 (13.5%)	0.51
ASA > 2	29 (1.7%)	168 (4.9%)	< 0.001	21 (1.7%)	13 (1.0%)	0.23
Preoperative ODI	40.9	47.5	< 0.001	41.3	41.4	0.91
Preoperative EQ-5D	0.34	0.25	< 0.001	0.4	0.3	0.80
Preoperative back pain	5.6	6.4	< 0.001	5.7	5.8	0.14
Preoperative leg pain	6.5	7.0	< 0.001	6.5	6.5	0.60
Emergency surgery	18 (1.0%)	1011 (29.1%)	< 0.001	11 (0.8%)	11 (0.8%)	–

Table 2 Complete case analyses and mixed linear model analysis for outcomes at 1 year in patients operated in private or public hospitals for lumbar disc herniation

Outcomes	Complete case analysis ($N = 3624$)						Difference in mean change between groups (95% CI)	P for equivalence	Mixed model analysis						Difference in mean change between groups (95% CI)	P for equivalence
	Private hospitals ($N = 1195$)			Public hospitals ($N = 2429$)					Private hospitals			Public hospitals				
	Baseline	1 year	Mean change	Baseline	1 year	Mean change			Baseline	1 year	Mean change	Baseline	1 year	Mean change		
Aggregate cohort																
ODI	40.9	11.9	28.8	47.5	15.7	32.3	− 3.5 − 5.0, − 1.9)	< 0.001	41.0	12.0	29.0	47.5	15.6	31.9	− 2.9 (− 4.3, − 1.5)	< 0.001
EQ-5D	0.34	0.80	0.45	0.25	0.74	0.50	− 0.05 (− 0.08, − 0.02)	–	0.34	0.80	0.46	0.24	0.74	0.50	− 0.04 (− 0.07, − 0.01)	–
Back pain	5.6	2.3	3.3	6.4	2.8	3.5	− 0.2 (− 0.4, − 0.004)	–	5.6	2.3	3.3	6.4	2.8	3.6	− 0.2 (− 0.4, − 0.01)	–
Leg pain	6.5	1.8	4.8	7.01	2.3	4.8	− 0.01 (− 0.2, 0.2)	–	6.5	1.8	4.7	7.01	2.3	4.8	− 0.03 (− 0.2, 0.2)	–
Matched cohort	Private hospitals ($N = 865$)			Public hospitals ($N = 881$)												
ODI	41.3	11.4	29.0	41.4	14.0	27.0	2.0 (− 0.3, 4.3)	< 0.001	41.3	12.0	29.3	41.4	14.4	27.0	2.3 (0.6, 4.0)	< 0.001
EQ-5D	0.35	0.82	0.46	0.34	0.78	0.42	0.04 (− 0.01, 0.1)	–	0.35	0.81	0.46	0.34	0.76	0.42	0.04 (− 0.01, 0.1)	–
Back pain	5.7	2.2	3.4	5.8	2.6	3.2	0.3 (− 0.1, 0.6)	–	5.7	2.3	3.4	5.8	2.7	3.2	0.3 (0.0, 0.5)	–
Leg pain	6.5	1.8	4.8	6.5	2.0	4.5	0.3 (− 0.04, 0.7)	–	6.5	1.8	4.8	6.5	2.1	4.4	0.4 (0.1, 0.6)	–

(0.46 vs 0.42 for EQ-5D; $P = 0.13$) and (3.4 vs 3.2 for back pain; $P = 0.16$). There was no difference between the two groups for leg pain. Duration of surgical procedures and length of hospital stays were lower in the private group compared to the public group (for the matched cohorts 47.9 vs 57.8 min; $P < 0.001$ and 0.7 vs 2.0 days; $P < 0.001$), as shown in Table 3. For the aggregate cohort, there was a significantly higher number of patients operated in a public hospital that experienced both perioperative complications and postoperative complications within 3 months (2.9% vs 1.4%; $P = 0.001$) and (6.5% vs 4.5%; $P = 0.020$), respectively. In the propensity-matched cohort, there were no differences in either perioperative or postoperative complications within 3 months between the two groups.

