Doctoral theses at NTNU, 2023:175

Vetle Vangen Lønne

Outcomes following surgery for degenerative spinal disease

Observational studies based on data from the Norwegian Registry for Spine Surgery and the Norwegian Labour and Welfare Administration

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

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ISBN 978-82-326-7054-3 (printed ver.)
ISBN 978-82-326-7053-6 (electronic ver.)
ISSN 1503-8181 (printed ver.)
ISSN 2703-8084 (online ver.)

Doctoral theses at NTNU, 2023:175

Printed by NTNU Grafisk senter

Kirurgi for degenerativ nakke- og rygglidelse

Sammendrag på norsk:

Lumbalt prolaps (LDH), lumbal spinal stenose (LSS) og degenerativ cervical myelopati (DCM) er degenerative lidelser i ryggraden som kan gi betydelige og av og til alvorlige plager for de som rammes. Målet med denne oppgaven var å studere resultater etter kirurgisk behandling for disse tilstandene, ved å bruke materiale fra Norsk ryggregister (NORspine) og NAV.

I studie 1 undersøkte vi resultat og komplikasjonsrate etter førstegangs lumbal mikrodiskektomi ved å bruke data fra et enkelt sykehus. Det primære utfallsmålet var endring i Oswestry Disability Index (ODI) etter et år. Vi fant signifikant forbedring i gjennomsnittlig ODI score ett år etter kirurgi. Vi fant også signifikant forbedring i alle sekundære utfallsmål. Det var totalt 18 kirurgiske komplikasjoner, og 63 medisinske komplikasjoner. Vannlatingsproblemer var den vanligste komplikasjonen 3 måneder etter kirurgi.

I studie 2 undersøkte vi endringer i smerter under seksuell aktivitet etter kirurgi for lumbal spinal stenose (LSS). Det primære utfallsmålet var endring i smerte under seksuell aktivitet etter ett år, målt ved seksjon nr. 8 i ODI. 12 954 pasienter ble inkludert, og 76.5% av disse fullførte et års oppfølging. Preoperativt svarte 26.4% at de hadde et normalt sexliv uten smerter, mens 57.8% svarte det samme etter ett år. Preoperativt rapporterte 10.5% av pasientene at smerter forhindret all seksuell aktivitet, sammenliknet med 5.3% etter ett år. Det å ha en partner, høyere utdanning, og å være i arbeid frem til datoen for kirurgi var prediktorer for forbedring i smerte under seksuell aktivitet. Bruk av tobakk, smertevarighet over tolv måneder, tidligere ryggkirurgi og komplikasjoner innen tre måneder var negative prediktorer.

I studie 3 undersøkte vi resultater etter dekompressiv kirurgi for DCM. Det primære utfallsmålet var endring i Neck Disability Index (NDI) ett år etter kirurgi. 905 pasienter ble inkludert. Vi fant signifikant forbedring målt ved alle pasient-rapporterte utfallsmål, inkludert NDI, EQ-5D, hodepine, nakke- og armsmerte NRS, og GPE. Det var signifikant forbedring både for mild og moderat-til-alvorlig DCM.

I studie 4 undersøkte vi grad av retur til arbeid (RTW) hos pasienter etter gjennomført dekompressiv kirurgi for DCM. Det primære utfallsmålet var RTW, definert som å være i jobb på et gitt tidspunkt postoperativt uten noen form for helserelatert ytelse fra NAV. Blant 439 pasienter operert for DCM mellom 2012 og 2018, mottok 20% av pasienten en form for økonomisk stønad ett år før kirurgi. Tolv måneder etter kirurgi hadde 65% returnert til arbeid. Etter 36 måneder hadde 75% returnert til arbeid. Pasientene som returnerte til arbeid var oftere ikke-røykere med høyere utdanning. De hadde mindre komorbiditet, flere hadde jobb, og flere hadde ingen stønad ett år før kirurgi. Gjennomsnittlige sykedager i året før kirurgi var færre i gruppen som oppnådde retur til arbeid, og de hadde signifikant lavere NDI- og EQ-5D-score før kirurgi.

Oppsummert viser denne oppgaven at kirurgi for degenerative rygglidelser er trygt og assosiert med gode resultater målt ved et bredt spekter av utfallsmål.

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Finansieringskilde: NTNU, Institutt for Nevromedisin og Bevegelsesvitenskap

Ovennevnte avhandling er funnet verdig til å forsvares offentlig for graden Doctor Philosophiae.
Disputas finner sted i Trondheim, 8. juni 2023

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Acknowledgements:

The research for this thesis was done between 2017 - 2022. During this time, I was completing my medical studies at the Norwegian University of Science and Technology (NTNU) in Trondheim, 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 started as a medical student research project and was later developed into a PhD thesis.

I know of no one else who has entered the field of medical research the way I did. In the spring of 2015, I was studying music, still working to be accepted to the medical program at NTNU. My father defended his PhD in April of that year, and I played a few songs on guitar as part of the entertainment before the doctoral dinner. During the dinner, I was approached by a man I did not know. The man introduced himself as Sasha Gulati and asked if I would be willing to play guitar in another doctoral dinner, in about six months. I said I would be happy to. When we met again six months later, I had been accepted to the medical program at NTNU and had started thinking about getting involved in research myself. We had a quick, but interesting discussion that evening (while I was tuning my guitar) and agreed to discuss further the following week. That discussion marks the earliest beginnings of this thesis.

I sincerely thank Sasha for being my main supervisor, mentor, and friend. He has been a constant source of inspiration, optimism, and support. He has never failed to provide quick guidance and feedback to all manner of questions, whether related to research, work, or life in general, and I am forever grateful for that.

I would also like to sincerely thank Karen Walseth Hara, my co-supervisor for this thesis, for introducing me to a topic of which I knew only the basics, with skill, enthusiasm, and patience. Øystein Petter Nygaard was co-supervisor on my medical student research project, and he and Tore Kristian Solberg are co-authors on all articles included in this thesis. They have contributed with their wealth of experience and skill to ensure the quality of my work is up to a high standard. Øyvind Salvesen has helped me navigate the jungle of medical statistics with insight and no small amount of very strong coffee. Further, I would like to thank all my co-authors for your skill and dedication. A warm thank you also to my colleagues at the Department of Neurosurgery for all that you have taught and continue to teach me.

A warm thank you to my family and friends for enduring my endless talks about spine surgery (“I have no clue what it is you are doing, but if you are working on it on the weekends again it better be good!”). A special thank you to my fellow PhD-students at The Office for helping me to stay sane through this process. Finally, a warm thank you to my wife Kristina for all your kindness and understanding, and for letting this thesis be part of our lives for many years now. This is teamwork!

Abbreviations

ASA	American Society of Anesthesiologists
BMI	Body mass index
CT	Computed tomography
DCM	Degenerative cervical myelopathy
EMS	European Myelopathy Score
EQ-5D	(EuroQol instrument)
GPE	Global Percieved Effect scale
HRQL	Health-related quality of life
JOA	Japanese Orthopedic Association
LDH	Lumbar disc herniation
LSS	Lumbar spinal stenosis
MCIC	Minimal clinically important change
MRI	Magnetic resonance imaging
NAV	(The Norwegian Labour and Welfare Administration)
NDI	Neck Disability Index
NORspine	The Norwegian Registry for Spine Surgery
NRS	Numerical rating scale
ODI	Oswestry Disability Index
PROMs	Patient-reported outcome measurements
RTW	Return to work

Publications included in the research thesis

The present PhD thesis is based on the following papers, which will be referred to in the text as paper 1, paper 2, paper 3, and paper 4:

Paper 1

Microdiscectomy for lumbar disk herniation: a single center observational study. Vetle Vangen-Lønne, Mattis A. Madsbu, Øyvind Salvesen, Øystein Nygaard, Tore K. Solberg, and Sasha Gulati; World Neurosurgery; 2020

Paper 2

Pain During Sex Before and After Decompressive Surgery for Lumbar Spinal Stenosis: A Multicenter Observational Study. Siril T. Holmberg*, Vetle Vangen-Lønne*, Agnete M. Gulati, Øystein P. Nygaard, Tore K. Solberg, Øyvind O. Salvesen, and Sasha Gulati; Spine; 2021

Paper 3

Surgery for degenerative cervical myelopathy: A nationwide registry-based observational study with patient reported outcomes. Sasha Gulati, Vetle Vangen-Lønne, Øystein P. Nygaard, Agnete M. Gulati, Tommy A. Hammer, Tonje O. Johansen, Wilco C. Peul, Øyvind O. Salvesen, and Tore K. Solberg; Neurosurgery; 2021

Paper 4

Return to work after surgery for degenerative cervical myelopathy: A nationwide registry-based observational study. Vetle Vangen Lønne, Sozaburo Hara, Sasha Gulati, Lene Aasdahl, Øyvind O. Salvesen, Øystein P. Nygaard, Tore K. Solberg, and Karen Walseth Hara; Acta Neurochirurgica; 2023 (In press)

*STH and VVL contributed equally on this publication

Complete list of publications

1. **Lumbar microdiscectomy in obese patients: a multicenter observational study.** Mattis A. Madsbu, Lise R. Øie, Øyvind Salvesen, Vetle Vangen-Lønne, Øystein Nygaard, Tore K. Solberg, and Sasha Gulati; World Neurosurgery (2018)

2. **Microdiscectomy for lumbar disk herniation: a single center observational study.** Vetle Vangen-Lønne, Mattis A. Madsbu, Øyvind Salvesen, Øystein Nygaard, Tore K. Solberg, and Sasha Gulati; World Neurosurgery (2020)

3. **Surgery for extraforaminal lumbar disc herniation - a single center observational study.** Samuel B. Polak, Mattis A. Madsbu, Vetle Vangen-Lønne, Øyvind Salvesen, Øystein Nygaard, Tore K. Solberg, Carmen L. A. M. Vleggeert-Lankamp, Sasha Gulati; Acta Neurochirurgica (2020)

4. **Pain during sex before and after decompressive surgery for Lumbar Spinal Stenosis: A Multicenter Observational Study.** *Siril T. Holmberg, *Vetle Vangen-Lønne, Agnete M. Gulati, Øystein P. Nygaard, Tore K. Solberg, Øyvind O. Salvesen, Sasha Gulati – Spine (2021) *STH and VVL contributed equally on this publication

5. **Pain during sex before and after decompressive surgery for Lumbar Disc Herniation – A Multicenter Observational Study.** Siril T. Holmberg, Vetle Vangen-Lønne, Agnete M. Gulati, Øystein P. Nygaard, Tore K. Solberg, Øyvind O. Salvesen, Sasha Gulati – Spine (2021)

6. **Surgery for degenerative cervical myelopathy – a single center observational study.** Sasha Gulati, Vetle Vangen-Lønne, Øystein P. Nygaard, Agnete M. Gulati, Tommy A. Hammer, Tonje O. Johansen, Wilco C. Peul, Øyvind O. Salvesen, and Tore K. Solberg; Neurosurgery (2021)

7. **Is surgery for recurrent lumbar disc herniation worthwhile or futile? A single center observational study with patient reported outcomes.** Vetle Vangen Lønne,