Discussion

To our knowledge, this is the first study to compare patient-reported outcomes between private and public hospitals. Despite differences in patients' baseline characteristics that may influence treatment outcomes, the effectiveness of lumbar microdiscectomy was equivalent in public and private hospitals in this registry-based multicenter observational study. This finding was consistent in both unmatched and propensity-matched populations.

Duration of surgery was shorter in private hospitals. This may in part be explained by the surgical team's experience. Unlike private hospitals, most public hospitals are teaching institutions where surgical residents and operating room staff are learning the procedure and working under guidance and supervision. It is also possible that surgical units specializing in fewer procedures, microdiscectomy being one of them, are prone to develop a more efficient take on the surgical technique and logistics, resulting in shorter operation time. They also avoid the burden of having a readiness for acute interventions that in the public part of this cohort was as high as 29.1%.

Longer hospital stays in public hospitals could partly be explained by the fact that public hospitals only received full reimbursement from Norwegian health authorities if the patients spent the first night following surgery in hospital. It is also rather common that patients originally referred to private hospitals are rejected when having comorbidities or other factors that may negatively influence outcomes and logistics [9]. Lumbar microdiscectomy seems to be a safe surgical procedure with few serious complications. In the aggregate cohort, there were slightly more perioperative complications within 3 months in the public group compared to the private group. These differences disappeared following propensity matching, supporting the evidence that "healthier" patients are treated in private hospitals [9].

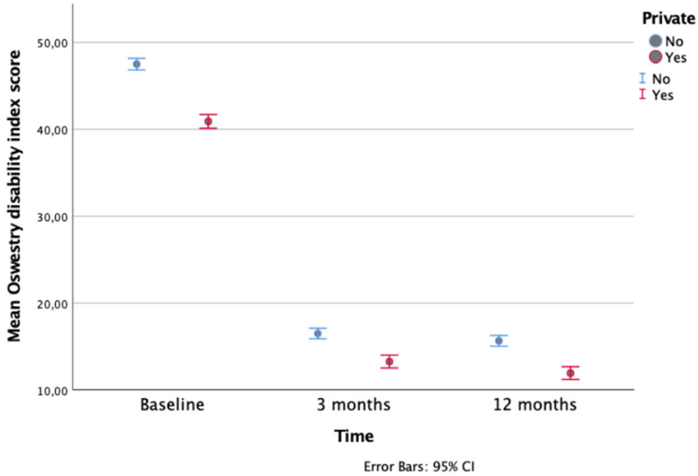

Fig. 1 Change in Oswestry disability index score after microdiscectomy for lumbar disc herniation in aggregate cohort during 1-year follow-up for patients operated in private versus public hospitals

Unlike private hospitals, most public hospitals are teaching institutions where surgical residents and operating room staff are learning the procedure and working under guidance and supervision. Our results are in line with a study showing that surgical treatment of LDH at public hospitals with dedicated training programs does not lead to inferior patient care [22].

Economic and social differences between patients and access to healthcare are not as big of a challenge in Norway compared to other parts of the world. This could in part explain our equivalent results. However, a systematic review from low- and middle-income countries showed that the private sector was not superior to the public when considering medical efficiency [2].

Considering the equivalence of surgical results between the two health care providers in our nationwide patient sample, one could argue that there is a widespread access to high quality surgical management of LDH in both private and public health care systems. The dilemma each patient should consider is then not the effectiveness and quality of the health care, but rather their own economical capacity and possible waiting time for surgery. The role of private health insurance also comes under scrutiny in a country where the public health care system is well functioning and provides all emergency and complex in-house medical treatment [11].

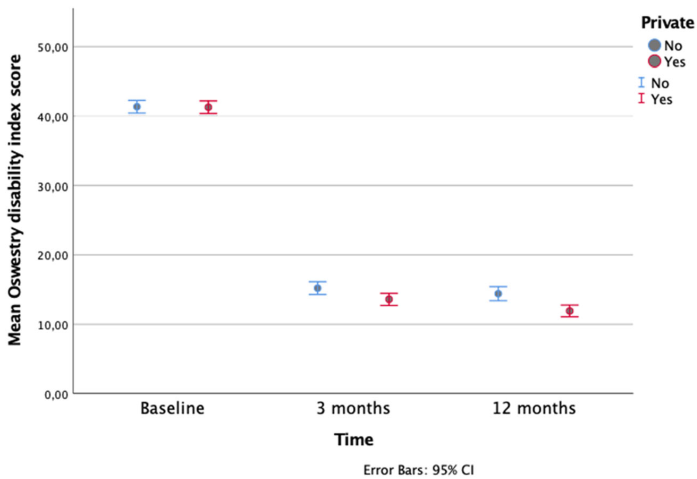

Fig. 2 Change in Oswestry disability index score after microdiscectomy for lumbar disc herniation in propensity-matched cohort during 1-year follow-up for patients operated in private versus public hospitals

Table 3 Operation time, complications, and events. Values are numbers (percentages) of participants unless stated otherwise

Variables	Aggregate cohort		*P* value	Propensity-matched cohort		*P* value
	Private hospitals (*n* = 1728)	Public hospitals (*n* = 3493)		Private hospitals (*n* = 1281)	Public hospitals (*n* = 1281)	
Operation time (min)	48.4	61.8	< 0.001	47.9	57.8	< 0.001
Days in hospital (no.)	0.7	2.2	< 0.001	0.7	2.0	< 0.001
Patients with complications (no.)	78 (4.5%)	250 (7.2%)	< 0.001	56 (4.7%)	76 (6.2%)	0.10
Perioperative complications (no.)	24 (1.4%)	100 (2.9%)	0.001	18 (1.4%)	30 (2.4%)	0.11
Dural tear or CSF leak	12 (0.7%)	61 (1.7%)	0.002	9 (0.7%)	21 (1.7%)	0.04
Nerve injury	6 (0.3%)	7 (0.2%)	0.38	4 (0.3%)	2 (0.2%)	0.69
Blood replacement or postoperative hematoma	8 (0.5%)	10 (0.3%)	0.32	6 (0.5%)	1 (0.1%)	0.13
Cardiovascular compl.	–	5 (0.1%)	0.18	–	–	–
Respiratory compl.	1 (0.1%)	1 (–)	0.55	1 (0.1%)	–	–
Anaphylactic reaction	3 (0.2%)	3 (0.1%)	0.40	2 (0.2%)	1 (0.1%)	1.0
Wrong level surgery	–	8 (0.2%)	0.06	–	1 (0.1%)	–
Complications within 3 months (no.)	55 (4.5%)	157 (6.5%)	0.02	24 (3.9%)	33 (5.3%)	0.29
Wound infection	41 (3.4%)	62 (2.6%)	0.17	18 (2.9%)	18 (2.9%)	1.0
Urinaty tract infection	3 (0.2%)	47 (1.9%)	< 0.001	2 (0.3%)	8 (1.2%)	0.11
Micturition problems	10 (0.8%)	47 (1.9%)	0.01	4 (0.6%)	7 (1.1%)	0.55
Pneumonia	3 (0.2%)	10 (0.4%)	0.56	2 (0.3%)	4 (0.6%)	0.69
Pulmonary embolism	1 (0.1%)	0 (–)	0.33	–	–	–
Deep venous thrombosis	–	2 (0.1%)	1.0	–	–	–
Reoperated within 90 days no. (%)	20 (1.2%)	44 (1.3%)	0.79	10 (0.8%)	10 (0.8%)	1.0