Mattis A. Madsbu, Øyvind Salvesen, Øystein Nygaard, Tore Solberg, Sasha Gulati; Brain and Spine (2022)

8. **Surgery for degenerative cervical myelopathy in patients with rheumatoid arthritis and ankylosing spondylitis: A nationwide registry-based observational study with patient reported outcomes.** Siril T. Holmberg, Tonje O. Johansen, Øyvind Salvesen, Vetle Vangen Lønne, Tore K. Solberg, Agnete M. Gulati, Øystein P. Nygaard, Sasha Gulati; Acta Neurochirurgica (2022)

9. **Surgery for degenerative cervical myelopathy in the elderly: a nationwide registry-based observational study with patient-reported outcomes.** Tonje O. Johansen, Vetle Vangen Lønne, Siril T. Holmberg, Øyvind O. Salvesen, Tore K. Solberg, Agnete M. Gulati, Øystein P. Nygaard, Sasha Gulati; Acta Neurochirurgica (2022)

10. **Effect of spinal cord burst Stimulation vs placebo stimulation on disability in patients with chronic radicular pain after lumbar spine surgery: A randomized clinical trial.** Sozaburo Harra, Hege Andersen, Ole Solheim, Sven M. Carlsen, Terje Sundstrøm, Greger Lønne, Vetle Vangen Lønne, Kristin Taraldsen, Erling A. Tronvik, Lise R. Øie, Agnete M. Gulati, Lisa M. Sagberg, Asgeir S. Jakola, Tore K. Solberg, Øystein P. Nygaard, Øyvind O. Salvesen, Sasha Gulati; JAMA (2022)

11. **Return to Work after Surgery for Cervical Radiculopathy: A Nationwide Registry-based Observational Study.** Sozaburo Hara, Vetle Vangen Lønne, Lene Aasdahl, Øyvind Salvesen, Tore Solberg, Sasha Gulati, Karen Walseth Hara; Spine (2023)

12. **Return to work after surgery for degenerative cervical myelopathy: A nationwide registry-based observational study.** Vetle Vangen Lønne, Sozaburo Hara, Sasha Gulati, Lene Aasdahl, Øyvind O. Salvesen, Øystein P. Nygaard, Tore K. Solberg, and Karen Walseth Hara; Acta Neurochirurgica (In press, 2023).

Summary in English:

Lumbar disc herniation (LDH), lumbar spinal stenosis (LSS) and degenerative cervical myelopathy (DCM) are degenerative spine conditions which can cause significant and sometimes severe disability for those affected. The aim of this thesis was to examine outcomes after surgery for these conditions, using prospectively collected data from The Norwegian Registry for Spine Surgery (NORspine) and the Norwegian Labour and Welfare Administration (NAV).

In paper 1, we examined outcomes and complications following first time lumbar microdiscectomy in an everyday clinical setting. The primary outcome was change in the Oswestry Disability Index (ODI) at one year. 1219 patients were included. We found significant improvement in mean ODI score one year after surgery. We also found significant improvement measured with all secondary outcomes. There were 18 surgical complications and 63 medical complications. The most common complication was micturition problems at three months following surgery.

In paper 2, we evaluated changes in pain during sexual activity after surgery for lumbar spinal stenosis (LSS). The primary outcome was change in pain during sexual activity at one year, assessed by item number eight of the Oswestry disability index (ODI) questionnaire. 12 954 patients were included, and 76.5% of these completed one-year follow-up. Preoperatively 26.4% of patients reported a normal sex-life without pain compared to 57.8% at one year. Preoperatively 10.5% of patients reported that pain prevented any sex-life compared to 5.3% at one year. Having a life partner, college education, and working until time of surgery were predictors of improvement in pain during sexual activity. Current tobacco smoking, pain duration >12 months, previous spine surgery, and complications occurring within three months were negative predictors.

In paper 3, we investigated clinical outcomes in patients undergoing decompressive surgery for DCM. The primary outcome was change in the Neck disability index (NDI) one year after surgery. 905 patients were included. There were significant improvements in all patient reported outcomes (PROMs) including NDI, EuroQol-5D, headache-, neck-, and arm pain NRS and Global Perceived Effect score. There were significant improvements in all PROMs for both mild and moderate-to-severe DCM.

In paper 4, we examined the return to work (RTW) rate in patients undergoing decompressive surgery for DCM. The primary outcome was RTW, defined as being at work at a given time postoperatively without a medical income-compensation benefit from NAV. Among 439 patients operated for DCM between 2012 and 2018, 20% of the patients received a medical income-compensation benefit one year before surgery. By 12 months after surgery, 65% had returned to work. By 36 months, 75% had returned to work. Patients that returned to work were more likely to be non-smokers and to have a college education. They had less comorbidity, more were employed, and more were without benefit one-year pre-surgery. Average days of sick leave in the year before surgery were significantly less in the RTW group, and they had a significantly lower baseline NDI and EQ-5D.

In summary, this thesis demonstrates that surgery for degenerative spine disease is safe and associated with favorable outcomes measured with a wide range of outcome measures.

Sammendrag på norsk:

Lumbalt prolaps (LDH), lumbal spinal stenose (LSS) og degenerativ cervical myelopati (DCM) er degenerative lidelser i ryggraden som kan gi betydelige og av og til alvorlige plager for de som rammes. Målet med denne oppgaven var å studere resultater etter kirurgisk behandling for disse tilstandene, ved å bruke materiale fra Norsk ryggregister (NORspine) og NAV.

I studie 1 undersøkte vi resultat og komplikasjonsrate etter førstegangs lumbal mikrodiskektomi ved å bruke data fra et enkelt sykehus. Det primære utfallsmålet var endring i Oswestry Disability Index (ODI) etter et år. Vi fant signifikant forbedring i gjennomsnittlig ODI score ett år etter kirurgi. Vi fant også signifikant forbedring i alle sekundære utfallsmål. Det var totalt 18 kirurgiske komplikasjoner, og 63 medisinske komplikasjoner. Vannlatingsproblemer var den vanligste komplikasjonen 3 måneder etter kirurgi.

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I studie 4 undersøkte vi grad av retur til arbeid (RTW) hos pasienter etter gjennomført dekompressiv kirurgi for DCM. Det primære utfallsmålet var RTW, definert som å være i jobb på et gitt tidspunkt postoperativt uten noen form for helserelatert ytelse fra NAV. Blant

439 pasienter operert for DCM mellom 2012 og 2018, mottok 20% av pasienten en form for økonomisk stønad ett år før kirurgi. Tolv måneder etter kirurgi hadde 65% returnert til arbeid. Etter 36 måneder hadde 75% returnert til arbeid. Pasientene som returnerte til arbeid var oftere ikke-røykere med høyere utdanning. De hadde mindre komorbiditet, flere hadde jobb, og flere hadde ingen stønad ett år før kirurgi. Gjennomsnittlige sykedager i året før kirurgi var færre i gruppen som oppnådde retur til arbeid, og de hadde signifikant lavere NDI- og EQ-5D-score før kirurgi.

Oppsummert viser denne oppgaven at kirurgi for degenerative rygglidelser er trygt og assosiert med gode resultater målt ved et bredt spekter av utfallsmål.

Introduction

Ever since mankind started walking upright on two legs, we have had to relate to a wide variety of conditions affecting our spine. The spine serves to keep the head and thorax in an upright position, ensures a complex set of motions along three axes, as well protecting the spinal cord and corresponding nerve roots (1). With such a complex set of tasks, any condition affecting the spine will also affect our ability to lead a normal life. I aim to investigate three of these conditions in this thesis. One is a rather common condition many will experience first-hand, one is common in the elderly, while one is less known, though no less disabling for those affected.

Pain radiating along the sciatic nerve distribution, aptly referred to as "sciatica", has been known to physicians for thousands of years (2). It is said that Hippocrates was the first physician to use the term "sciatica", a word derived from the Greek word for hip, *ischios.* Its relation to an intervertebral disc herniation compressing a nerve root was not, however, fully established until 1934 (3). Since then, lumbar disk herniation (LDH) has been established as one of the leading causes of sciatic pain in the adult population (4). A term often used in concordance with sciatica is "radiculopathy". Radiculopathy describes pain radiating down the legs, often characterized as sharp, burning or electric (5). Radiculopathy is most often due to irritation of a specific nerve, and the pain may follow this nerves dermatomal distribution. This pain distribution, along with a thorough clinical history and physical examination, will help the clinician decide on further diagnostic steps (5).

Lumbar spinal stenosis (LSS) is a prevalent condition in the elderly population, resulting from a degenerative aging process in the lumbar spine (6). LSS is characterized by pain, numbness, and weakness in the lower extremities, often in relation to low back pain (7-9). As many other conditions may yield a similar set of symptoms, a radiological image confirming a narrowing of the lumbar spinal canal is also required for the diagnosis to be certain (6, 10).

Degenerative changes in the spine yield different clinical symptoms according to where the changes take place. Degenerative changes in the cervical spine might lead to degenerative cervical myelopathy, the most common cause of spinal cord impairment in adults (11). The term was coined as late as 2015, seeking to unify previously used terms of cervical

spondylotic myelopathy (CSM) and ossification of the posterior longitudinal ligament (OPLL) (12).

Although LDH, LSS and DCM differ in clinical symptoms, epidemiology, and localization, they all have the potential to cause a wide variety of problems for those affected. Surgical treatment has shown favorable results for all three conditions. But when is surgery successful, and how do you measure it? Since the 1980s, one of the preferred ways of measuring outcome after surgery has been to use a patient-reported outcome measure (PROM) (13). A patient-reported outcome measure is defined as being "any report of the status of a patient´s health condition that comes directly from the patient without interpretation of the patient´s response by a clinician or anyone else" (14). Over the years many different outcome measures have been devised to measure success after medical treatments, and every author needs to evaluate which PROMs might be best suited to their research project.

PROMs are not the only way to determine if a treatment is successful or not. Return to work (RTW) after surgery is an increasingly popular outcome due to the significant number of work hours lost because of neck- and back-related pathology (15). As the working population continues to grow older and wishes to stay active and working, knowledge about RTW is also of interest as it can serve as a marker for a successful outcome after treatment.

Aims of the thesis

- To measure clinical outcomes at one year following first time single-level lumbar microdiscectomy for patients operated at St. Olavs Hospital, Norway, using data from the Norwegian Registry for Spine Surgery (NORspine)
- To evaluate changes in pain during sexual activity after microdecompression or laminectomy for LSS using data from NORspine
- To investigate clinical outcomes in patients undergoing decompressive surgery for DCM, using data from NORspine
- To examine the RTW rate in patients undergoing decompressive surgery for DCM, using data from NORspine and the Norwegian Labour and Welfare Administration (NAV)

What is lumbar disc herniation?

Lumbar disc herniation occurs when intervertebral disk material (annulus fibrosus and/or nucleus pulposus) displaces beyond the normal margins of the disk space, potentially compressing nerve roots (4). This may cause pain radiating along the distribution of the affected nerve root, often referred to as “sciatica” or “radiculopathy” (2, 5). Lumbar disc herniation is one of the most common cause of radiculopathy in the adult population (4). Radiculopathy is believed to be both due to the mechanical process of the herniation compressing the nerve but is also a biochemical process. Contact between the nucleus pulposus and the nerve root might be needed to trigger the necessary inflammation for mechanical compression to cause pain (16). Thus, disc herniations can be asymptomatic and are rather common incidental findings on MRI scans. The chance of developing asymptomatic disc herniations also increases with age (17). Herniation can occur in all spine levels, but according to multiple studies, at least 95% of herniated discs are located in the L4/L5 or L5/S1 levels (18, 19). Both genetic and environmental factors seem to play a role in causing disc herniations.