Study strengths and limitations

The major strength of this study is our use of propensity-matched groups to minimize confounding factors. Other strengths include the large sample size, pragmatic study design based on prospective registry data with high external validity, use of patient-reported outcome measures, and protocol-based statistical analyses with blinded assessment of main outcome measures. The main limitation was the lack of randomization. Even though propensity-matched patient groups adjusts for known interactions, while unlikely, residual or introduction of confounding cannot be ruled out. Another weakness was the loss to follow-up of 30.6% of participants regarding Oswestry disability index scores at 1 year. A previous study on a similar population from the NORspine registry showed no difference in outcomes between non-responders and responders [21]. The minor differences in baseline characteristics between non-responders and responders at 1 year are not likely to influence our results [7, 13–15]. Also, we are lacking data on exact amounts of costs, payment, and reimbursements, inhibiting us from performing cost-effectiveness analyses.

Conclusion

At 1 year, the effectiveness of microdiscectomy for lumbar disc herniation was equivalent for patients operated in private compared to public hospitals. However, patients operated in private clinics were managed more efficiently. Favorable outcomes were observed at 1 year in both treatment groups.

Acknowledgments We thank the Norwegian Registry for Spine Surgery (NORspine). We thank all patients and spine surgeons who participate in NORspine registration.

Data sharing All data is shared.

Authors' contribution All authors read and approved the final manuscript. MAM is the guarantor and originally conceived the study with SG. SG and MAM were involved in the study design, collection of data, statistical analysis, and writing of the manuscript. TKS and ØPN took part in collection of data and writing of manuscript. ØS and SMC took part of study design, statistical analyses and writing of manuscript. SW and KO were involved with study design and writing of manuscript.

Funding information The registry receives funding from the University of Northern Norway and Norwegian health authorities.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was approved by the regional committee for medical research in central Norway (ID2016/840) and all participants provided written informed consent. The Data Inspectorate of Norway approved the registry protocol.