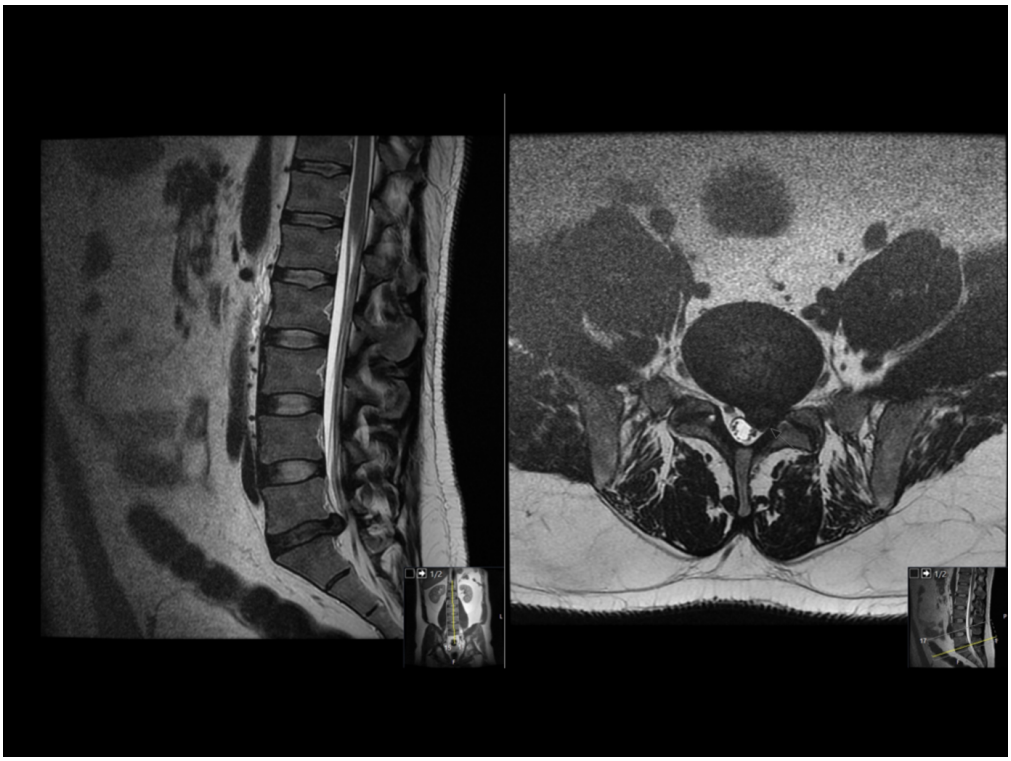

Figure 1. T2-weighted sagittal and axial MR images of lumbar disc herniation at the L5/S1 level with compression of the left S1 nerve root (provided by Prof Sasha Gulati).

Clinical features of lumbar disc herniation

Pain in the lower back and legs are common symptoms and may be due to multiple causes. Lumbar spinal stenosis, spondylolisthesis, and fracture can all give similar symptoms. After these have been ruled out, approximately 85% of patients with radiculopathy are found to have a herniated intervertebral disc (4). Radiculopathy may begin either slowly and gradually or suddenly and is characterized by sharp and aching pain radiating down the foot (20). When the L4 root is compressed, the pain typically located anterolateral in the thigh and to the medial side of the knee, and further down to the medial side of the foot. L5 compression often leads to pain distribution dorsolateral in the thigh and leg, and out to the dorsal side of the foot. S1 compression often yields radiating pain on the lateral side of the thigh and leg, down to the fifth toe. Low back pain might accompany radiculopathy but is not a consistent feature. Patients may also have paresthesias according to the distribution of the affected nerve root, and weakness in the same area. Deep tendon reflex patterns might also be affected by the condition, causing weakened reflexes according to the affected nerve root.

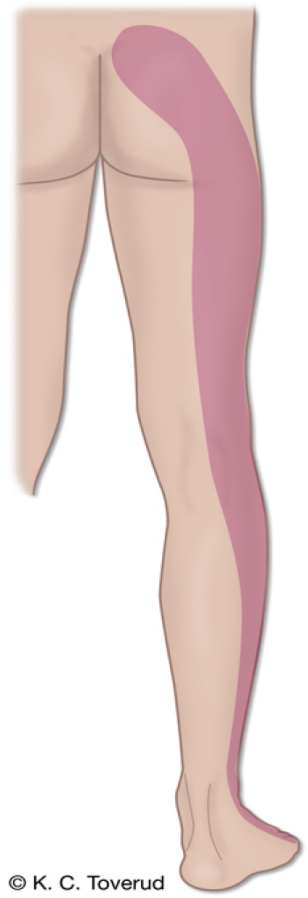

Figure 2. Typical pain distribution following the L5-dermatome. Reproduced with permission from K. C. Toverud

Examination of a patient with suspected lumbar disc herniation involves a thorough clinical history, and a physical examination centered around detecting impaired walking, paresis, sensory deficits, and impaired reflexes. A variation of the straight-leg-raising test (Lasègue´s test) is often used. The test is considered positive when, with the patient in the supine position, raising the leg on the affected side with the knee extended reproduces pain that radiates to below the knee when the angle of the leg is between 30 and 70 degrees (20). The sensitivity of the test for disc herniation is approximately 90%, but the specificity is low (21).

Treatment of lumbar disc herniation

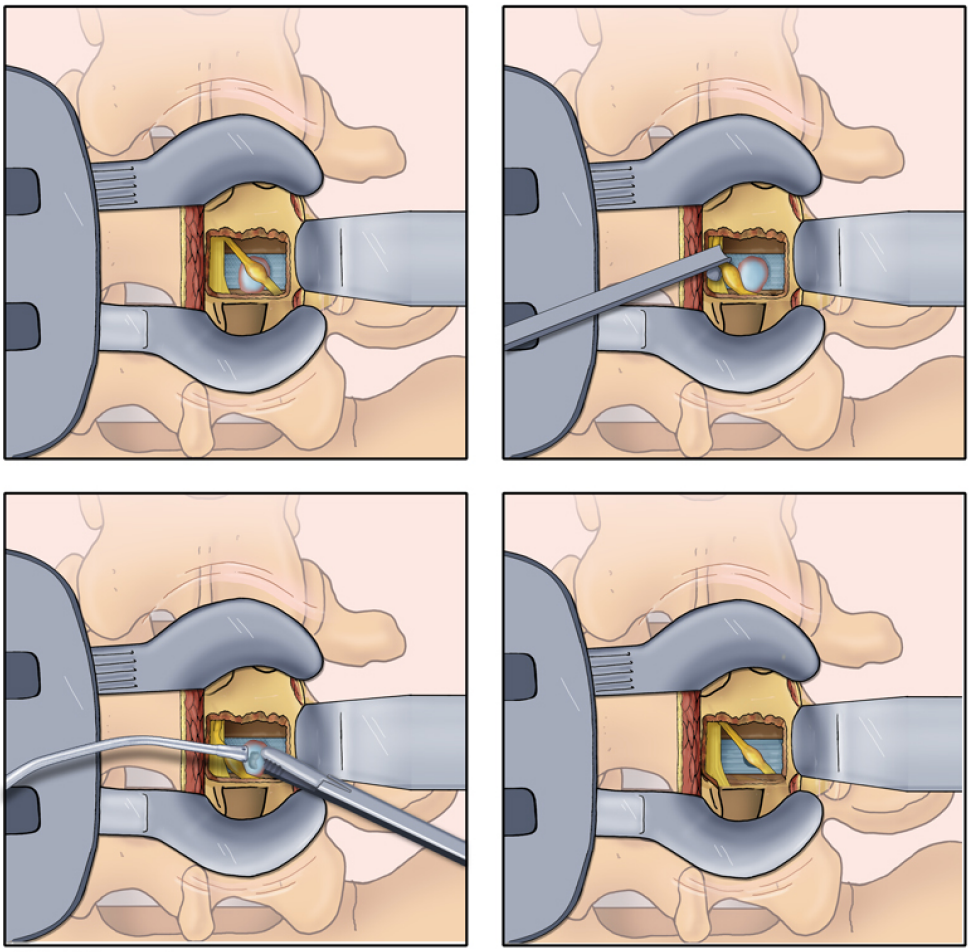

Figure 3. Illustration of a micodiscecomy using Caspar retractors. Reproduced with permission from K. C. Toverud

One-third of the patients with radiculopathy improve within two weeks after onset. Symptoms resolve in three-quarters of patients within 3 months after onset (22). Surgery is typically offered to patients with persisting pain in the lower back radiating down the legs despite conservative treatment, intractable pain, or acute serious paresis including cauda equine syndrome (4). For those who require surgery, lumbar microdiscectomy is the most common surgical procedure (23). The procedure involves preoperative fluoroscopy for detection of the target level, paramedian or median skin incision of about 3 cm, straight or curved opening of the paravertebral muscular fascia, and subperiosteal release of the paravertebral muscles from the spinous process and basal lamina above and occasionally below the target disc-level. Self-

retaining retractors (typically Caspar or Piccolino retractors) are introduced and an operating microscope is used for magnification. Following flavectomy and required bony decompression (i.e. arcotomy and/or partial medial facetectomy), the dural sac and nerve root are carefully mobilized medially and the herniated disc evacuated. Removal of the disc herniation might involve entering the disc space or just removing a free sequestrated disc fragment (sequestrectomy). New methods of treatment for lumbar disc herniation are constantly being developed. A recent multicenter, randomized controlled trial comparing percutaneous transforaminal endoscopic discectomy (PTED) with conventional open microdiscectomy found PTED to be non-inferior in reduction of leg pain after surgery (24).

What is lumbar spinal stenosis

Lumbar spinal stenosis (LSS) is a term used to describe patients with symptoms related to anatomical reduction (stenosis) of the lumbar spinal canal (25). The most common cause of LSS is spondylosis; a degenerative process with hypertrophy of facet joints and ligaments and bulging of the intervertebral disc (26-28). This slowly progresses with age, gradually yielding symptoms from the affected level. Thus, degenerative LSS is rare in patients younger than 50 years old (25). Both direct compression of the nerve root and restriction of the blood supply to the nerves are believed to play a part in the symptom development (10).To be given the clinical diagnosis of LSS, both characteristic symptoms and a radiological or anatomical confirmation of stenosis in the spinal canal are needed (6, 10). Magnetic resonance imaging (MRI) is the preferred method of choice for radiologic assessment of LSS (29). Evaluation is usually based on a quantification of the stenosis at the narrowest place in axial view. Dural sac cross-sectional area (DSCA) is frequently used to quantify the available space in patients with central LSS (30). Schizas et al. has proposed a morphological grade of central LSS from A to D, based on the space available for the nerve rootlets within the cerebrospinal fluid in the dural sac and the presence of epidural fat (31). This morphological grading system has been validated in a study that found high inter- and intraobserver agreement between clinicians and radiologists (30). Not all patients with stenosis on radiological imaging experience symptoms. Some patients have significant narrowing if the spinal canal on MRI (32), without experiencing any symptoms. Others may have severe symptoms with only minor stenosis visible on MRI (33). A multicenter observational study from 2016 found no association between severity of the stenosis on preoperative MRI and preoperative disability, pain or surgical outcomes at 1 year (34).