References

1. Arts MP, Brand R, van den Akker ME, Koes BW, Bartels RH, Peul WC, Leiden-The Hague Spine Intervention Prognostic Study G (2009) Tubular diskectomy vs conventional microdiskectomy for sciatica: a randomized controlled trial. JAMA 302:149–158. https://doi.org/10.1001/jama.2009.972
2. Basu S, Andrews J, Kishore S, Panjabi R, Stuckler D (2012) Comparative performance of private and public healthcare systems in low- and middle-income countries: a systematic review. PLoS Med 9:e1001244. https://doi.org/10.1371/journal.pmed.1001244
3. Brox JI, Reikeras O, Nygaard O, Sorensen R, Indahl A, Holm I, Keller A, Ingebrigtsen T, Grundnes O, Lange JE, Friis A (2006) Lumbar instrumented fusion compared with cognitive intervention and exercises in patients with chronic back pain after previous surgery for disc herniation: a prospective randomized controlled study. Pain 122:145–155. https://doi.org/10.1016/j.pain.2006.01.027
4. Deyo RA, Mirza SK (2016) Clinical practice. Herniated lumbar intervertebral disk. N Engl J Med 374:1763–1772. https://doi.org/10.1056/NEJMcp1512658
5. Fairbank JC, Couper J, Davies JB, O'Brien JP (1980) The Oswestry low back pain disability questionnaire. Physiotherapy 66:271–273
6. Giannadakis C, Nerland US, Solheim O, Jakola AS, Gulati M, Weber C, Nygaard OP, Solberg TK, Gulati S (2015) Does obesity affect outcomes after decompressive surgery for lumbar spinal stenosis? A multicenter, observational, registry-based study. World Neurosurg 84:1227–1234. https://doi.org/10.1016/j.wneu.2015.06.020
7. Giannadakis C, Solheim O, Jakola AS, Nordseth T, Gulati AM, Nerland US, Nygaard OP, Solberg TK, Gulati S (2016) Surgery for lumbar spinal stenosis in individuals aged 80 and older: a multicenter observational study. J Am Geriatr Soc 64:2011–2018. https://doi.org/10.1111/jgs.14311
8. Grotle M, Brox JI, Vollestad NK (2003) Cross-cultural adaptation of the Norwegian versions of the Roland-Morris disability questionnaire and the Oswestry disability index. J Rehabil Med 35:241–247
9. Grotle M, Solberg T, Storheim K, Laerum E, Zwart JA (2014) Public and private health service in Norway: a comparison of patient characteristics and surgery criteria for patients with nerve root affections due to disc herniation. Eur Spine J 23:1984–1991. https://doi.org/10.1007/s00586-014-3293-z
10. Gulati S, Madsbu MA, Solberg TK, Sorlie A, Giannadakis C, Skram MK, Nygaard OP, Jakola AS (2017) Lumbar microdiscectomy for sciatica in adolescents: a multicentre observational registry-based study. Acta Neurochir 159:509–516. https://doi.org/10.1007/s00701-017-3077-4
11. Gulati S, Solheim O, Carlsen SM, Oie LR, Jensberg H, Gulati AM, Madsbu MA, Giannadakis C, Jakola AS, Salvesen O (2018) Risk of intracranial hemorrhage (RICH) in users of oral antithrombotic drugs: nationwide pharmacoepidemiological study. PLoS One 13:e0202575. https://doi.org/10.1371/journal.pone.0202575
12. Knutsson B, Michaelsson K, Sanden B (2013) Obesity is associated with inferior results after surgery for lumbar spinal stenosis: a study of 2633 patients from the Swedish spine register. Spine (Phila Pa 1976) 38:435–441. https://doi.org/10.1097/BRS.0b013e318270b243
13. Madsbu MA, Oie LR, Salvesen O, Vangen-Lonne V, Nygaard OP, Solberg TK, Gulati S (2018) Lumbar microdiscectomy in obese patients: a multicenter observational study. World Neurosurg 110:e1004–e1010. https://doi.org/10.1016/j.wneu.2017.11.156
14. Madsbu MA, Salvesen O, Werner DAT, Franssen E, Weber C, Nygaard OP, Solberg TK, Gulati S (2018) Surgery for herniated lumbar disc in daily tobacco smokers: a multicenter observational study. World Neurosurg 109:e581–e587. https://doi.org/10.1016/j.wneu.2017.10.024
15. Madsbu MA, Solberg TK, Salvesen O, Nygaard OP, Gulati S (2017) Surgery for herniated lumbar disk in individuals 65 years of age or older: a multicenter observational study. JAMA Surg 152:503–506. https://doi.org/10.1001/jamasurg.2016.5557
16. Nerland US, Jakola AS, Giannadakis C, Solheim O, Weber C, Nygaard OP, Solberg TK, Gulati S (2015) The risk of getting worse: predictors of deterioration after decompressive surgery for lumbar spinal stenosis: a multicenter observational study. World neurosurgery 84:1095–1102. https://doi.org/10.1016/j.wneu.2015.05.055
17. Nerland US, Jakola AS, Solheim O, Weber C, Rao V, Lonne G, Solberg TK, Salvesen O, Carlsen SM, Nygaard OP, Gulati S (2015) Minimally invasive decompression versus open laminectomy for central stenosis of the lumbar spine: pragmatic comparative effectiveness study. BMJ 350:h1603. https://doi.org/10.1136/bmj.h1603
18. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, Bouter LM, de Vet HC (2008) Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976) 33:90–94. https://doi.org/10.1097/BRS.0b013e31815e3a10
19. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JA, Tans JT, Thomeer RT, Koes BW, Leiden-The Hague Spine Intervention Prognostic Study G (2007) Surgery versus prolonged conservative treatment for sciatica. N Engl J Med 356:2245–2256. https://doi.org/10.1056/NEJMoa064039
20. Solberg TK, Olsen JA, Ingebrigtsen T, Hofoss D, Nygaard OP (2005) Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. Eur Spine J 14:1000–1007. https://doi.org/10.1007/s00586-005-0898-2
21. Solberg TK, Sorlie A, Sjaavik K, Nygaard OP, Ingebrigtsen T (2011) Would loss to follow-up bias the outcome evaluation of patients operated for degenerative disorders of the lumbar spine? Acta Orthop 82:56–63. https://doi.org/10.3109/17453674.2010.548024
22. Stienen MN, Smoll NR, Hildebrandt G, Schaller K, Gautschi OP (2014) Early surgical education of residents is safe for microscopic lumbar disc surgery. Acta Neurochir 156:1205–1214. https://doi.org/10.1007/s00701-014-2070-4