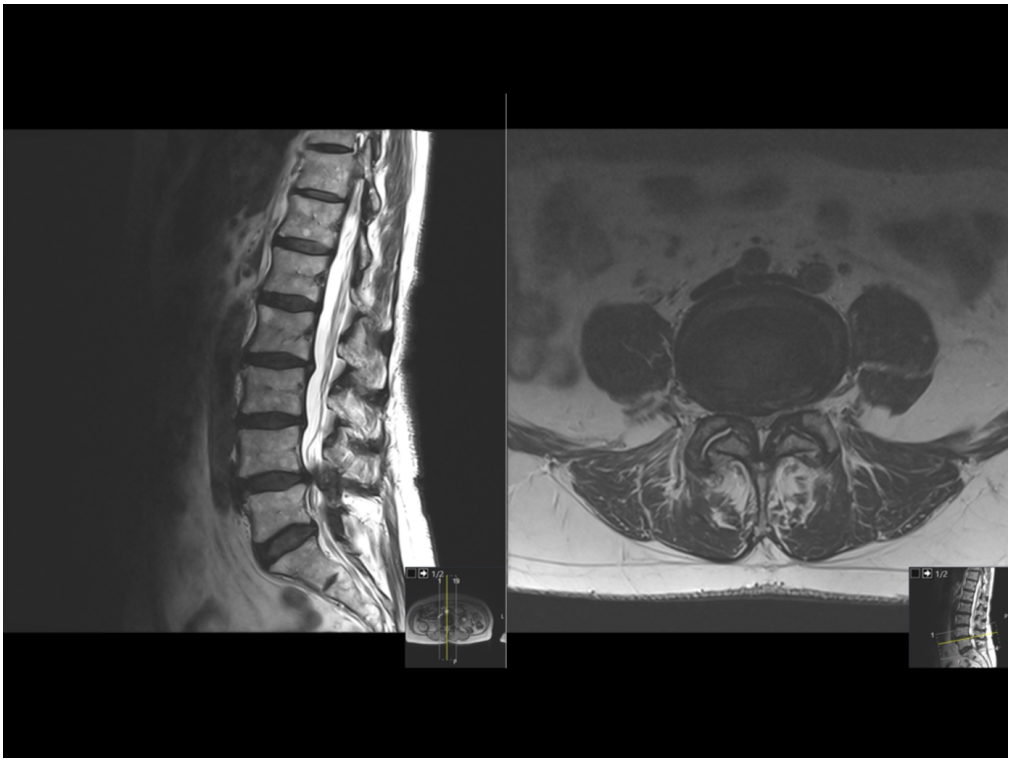

Figure 4. T2-weighted saggital and axial MR images of lumbar spinal stenosis due to ligament and facet joint hypertrophy and an intervertebral disc bulge (provided by Prof Sasha Gulati).

Clinical features of lumbar spinal stenosis

The most common symptom associated with LSS is neurogenic claudication, with symptoms in the gluteal area, groin, and thigh, as well as radiation down the posterior part of the leg to the feet (6, 10). Patients may also experience a sensation of fatigue or heaviness in the leg, as well as paresthesia and weakness (6). Symptoms can be both unilateral and bilateral, the latter being the most common. Pain in the lower back might also be present but is not a consistent finding (25). Symptoms are often relieved by flexion of the lumbar spine which is a key clinical features of LSS (25). Neurological testing in patients with LSS is often negative, as symptoms usually appear after the patients have been walking for a certain distance (6).

Treatment of lumbar spinal stenosis

LSS is the most common indication for spine surgery for patients older than 65 years (35, 36). Even so, treatment for LSS depends on the degree of symptoms and the patient's general health. Non-operative treatment options include physical therapy, cognitive behavioral

therapy and education, and pharmacotherapy (37). The role of non-operative treatment options for LSS remains unclear. A randomized controlled trial (RCT) from 2008 comparing surgical approach for LSS with a non-surgical approach found that patients with LSS without degenerative spondylolisthesis who underwent surgery showed significantly greater improvement measured by a wide range of outcome measures than patients who did not receive surgical treatment (38). An RCT from 2015 comparing surgery to physical therapy found that patients with LSS who were surgical candidates experienced similar long-term functional gains with surgical decompression as with "evidence-based physical therapy" (39). Even so, if conservative treatment does not yield sufficient improvement, a surgical approach is often advised (6). There are multiple different surgical techniques for treatment of LSS, but the main principle is decompression of the nerve structures. Microsurgical decompression and laminectomy remain two of the most common (40). Several studies have shown equivalent outcomes and similar safety profiles following laminectomy and microsurgical decompression for LSS (40-42). When a laminectomy is performed, the spinous process and the lamina of the involved levels as well as the medial aspects of the facet joints are resected (41). Microdecompression via a smaller skin incision can be performed using a bilateral or unilateral approach depending on the surgeon's preference and the patient's anatomy and symptoms. Unlike a laminectomy, the spinous process and the supraspinous and interspinous ligaments are left intact during a microdecompression (41). An operating microscope is used, whereas laminectomy procedures can be performed either with or without visual enhancement such as an operating microscope or surgical loupes. Several different decompression techniques may yield a good outcome. An RCT from 2022 comparing 3 different minimally invasive surgical techniques for LSS found no difference in effectiveness although surgical time did differ (43). As the use of surgery for treatment of LSS has increased, laminectomy has increasingly been supplemented with lumbar fusion, especially in the US. The intention has been to minimalize the chance of future deformity and instability (44). This is a controversial topic. A Swedish RCT from 2016 randomizing patients with LSS to decompressive surgery with or without fusion found no clinical benefit from fusion after 2 years of follow-up (45). Further, they found that fusion surgery is a more complex, more expensive procedure, and associated with an increased risk of complications in the elderly. A Norwegian RCT randomizing patients with LSS and spondylolisthesis to decompression with or without fusion found decompression alone to be non-inferior to decompression with fusion, although with slightly higher reoperation rate in the no-fusion group (46). An American RCT from 2016 randomizing patients with LSS and stable spondylolisthesis to laminctomy with or

without fusion found slightly greater improvement in the fusion group measured with the SF-36 score (47). This study included only 66 patients, the rate of reoperation in the non-fusion group was uncommonly high (34%), and the primary endpoint was changed from the original protocol to publishing. A study from 2019 comparing surgical practice variation and clinical outcomes in Norway, Sweden and Denmark found similar indications for surgery but significant differences in the use of fusion surgery (48). Nevertheless, outcomes after surgery were similar in all three countries.

What is degenerative cervical myelopathy?

Degenerative cervical myelopathy (DCM) is a progressive spine disorder and the most common cause of spinal cord impairment (11, 49-51). Degenerative changes in the cervical spine such as disk herniation, ligament hypertrophy or ossification, and osteophyte formation may lead to compression and dysfunction of the spinal cord (11, 52). The degenerative changes that lead to compression in the neck are often called spondylosis. The prevalence of spondylosis increase with age, and DCM is therefore uncommon before the age of 40 (53). The epidemiology of DCM is poorly understood, and exact numbers of prevalence or incidence are not known. The prevalence of surgically treated DCM in Europe has been estimated between 1.6 to 4.7 per 100,000 inhabitants (54, 55).

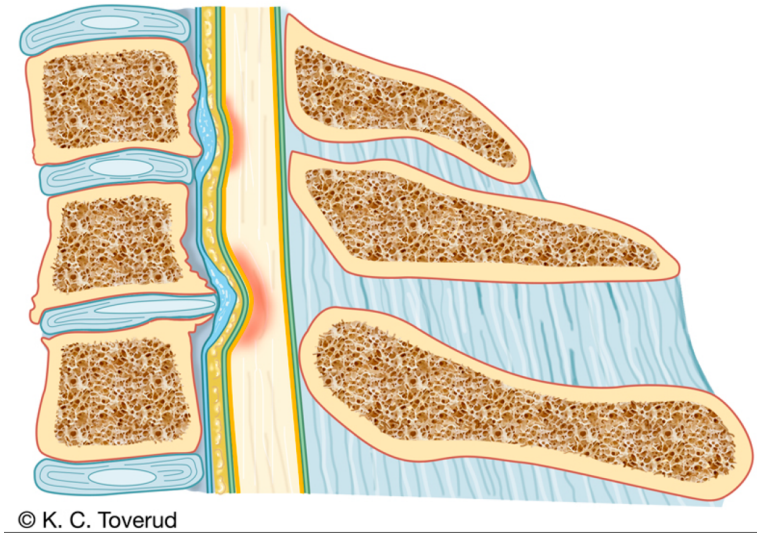

Figure 5. Degenerative changes in the cervical spine may lead to compression of the spinal cord. Reproduced with permission from K. C. Toverud

Clinical features of DCM

Symptoms of DCM include pain and stiffness in the neck, pain and numbness in limbs, poor coordination, imbalance, gait problems, loss of dexterity and incontinence, and shock-like paresthesias with neck flexion (Lhermitte sign) (53, 56, 57).

The symptoms of DCM are non-specific and subtle and overlap with other neurological conditions, which make diagnosing the condition early a challenge. It is not uncommon for DCM to be misinterpreted as a peripheral nerve condition, such as carpal tunnel syndrome (57). Lack of awareness and incomplete neurological assessment can also delay diagnosis, (58) which may increase patients´ risk of developing life-long disability and impaired quality of life (59, 60).

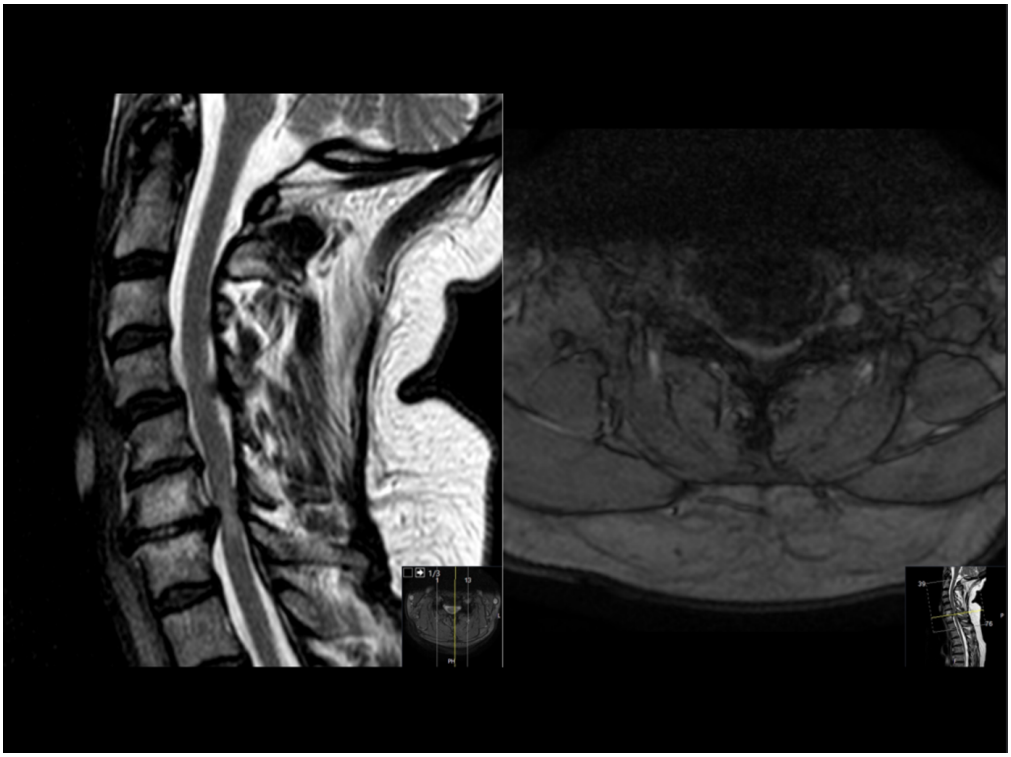

Figure 6. T2-weighted sagittal and axial MR images of a patient with severe degenerative cervical myelopathy due to disc herniation, ligament hypertrophy, and osteophyte formation at the C6/C7 level. On the sagittal images, one can see intramedullary signal changes. (Images provided by Prof. Sasha Gulati).

Treatment of DCM

International guidelines from AOSpine (52, 61) advise that all patients with DCM should be assessed by a surgeon specializing in the field. It is important to refer patients with suspected DCM promptly to MRI and a specialist for consideration of decompressive surgery, as delayed diagnosis and treatment can lead to unnecessary residual symptoms and worsening of disability. For non-myelopathic patients without radiculopathy and only radiological evidence of cervical cord compression, prophylactic surgery is not recommended (52, 53). These patients should be followed clinically if feasible and counseled as to potential risks of progression and advised to seek medical attention if symptoms should develop. Regular follow-up and help with pain management might be offered if patients have a mild, stable DCM. Surgery is recommended in patients with moderate or severe DCM, and in patients who have experienced progression of symptoms (52).

Methodological considerations

Study population

Data were collected through the Norwegian Registry for Spine Surgery (NORspine) and the Norwegian Labour and Welfare Administration (NAV).

NORspine:

NORspine is a comprehensive nationwide registry for quality control and research (62). It provides data on demographics, lifestyle, comorbidity, diagnoses, clinical and radiological findings, surgical procedures, and complications, as well as PROMs before and after spinal surgery (63, 64). All patients in all four articles are included in NORspine, and all centers for spine surgery in Norway currently report to NORspine. Participation in NORspine by either providers or patients is not mandated, nor is participation required as a necessary condition for a patient to gain access to health care or for a provider to be eligible for payment for the health care service. On admission for surgery, the patients completed a self-administered questionnaire, which included questions about demographics and personal characteristics in addition to patient reported outcome measures (PROMs). Using a standard registration form, surgeons recorded data on diagnosis, the severity of the diagnosis, comorbidity, American Society of Anesthesiologists grade, image findings, and surgical procedure. The NORspine registry distributed self-administered questionnaires to the patients by mail three and 12 months after surgery. Non-responders received one reminder with a new copy of the questionnaire. Surgeons provided the following data on perioperative complications: unintentional durotomy, nerve root injury, wrong level of surgery, misplacement of implant, intraoperative hemorrhage requiring blood replacement, respiratory complications, anaphylactic reaction, spinal cord injury, esophageal injury, major vessel injury, cardiovascular complications, and other nerve injuries. Patients reported the following complications if occurring within three months: wound infection, urinary tract infection, pneumonia, pulmonary embolism, deep vein thrombosis, dysphagia, dysphonia, and new-onset arm or leg weakness.

Norwegian Labour and Welfare Administration (NAV)

Norway has a comprehensive national insurance scheme administered by the Norwegian Labour and Welfare Service (NAV). Economic loss due to sickness and injury is generously compensated. Medical benefits issued by NAV are summarized as follows:

- Sickness benefit (temporary and short-term: partial or full): Every member of the society who has worked in Norway continuously for six weeks is entitled to a sickness benefit for the first 12 months of sick leave. This compensates previous salary with 100% coverage, with some limitations regarding size of the salary.

- Work assessment allowance (temporary and long-term: partial or full): Persons who cannot resume work after this period and are under ongoing medical treatment or with a possibility of improving may apply for a benefit termed work assessment allowance for the next 36 months. This compensates on average about 66% of the income. In addition, persons may be entitled to work assessment allowance without working experience if their ability to work is impaired due to illness or injury (e.g., students, handicapped, refugees with health problems). Sickness benefits and work assessment allowance are mutually exclusive.

- Disability benefit: Disability benefits may be warranted for those permanently disabled to work, either partially or fully. Patients with partial disability benefits are considered actively working, albeit with a reduced work capacity.

Ethical approval

The regional committee for medical research in Central-Norway (2016/840) approved all studies, and all participants provided written informed consent.

User involvement

A member from The Norwegian Back Pain Association reviewed the study protocols and provided feedback concerning the study designs.

Outcome measures

Oswestry Disability Index

The Oswestry Disability Index (ODI) was first published in 1980, and has since emerged as one of the most recommended PROMs for spinal disorders (65). It is one of the recommended standardized PROMs in research on low back pain (66), and has been widely used in different studies and settings (67-71). It contains ten questions on the limitations of activities of daily living, each rated on a scale of 0 to 5 points. The points are summarized and converted into a percentage score from 0 to 100, with a lower score indicating less severe pain and disability. Patients are asked to score questions regarding pain intensity, ability to care for oneself, lifting, ability to walk, sit and stand, social life, sexual function, ability to travel, and quality of sleep (72). Item no. 8, used as our primary outcome measure in paper 3, contains the following response alternatives: My sex life is normal and causes no extra pain (0p), my sex life is normal but causes some extra pain (1p), my sex life is nearly normal but causes some extra pain (2p), my sex life is severely restricted by pain (3p), my sex life is nearly absent because of pain (4p), pain prevents any sex life at all (5p).

Pros and cons

ODI was developed to measure disability in patients with low back pain (65), and multiple studies has examined its validity. A study from 1997 comparing replies in version 2.0 of the ODI to actual patient behavior shows that it correlates well for sitting and walking, but less so for lifting (73). A study examining the Norwegian validated version of ODI 2.0 concludes that its validity in Norwegian is sufficient (74). A consequence of the popularity and widespread use of the ODI is that it exists in many different versions, and in many different languages (65). Some versions exist where entire sections (i.e. section 8 – the questions on sexual activity) has been left out (75, 76). Other versions scores remaining sections from 1-6 instead of 0-5 (77). This makes direct comparison between studies and countries a challenge, as it is sometimes hard to establish exactly which version of the ODI that has been used. Translation of the original English version of the ODI should be validated, which is not always the case (65, 74). Change in ODI can be reported as a raw score, change in score from baseline to follow-up, or as percentage change from baseline to follow-up. The minimal important clinical difference for mean change in ODI score is calculated to 20 points (78). A recent study comparing these three outcomes suggest that ODI raw score and ODI percentage

change were more accurate measures, while also underlining the importance of taking baseline ODI scores into account when interpreting change in ODI (79).

EuroQol-5D

The EQ-5D is a generic health-related quality of life (HRQL) instrument. It was originally designed for comparing therapeutic effects in different diseases, and for cost utility analyses (80). It was designed to be self-administered, short enough to be used together with other measures, and with extensive cultural and language evaluations (80, 81). Five dimensions are measured: Self-care, mobility, anxiety/depression, pain, and activities of daily life. Each dimension is described by three possible answers: no, mild to moderate and severe. An index value for health status is generated for each patient. Scores range from -0.6 to 1, where 1 corresponds to perfect health. Effect size estimations were used to evaluate the magnitude of changes.(82) EQ-5D also contains a vertical visual analog scale (EQ-VAS), ranging from 0 to 100 (lower scores indicate poorer health).

Pros and cons

The EQ-5D is brief, efficient for the investigator to administer and for the patient to complete, and highly acceptable to both investigators and respondents (83). Being a generic health-related Quality of Life (HRQL) instrument, the EQ-5D can be used to compare treatments across different conditions and diseases, and thus aiding decisionmakers in setting priorities and dividing resources (80, 84). Disease-specific HRQL cannot be used to compare outcomes across different conditions. On the other hand, it has been argued that generic questionnaires are less responsive and too general to assess specific conditions (80, 85-87). However, when it comes to low back pain, a study comparing the performance of EQ-5D against the ODI found that the EQ-5D is a valid, reliable and responsive instrument when assessing patients undergoing low-back surgery (80).

Neck Disability Index

The NDI was originally published in Canada in 1991 (88). It is a self-reported questionnaire derived from the ODI. It covers 10 items of disability related to neck-pain, with 6 response categories (0-5) and a total score ranging from 0 to 50. It has been translated and adapted to numerous other languages and cultures since its inception (89-92).

Pros and cons

The NDI is currently the most used and best examined neck-specific PROM (89, 93).
A study from 2012 states that the NDI shows positive results for internal consistency, content validity, structural validity, hypothesis testing and responsiveness, but a negative result for reliability (94) They did, however, recommend NDI over other neck-specific outcome measures, as it is the most researched questionnaire, and with most of its measurement properties being adequate (94).

The European Myelopathy Score

The European Myelopathy Score (EMS) was developed as a European counterpart to the Japanese Orthopedic Association (JOA) score. It rates the 4 major neural systems, the impairment of which contributes to the clinical picture of DCM: (a) the upper motor neuron with signs of spasticity as well as bladder and bowel disturbances; (b) the lower motor neuron with impairment of hand function; (c) the posterior roots with upper limb radicular deficits and paresthesias; and (d) the posterior columns with proprioceptive sensory loss, disturbed coordination, and ataxia (95, 96). It contains 5 subscores, with the total score ranging between 5 and 18. The lower the score, the more severe the deficits. Scores ≥13 were classified as mild DCM and scores between 5 and 12 points were classified as moderate-to-severe DCM (96). There is no consensus of the minimal clinically important change (MCIC) for EMS, but even a small change in severe DCM might be considered important in daily function.

Pros and cons

The EMS was developed when attempts to apply the JOA score to western patients yielded several difficulties. The first criterion on the JOA score rates a patient's ability to eat with chopsticks, a skill that is less relevant and less common among the western population (96). Using this criterion on western patients would rate most patients with impairments in their upper limb function, regardless of the severity of their DCM symptoms. Further, the JOA score does not evaluate all four major neural systems, as the EMS was developed to do. Despite this, a modified version of the JOA score (modified JOA, mJOA) is currently the recommended disease-specific PROM (52). Using only the EMS as an outcome measure might make comparison with new studies a challenge, as they might be using the mJOA as their outcome measure of choice.

The Global Perceived Effect scale

The Global Perceived Effect scale is a tool that simply asks: are you feeling better or worse? It asks patients to rate, on a numerical scale how much their condition has deteriorated or improved since a specific point in time (97).