23. Team. RDC (2007) R a language and environment for statistical computing. R Foundation for Statistical Computing
24. Twisk J, de Boer M, de Vente W, Heymans M (2013) Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. J Clin Epidemiol 66:1022–1028. https://doi.org/10.1016/j.jclinepi.2013.03.017
25. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S (2007) The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 370:1453–1457. https://doi.org/10.1016/S0140-6736(07)61602-X

Comments

The microsurgical treatment of lumbar disc herniation (LDH) is one of the most commonly performed procedures in neurosurgery. For its relatively minor degree of complexity, lumbar microdiscectomy can be performed by supervised trainees without increasing the risk of complications and adverse outcome. Training the next generation of spine surgeons typically takes place in public hospitals and - as this paper illustrates - on a selected cohort of patients that are older, smoke more, have a lower educational level but suffer from more comorbidities and higher baseline case severity. Considering the teaching aspect, it is not surprising that the OR time is longer (62 vs. 48 min) & the rate of incidental durotomies is somewhat higher in patients treated at public hospitals (1.7% vs. 0.7%), even in the propensity-matched models. Nonetheless, both - patients treated in public or private hospitals - benefit substantially from the operation and the rates of nerve injuries (ca. 0.2%) or 90-day re-operations (ca. 1.2%) are similarly low. To me, this work underlines today's high standards of surgical teaching in the OR, which becomes increasingly important in times of decreasing working time & OR exposure of neurosurgical trainees.

Martin N. Stienen
Zurich / Stanford

Affiliations

Mattis A. Madsbu[1,2] · **Øyvind Salvesen**[3] · **Sven M. Carlsen**[4,5] · **Steinar Westin**[3] · **Kristian Onarheim**[6] · **Øystein P. Nygaard**[1,2,7] · **Tore K. Solberg**[8,9,10] · **Sasha Gulati**[1,2,7]

1 Department of Neurosurgery, St. Olavs University Hospital, Trondheim, Norway

2 Department of Neuroscience, Norwegian University of Science and Technology (NTNU), Trondheim, Norway

3 Department of Public Health and Nursing, Norwegian University of Science and Technology (NTNU), Trondheim, Norway

4 Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU), Trondheim, Norway

5 Department of Endocrinology, St Olavs Hospital, Trondheim, Norway

6 Central Norway Regional Health Authority, Stjørda, Norway

7 National Advisory Unit on Spinal Surgery, St. Olavs University Hospital, Trondheim, Norway

8 The Norwegian National Registry for Spine Surgery, University Hospital of Northern Norway (UNN), Tromsø, Norway

9 Department of Neurosurgery, University Hospital of Northern Norway (UNN), Tromsø, Norway

10 Institute of Clinical Medicine, The Arctic University of Norway (UIT), Tromsø, Norway

ISBN 978-82-326-5546-5 (printed ver.)
ISBN 978-82-326-6506-8 (electronic ver.)
ISSN 1503-8181 (printed ver.)
ISSN 2703-8084 (online ver.)

NTNU
Norwegian University of
Science and Technology