Pros and cons

The GPE is a single question, which makes it easy to understand for both patients, researchers, and clinicians. Scales of this format is recommended as a core outcome measure in chronic pain research (98), and might serve to bridge the gap between clinical trials and clinical practice (99). The GPE also serves as an "anchor" to test measurement properties of other outcome measures (97, 100). Single item measures are easy and quick to administer compared to larger and more detailed outcome measures. As a single item measure, there has been concerns about the test-retest reliability of the GPE scale, as the reliability of a scale is related to the number of items on that scale (101, 102). It has also been suggested that there are validity issues with the GPE scale. Patients may have difficulty recalling their previous status and might be influenced by their current status when scoring their improvement, especially if the time period from the intervention to the testing increases (97, 103). A study from 2010 found that the test-retest reliability of the GPE scale is good, but that the patients are indeed likely to be influenced by the severity of their symptoms at the time when the test is administered (97). This meant that patients with severe symptoms at the time of testing were more likely to score little improvement, whereas patients with mild symptoms were more likely to score a large improvement.

Numeric rating scale

The NRS is a unidimensional self-report measure that ask patients to quantify their pain intensity by a single, general rating. The most common rating scales ask patients to their pain on a scale of 0-10 with 0 representing no pain and 10 representing the worst pain imaginable or ever experienced by the patient (104).

Pros and cons

The NRS for pain has shown good validity and are frequently used in research on back pain (74). With unidimensional ratings of pain intensity, the researchers must be keenly aware of

exactly what they ask their patients to score. Patients can be asked to score their pain severity (i.e. average pain, most severe pain, least pain), circumstances when their pain is better or worse (pain when resting vs. pain when moving) and pain during a set time frame (current pain vs. pain in the past week or month) (104). All questions relate to pain, but they all yield different information, which is important to be aware of when interpreting the result.

Return to work

Return to work is increasingly used as a functional outcome in clinical studies. This is due to the significant number of work hours lost because of neck- and back-related pathology (15). RTW can be defined differently depending on the research question, the available data and the focus of the researchers. In paper 4, we defined RTW as being at work at a given time postoperatively without a medical income-compensation benefit from NAV.

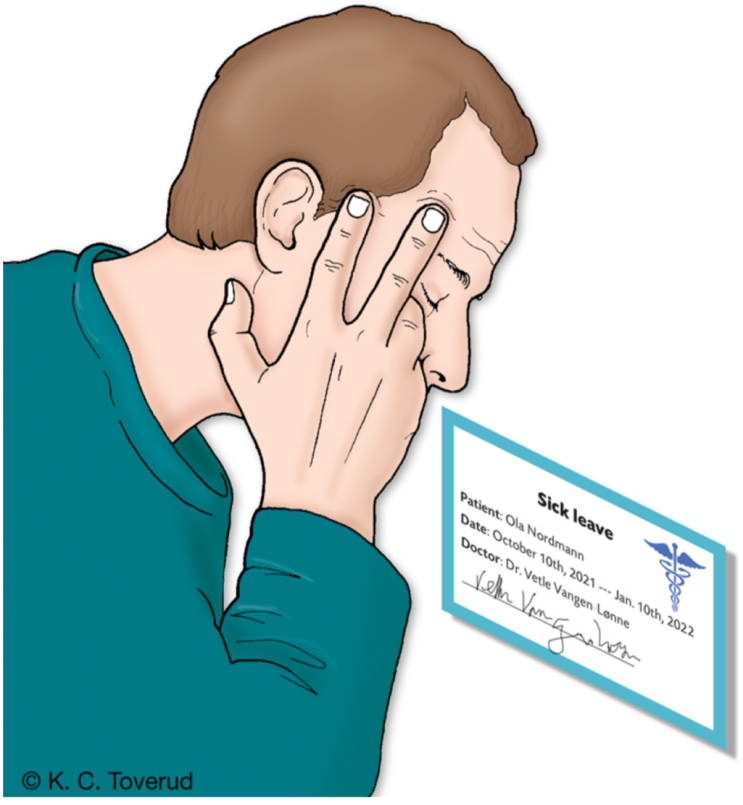

Figure 7. Reproduced with permission from K. C. Toverud.

Pros and cons

As the working population grows older and wishes to stay active, knowledge about RTW is becoming increasingly important. RTW is a practical measure that provides a different perspective than PROMs when exploring whether a treatment is successful. Much of the existing literature on RTW after spine surgery is, however, based on self-reported measures, and therefore have limited external validity (105). RTW is not a standardized measure, and many different definitions of RTW exists (106, 107). As a result, there is extensive variability among different trials that focus on work participation (108). Different cultures and systems for compensation also make direct comparison with studies from other countries a challenge. The lack of consistency and comprehensiveness of RTW as a measure has been described as one of the factors that limits the field of RTW research (109). Fixing the biomedical problem has long been the priority to achieve RTW. A modern understanding of RTW includes a biopsychosocial perspective (110), and keeping in mind that reasons for sick leave are complex and not limited to physical function.

Clinical outcomes

Clinical outcomes in paper 1

In paper 1 we used version 2.0 of the Oswestry Disability Index (ODI), which has been validated in Norwegian, as our primary outcome measure (72, 74). Changes in generic health-related quality of life were measured with the generic EuroQol 5 Dimensions (EQ-5D) between baseline and one-year follow-up (80). The intensity of pain was graded on two separate numerical rating scales (NRS) of 0-10 for back pain and leg pain. We also evaluated the duration of procedures, length of hospital stays, repeated surgery at the index level within 3 months of the initial surgery, and both surgeon and patient-reported complications.

Clinical outcomes in paper 2

The primary outcome in paper 2 was change in item number 8 in the Oswestry disability index (ODI) version 2.0 validated in Norwegian (74). Item no. 8 contains the following response alternatives:

0p My sex life is normal and causes no extra pain
1p My sex life is normal but causes some extra pain
2p My sex life is nearly normal but is very painful
3p My sex life is severely restricted by pain
4p My sex life is nearly absent because of pain
5p Pain prevents any sex life at all

Secondary outcome measures were changes in ODI, EQ-5D, NRS leg- and back pain between baseline and 1-year follow-up.

Clinical outcomes in paper 3

The primary outcome measure in paper 3 was change in the Neck Disability Index (NDI) between baseline and one year. Secondary outcome measures were changes at one year in the European Myelopathy Score (EMS), EQ-5D, and numeric rating scales (NRS) for headache, neck pain, and arm pain. In addition, we report complications occurring within 3 months and patients' perceived benefit of surgery assessed by the Global Perceived Effect scale (GPE) at one year.

Clinical outcomes in paper 4

Our primary outcome in paper 4 was RTW, defined as being at work at a given time postoperatively without a medical income-compensation benefit from NAV. We calculated the grades of received benefits (partial or full sick leave, partial or full work assessment allowance, partial or full disability benefit) for each day from one year before to three years after surgery. The benefits were then grouped into five categories: no medical benefit, partial medical benefit of any kind, full sickness benefit, full work assessment allowance, and full disability benefit. We then examined the data on a group level and explored the trends in sick leave and RTW for our patient group. Secondary outcome measures were changes at one year in the European Myelopathy Score (EMS), NDI, EQ-5D, and numeric rating scales (NRS) for headache, neck pain, and arm pain. In addition, we report complications occurring within 3 months and patients' perceived benefit of surgery assessed by the Global Perceived Effect scale (GPE) at one year.

Statistical analyses

All statistical analyses were performed with SPSS version 26.0 (IBM Corporation), STATA version, 16.1 and 17.0 (StataCorp., College Station, TX), or Software R version 3.6.3. For statistical comparison tests, we defined the significance level as $P \leq 0.05$. Figures were created using SPSS version 26.0 and Microsoft Excel version 16.38 (Microsoft corp.). Mixed linear model analyses were used in paper 1, 2 and 3 for handling missing data. This was in line with previous studies showing that imputations are not needed before performing a mixed model analysis on longitudinal data (111, 112). In the mixed model, patients were not excluded from the analysis if a variable was missing at some, but not all, time points after baseline.

Summary of papers

Paper 1

Microdiscectomy for lumbar disk herniation: a single center observational study. Vetle Vangen-Lønne, Mattis A. Madsbu, Øyvind Salvesen, Øystein Nygaard, Tore K. Solberg, and Sasha Gulati; World Neurosurgery; 2020

Objective

To examine outcomes and complications following first time lumbar microdiscectomy in an everyday clinical setting.

Methods

Prospective data for patients operated at the Department of Neurosurgery, St. Olavs Hospital, Norway, were obtained from the Norwegian Registry for Spine Surgery from May 2007 throughout July 2016. The primary outcome was change in ODI at one year. Secondary endpoints were change in quality of life measured with EQ-5D, back and leg pain measured with NRS, and perioperative complications within three months of surgery.

Results

For all patients (n=1219) enrolled in the study, the mean improvement in ODI at one year was 33.3 points (95% CI, 31.7 to 34.9; P < 0.001). The mean improvement in EQ-5D at one year of 0.52 points (95% CI 0.49 to 0.55; P <0.001) represents a large effect size (Cohens D = 1.6). The mean improvement in back pain and leg pain NRS were 3.9 points (95% CI 3.6 – 4.1, P <0.001) and 5.0 points (95% CI 4.8 – 5.2, P <0.001), respectively. There were 18 surgical complications in a total of 1219 patients, and 63 medical complications in a total of 846 patients. The most common complication was micturition problems at three months following surgery (n=25, 2.1%). In a multivariable analysis, ODI 21-40 (HR 14.5, 95% CI 1.1 to 27.9, P = 0.035), ODI 41-60 (HR 27.5, CI 13.4 to 41.7, P < 0.001), ODI 61-80 (HR 47.4, CI 33.4 to 61.4, P < 0.001) and ODI > 81 (HR 66.7, CI 51.1 to 82.2, P < 0.001) were identified as positive predictors for ODI improvement at one year, whereas age ≥ 65 (HR -0.9, 95% CI -0.3 to -1.5, P = 0.004) was identified as a negative predictor for ODI improvement.

Conclusions

Microdiscectomy for lumbar disc herniation is an effective and safe treatment.

Paper 2

Pain During Sex Before and After Decompressive Surgery for Lumbar Spinal Stenosis: A Multicenter Observational Study. Siril T. Holmberg MS*, Vetle Vangen-Lønne*, Agnete M. Gulati, Øystein P. Nygaard, Tore K. Solberg, Øyvind O. Salvesen, and Sasha Gulati; Spine; 2021

Objective

The aim of this study was to evaluate changes in pain during sexual activity after surgery for lumbar spinal stenosis (LSS).

Methods

Data were retrieved from the Norwegian Registry for Spine Surgery. The primary outcome was change in pain during sexual activity at one year, assessed by item number eight of the Oswestry disability index (ODI) questionnaire. Secondary outcome measures included ODI, EuroQol-5D (EQ-5D), and numeric rating scale (NRS) scores for back and leg pain.

Results

Among the 12954 patients included, 9908 (76.5%) completed one-year follow-up. At baseline 9579 patients (73.9%) provided information about pain during sexual activity, whereas 7424 (74.9%) among those with complete follow-up completed this item. Preoperatively 2528/9579 patients (26.4%) reported a normal sex-life without pain compared to 4294/7424 patients (57.8%) at one year. Preoperatively 1007 (10.5%) patients reported that pain prevented any sex-life, compared to 393 patients (5.3%) at one year. At baseline 7051 of 9579 patients (73.6%) reported that sexual activity caused pain, and among these 3145 of 4768 responders (66%) reported an improvement at one year. A multivariable regression analysis showed that having a life partner, college education, and working until time of surgery were predictors of improvement in pain during sexual activity. Current tobacco smoking, pain duration >12 months, previous spine surgery, and complications occurring within three months were negative predictors.

Conclusion

This study clearly demonstrates that a large proportion of patients undergoing surgery for LSS experienced an improvement in pain during sexual activity at one year.

Paper 3

Surgery for degenerative cervical myelopathy: A nationwide registry-based observational study with patient reported outcomes. Sasha Gulati, Vetle Vangen-Lønne, Øystein P. Nygaard, Agnete M. Gulati, Tommy A. Hammer, Tonje O. Johansen, Wilco C. Peul, Øyvind O. Salvesen, and Tore K. Solberg; Neurosurgery; 2021

Objective

To investigate clinical outcomes in patients undergoing decompressive surgery for degenerative cervical myelopathy (DCM).

Methods: Nationwide prospective data obtained from the Norwegian Registry for Spine Surgery. The primary outcome was change in the Neck disability index (NDI) one year after surgery. Secondary endpoints were the European Myelopathy Score (EMS), quality of life (EuroQoL EQ-5D), numeric rating scales (NRS) for headache, neck pain, and arm pain, complications, and perceived benefit of surgery assessed by the Global Perceived Effect scale (GPE).

Results

We included 905 patients operated between January 2012 to June 2018. There were significant improvements in all patient reported outcomes (PROMs) including NDI (mean -10.0, 95% CI -11.5 to -8.4, $p<0.001$), EMS (mean 1.0, 95% CI 0.8 to 1.1, $p<0.001$), EQ-5D index score (mean 0.16, 95% CI 0.13 to 0.19, $p<0.001$), EQ-5D visual analogue scale (mean 13.8, 95% CI 11.7 to 15.9, $p<0.001$), headache NRS (mean -1.1, 95% CI -1.4 to -0.8, $p<0.001$), neck pain NRS (mean -1.8, 95% CI -2.0 to -1.5, $p<0.001$), and arm pain NRS (mean -1.7, 95% CI -1.9 to -1.4, $p<0.001$). According to GPE assessments, an improvement was reported by 496 out of 697 patients (71.2%). There were significant improvements in all PROMs for both mild and moderate-to-severe DCM. Mixed linear model analyses showed similar results for all PROMs. In total, 251 patients (27.7%) experienced complications/adverse effects within three months of surgery.

Conclusion

Surgery for DCM is associated with significant and clinically meaningful improvement across a wide range of PROMs at one year.

Paper 4

Return to work after surgery for degenerative cervical myelopathy: A nationwide registry-based observational study. Vetle Vangen Lønne, Sozaburo Hara, Sasha Gulati, Lene Aasdahl, Øyvind O. Salvesen, Øystein P. Nygaard, Tore K. Solberg, and Karen Walseth Hara; Acta Neurochirurgica; 2023 (In press)

Objective

Few studies of high quality exist on return to work (RTW) rate after surgery for degenerative cervical myelopathy (DCM). This study aims to examine the RTW rate in patients undergoing surgery for DCM.

Methods

Nationwide prospectively collected data were obtained from the Norwegian Registry for Spine surgery and the Norwegian Labour and Welfare Administration. The primary outcome was return to work, defined as being at work at a given time postoperatively without any medical income-compensation benefits. Secondary endpoints included the Neck Disability Index (NDI) and quality of life measured by Euroqol-5D (EQ-5D).

Results

Among 439 patients operated for DCM between 2012 and 2018, 20% of the patients received a medical income-compensation benefit one year before surgery. By 12 months after surgery, 65% had returned to work. By 36 months, 75% had returned to work. Patients that returned to work were more likely to be non-smokers and to have a college education. They had less comorbidity, more were employed, and more were without benefit one-year pre-surgery. Average days of sick leave in the year before surgery were significantly less in the RTW group, and they had a significantly lower baseline NDI and EQ-5D.

Conclusion

At 12 months following surgery, 65% had returned to work. At the end of the 36-month follow-up period, 75% had returned to work, 5% less than the working percentage in the beginning of the follow-up period. This study demonstrates that a large percentage of patients return to work after surgical treatment for DCM.

Discussion

In paper 1, we found that lumbar microdiscectomy is an effective and safe treatment for patients with symptomatic LDH. Paper 2 found that a large proportion of patients that undergo surgery for LSS experience an improvement in pain during sexual activity at one year. Paper 3 found that surgery for DCM is associated with significant improvement across a wide range of PROMs at one year. Surgical treatment cannot only arrest further progression of myelopathy, but also improve functional status, neurological outcomes, and quality of life. Paper 4 demonstrated that a large percentage of patients return to work after surgical treatment for DCM.

Outcomes following surgery for LDH:

Our study examining outcome after microdiscectomy for LDH adds to an increasing amount of evidence that lumbar microdiscectomy is an effective and safe treatment for patients with symptomatic LDH, although there is still room for improvements. Among the patients with complete follow-up, 69% experienced no or minimal disability at one year (i.e. an ODI score between zero and twenty). In our study, 26 (3.1%) patients experienced a clinically significant deterioration in ODI one year after surgery.

In line with previous studies, increasing ODI score at baseline was identified as the most important positive predictor for ODI improvement (113-115). Obesity has previously been reported as a negative predictor in terms of improvement following spine surgery (113, 116, 117). In the SPORT study, BMI <30 was associated with greater improvement in ODI after surgery. Obese patients were also found to have a significantly worse outcome after surgery than non-obese patients (118). We were unable to confirm high BMI as a negative predictor for ODI improvement. Moreover, a recent study from the NORspine registry demonstrated similar PROMs for obese and non-obese patients after surgery for LDH, although obese patients (BMI ≥ 30) had slightly longer hospital stays and increased risk of minor complications.

Age above 65 was also identified as a negative predictor in our study population. However, in a recent NORspine study it was clearly shown that patients above 65 years of age experienced similar improvement as younger patients, but with a slightly elevated risk of minor

complications and longer hospital stays (115). The hazard ratio for age above 65 was also notably weak, indicating this as a weak negative predictor in our study. Smoking, female sex, and ASA grade >2 were not established as negative predictors in our study. These predictors have, however, been identified as negative predictors in similar studies. (116, 117). Given that this is a single-center study, our sample size is limited compared to many of these studies, which might explain why we were not able to establish smoking, female sex, and ASA >2 as negative predictors.

Although minimally invasive procedures such as lumbar microdiscectomy and microdecompression may not impact long-term outcomes compared to open procedures, the benefits in terms of rapid recovery following surgery, early mobilization, and shorter hospital stays are obvious (42, 119). Microdiscectomy remains the gold standard for surgical treatment of LDH, although new methods of treatment for lumbar disc herniation are constantly being developed. Results from randomized double-blinded study with 328 patients concluded that conventional diskectomy were as effective as tubular diskectomy, and suggested that tubular discectomy resulted in more leg- and backpain post-surgery, although the difference was not statistically significant (23). A meta-analysis investigating the effectiveness of microdiscectomy vs other surgical techniques when treating LDH suggested that percutaneous endoscopic lumbar discectomy had a lower risk of overall complications (120). Further, in selected patients without serious comorbidity, hospital discharge on the day of surgery appears to be safe (121). A recent multicenter, randomized controlled trial comparing percutaneous transforaminal endoscopic discectomy (PTED) with conventional open microdiscectomy found PTED to be non-inferior in reduction of leg pain after surgery, and that PTED might serve as an equal option to microdiscectomy (24).

A subject not touched upon is surgical management of LDH versus a conservative approach. It is suggested that radiculopathy resolves on its own within two weeks in one-third of the patients, and within three months for three-quarter of the patients (20, 22). No single form of physical therapy or has proven to be superior to others, although it seems unlikely that physical therapy is harmful in any way (20). The advice of bed rest for radiculopathy has no proven effect and is largely abandoned today (122). Conservative treatment strategies often include pain management through oral medication and physical activity, the latter being self-limiting depending on the amount of discomfort it causes for the patient. The main advantage of surgery is that it yields earlier relief of the pain. If one does not recover from radiculopathy

within four to six weeks, a surgical approach is usually considered. A single center study from 2020 randomized 376 patients with radiculopathy persisting for four to twelve months to either surgery or conservative care. Surgery was found to be superior in terms of pain relief at six months (123). Similar results were found in the SPORT-study, which recruited patients with a shorter duration of radiculopathy (124).

In total, 1.5% of the patients in study 1 experienced perioperative complications and 5.2% of the patients who completed the three months follow-up reported complications following hospital discharge. A meta-analysis published in 2020 reported mean complication rates were reported to be 6.4% for perioperative complications and 10.2% for postoperative complications. The pooled mean complication rate was reported as 16.8%. The perioperative complication rates ranging from 0 to 9.4%, and total complication rates ranged from 4.5% to 25% (120). The included studies had substantially smaller sample sizes than our study, ranging from 14 to 500 patients, and mean values were reported as unweighted averages. Microdiscectomy remains a safe and effective treatment for lumbar disc herniation

Change in sexual function after surgery for LSS

Our study examining sexual function before and after surgery for LSS demonstrates that a large proportion of patients experience an improvement in pain during sexual activity at 1 year after surgery. Among the patients who reported pain during sexual activity prior to surgery, approximately 66% experienced an improvement at 1 year measured with item no. 8 in the Norwegian validated version of ODI 2.0. Further, we found a large reduction in the percentage of patients who reported that pain prevented any sexual activity at all at the end of follow-up. We also found clinically important improvements in all PROMs at 1 year, and few serious complications. This study demonstrates that elderly patients can participate in surgical outcomes research also for a sensitive and sometimes taboo-associated topic such as sexual function.

The baseline factors of having a life partner, college education, and working until the time of surgery were associated with improvement in pain during sexual activity.
Higher preoperative ODI score and increasing preoperative back pain related disability have also been identified as strong predictors for overall improvement in other studies (125-128). Duration of pain exceeding one year prior to surgery for LSS seems to be a negative predictor for improvement in pain during sexual activity, adding to the evidence that chronicity is

associated with unfavorable outcomes and that timing of surgery might be important (129-133). Complications within three months after surgery and previous spine surgery were also found to be negative predictors. Previous surgery at the same or different lumbar level has earlier been identified as a predictor for deterioration in patient-reported pain and disability in patients with LSS (128), however these predictors did not have any influence on improvement in pain during sex one year after surgery. Among the subgroup of patients with cauda equina syndrome, a univariable analysis did not indicate any impact on the prognosis of improvement in pain during sex one year after surgery. Tobacco smoking was also identified as a negative predictor, supporting the existing evidence that smoking is associated with inferior outcomes following surgery (134). Previous studies have shown that tobacco smokers are less likely to achieve clinically important improvement measured with several different PROMs following surgery for degenerative lumbar spine conditions and more likely to experience postoperative complications (116, 127, 134). However, smoking may be a marker for other characteristics responsible for the association that are unadjusted for in the regression model, such as anxiety and depression. Further, it is known that patient reported quality of life is lower among smokers in a general population, which may affect their measured outcomes (135).

In a recent study on patients undergoing surgery for lumbar disc hernation, we found that 65.1% of patients reported a normal sex-life without pain at one year compared to 57.8% in the present study(136). Patients operated for LSS are typically older than those operated for lumbar disc herniation, and this might in part explain the observed difference. There is a wide range of factors that may impact sexual health with age, including comorbidity that can limit physical activity and contribute to pain during sexual activity (137, 138). Moreover, elderly patients are more likely to experience complications following surgery, and this may also influence the outcome. Still, there is solid evidence showing that both lumbar microdiscectomy and decompressive surgery for lumbar spinal stenosis can substantially improve functional status and quality of life in selected elderly patients including those with comorbidity (112, 125, 139).

Previous studies on sexual function in patients undergoing spine surgery have focused on fusion procedures for chronic low back pain (140, 141). With the role of fusion surgery for LSS coming under increasing scrutiny because of increased costs, risk of complications, and questionable added value compared to decompressive surgery alone (35, 142-145), it is

important to assess changes in sexual function following common and less invasive spine procedures such as microsurgical decompression and laminectomy.

We found a strong correlation between pain during sexual activity at one year and patients' perceived overall health status (paper 2, Figure 2). A recent study involving US adults showed that sexual health is in fact a highly important aspect in quality of life (146). Sexual health and function are of course multifaceted and not only limited to pain during sexual activity as we measured in our study.

Outcome following surgery for DCM

Our nationwide study shows that surgery for DCM is associated with significant and clinically relevant improvements across the whole range of PROMs at one year. Favorable outcomes were observed for both mild and moderate-to-severe DCM, with the largest effects observed in the latter more severely disabled group. Our study adds to the evidence from previous observational studies that surgical treatment cannot only arrest further progression of myelopathy, but also improve functional status, neurological outcomes, and quality of life. (147-149) Although >70% of responders perceived a benefit from surgery, a substantial placebo effect cannot be ruled out following such complex treatment (150). Risk associated with surgery for DCM is not negligible and should be communicated to patients before surgery. Patients should also be informed that complete resolution of symptoms is unlikely following surgery. Life-threatening complications and early reoperations are fortunately rare. In our study, 27.7% of responders experienced adverse effects or complications within three months and 15.8% perceived a clinical worsening.

There are no randomized trials comparing surgical and non-surgical management of patients with moderate-to-severe DCM. In a recent trial, adjuvant treatment perioperatively with riluzole (Aventis Pharma) did not improve functional recovery beyond decompressive surgery in patients with moderate-to-severe DCM (151). Until recently there has been limited evidence to guide clinical management of mild DCM (52). In a large and recent prospective study on mild DCM with two years follow-up, significant gains in a wide range of PROMs were observed following surgery (152). Two small, randomized trials in patients with mild-to-moderate DCM found no differences in neurologic outcomes at two years between those who received conservative versus surgical treatment (153, 154). Still, most patients in our study had mild DCM and significant improvements were observed for all PROMs. However, these

improvements were smaller compared to patients with moderate-to-severe DCM. Although we have detailed clinical data at the time of surgery, little is known about the dynamics of symptoms, disability, and neurological functioning preceding surgery. A recent study showed that machine learning algorithms might become useful to identify patients with mild DCM that will benefit from surgery (155). The phenotype of mild DCM needs to be acknowledged, and a recent study reported that neck pain, motor symptoms, and female gender were associated with greater impairment of quality of life and greater response to surgery (156). The optimal timing for surgical treatment for mild DCM remains uncertain. Additional observational studies or clinical trials should be encouraged to clarify the natural course of the disease and evaluate surgery and structured rehabilitation for patients with mild DCM.

A hot topic within surgical management of DCM is whether to choose an anterior or posterior surgical approach. Both approaches have their pros and cons, and both are capable of yielding good results (157). A propensity-score matched study from 2019 performed on 13 884 patients showed that posterior cervical decompression and fusion (PCDF) were associated with a longer hospital stay, as well as a higher rate of postoperative complications (myocardial infarction, deep vein thrombosis, neurological complication, hardware-related complications, wound infection, cerebrospinal fluid leak) (158). Anterior cervical decompression and fusion (ACDF) were associated with an increased risk of postoperative hematoma, hoarseness, and dysphagia. A randomized clinical trial from 2021 comparing clinical outcomes in ventral (anterior) vs dorsal (posterior) approach showed no clinically significant difference at one year after surgery between the two approaches (159). In Norway, ACDF and posterior laminectomy without fusion are the two most common surgical approaches. Norwegian surgeons are in general more hesitant to perform posterior fusion surgery for this patient group, in contrast to American spine surgeons. This makes direct comparison with American studies a challenge. The efficacy and effectiveness of different surgical treatments is an interesting and much-debated topic (160)(149, 161)(162). Unfortunately, further examination into this subject was beyond the scope of paper 3 as we did not have detailed enough information to compare the effectiveness of different surgical procedures.

Return to work after surgery for DCM

This study examined patterns for returning to work after surgery for DCM as well as predictors for achieving RTW. In total, 50% of the patients returned to work after 5 months, and by 12 months 65% of the patients had returned to work. At the end of the follow-up period at 36 months, 75% had returned to work, 5% less than the working percentage in the beginning of the follow-up period.

In addition to pain, physical disability, and health related quality of life, RTW is increasingly acknowledged as a core outcome measure in spine surgery (15, 163). Recent studies have shown considerable improved physical function after surgery for DCM which may provide new opportunities to patients who were previously unable to work (61, 164, 165). Although surgery for DCM results in statistical and clinical meaningful improvement, this is not a guarantee for returning to work. Even so, larger percentage of patients operated on for DCM achieved RTW than in a similar study examining RTW after surgery for cervical radiculopathy (105).

To our knowledge, this is the largest study to date examining RTW after surgery for DCM. Direct comparison with other studies examining RTW-rate after surgery for DCM is challenging (15, 166, 167). Differences in cohort selections, welfare systems, authors definition of RTW and health care policies in individual countries contributes to this. A study examining RTW for 102 non-retired patients found that 58.8% of the total population achieved RTW at 1 year, while 75.9% of the population who were working pre-surgery achieved RTW (166). Like our study, working pre-surgery was associated with RTW. This study did, however, include all patient who were considered "non-retired", and had a smaller sample size than our study. A study from 2018 examining RTW after cervical spine surgery found that 82% achieved RTW after three months (15). They found that patients who achieved RTW were more likely to have higher education, 100% employment, and lower NDI at baseline and three months. However, this study included patients operated for both cervical myelopathy and radiculopathy and included only patients who were working pre-surgery. A study from 2020 examined RTW, among other outcomes, in 219 patients operated for cervical myelopathy (167). They found that 96% of patients with mild DCM 100% of patients with moderate DCM and 84% of

patients with severe DCM achieved RTW. They did not, however, define RTW clearly in their study, and only reported it as a secondary outcome.

College education, female sex, and less than 90 days of sick leave in the year before surgery, as well as NDI and EQ-5D at 12 months, had the strongest effect on RTW in this study. A study from 2021 examining work ability measured with the Work Ability Index score (WAI) after surgery for cervical radiculopathy found that thoughts of being able to work within the next six months, NDI score and work-related neck load explained 59% of the variance in WAI after 2 years of follow-up (168). A study from 2021 identified occupational profile as a predictor for RTW after surgery for DCM, with manual laborers having the lowest RTW rate (169). We did not have access to specific occupation in this study, and more research is needed to establish the relationship between occupational factors and RTW rate after surgery for DCM. A study from 2013 examining prognostic factors for RTW in patients with sciatica found that less sciatica bothersomeness at baseline and duration less than 3 months predicted faster RTW (170). Less than 90 days of sick leave in the year before surgery were associated with higher chances of RTW in our study, indicating that both manageable symptoms and a shorter symptom duration before surgery are associated with achieved RTW.

In addition to being less likely to have a college education and employment, the patients that did not return to work were more likely to receive some sort of benefit one year pre-surgery and had more comorbidity overall. This group might benefit from counseling from primary care providers, employers, or social insurance supervisors. Identifying individuals at risk for not returning to work remains a challenge for all health care providers, and more research is required to help as many as possible return to work after surgery.

Strengths and limitations

Our studies are strengthened by a large number of patients, high external validity, prospective data collection, and widely applied and validated outcome measures (72, 74, 80, 111, 171). Data from NAV have little missing information and using their registry data instead of self-reported data eliminates the possibility of recall bias when examining RTW.

One of the main limitations for all studies is the relatively high loss to follow-up at one year for multiple primary outcome measures. Missing data in spine registries remain a concern and may introduce bias (172). It seems that elderly NORspine participants >65 years are more likely to complete one-year follow-up (115). However, two NORspine study show no difference in outcomes between responders and non-responders (173, 174)

Paper 1:

Our study on LDH set out to examine outcomes after only one year, and a longer follow-up period could provide more information on long-term outcomes for lumbar microdiscectomy. Other studies examining outcomes after surgery for lumbar disc herniation have managed longer follow-up times (175-177). A study examining long-term results in the SPORT study concluded that improvement after surgery seemed to peak at six months post-treatment, and persisted through an eight-year follow-up period (175). We chose ODI mean change as our primary outcome measure in this study, although raw scores were also reported. A study from 2020 suggest that ODI raw score and ODI percentage change are more accurate measures, which may warrant increasing use of these measures as primary outcomes in the future (79). We only included patients who received operative treatment. We did not have a conservative treatment group to compare with, and there is, unfortunately, no information in the NORspine registry regarding conservative management before surgery. Future studies comparing surgical to well-defined non-surgical interventions are still warranted.

Paper 2:

The main limitations of this study were the inability to capture other aspects of sexual health and function such as enjoyment, desire, genital sensation, ability to achieve orgasm and ejaculation. It is therefore especially difficult to assess changes in sexual function in the subgroup of patients with cauda equina syndrome. Pain with sex life was determined using one question from the ODI, and the validity of the study might be enriched by using a survey

that more comprehensively addresses sexual function. Further, we do not know whether patients who reported that pain did not limit sexual function actually resumed an active sexual life or were limited by other factors. Degenerative spondylosis is usually a continuous process and although we found favorable outcomes at one year, a longer follow-up may be warranted to detect the effect of surgery on progression of spondylosis.

Paper 3:

In this study, NDI was our primary outcome. The modified Japanese Orthopedic Association (mJOA) scale is currently the recommended disease-specific PROM for DCM. The mJOA is not included in NORspine and may perhaps make it more challenging to compare our results with other studies. This is to some extent alleviated by the use of the NDI and EQ-5D which are included in several recent studies on DCM. NORspine started including patients several years before the current practice guidelines were published (52). Solely assessing the myelopathy is likely insufficient to fully understand clinical outcome in its totality, and combinations of questionnaires are recommended (156, 178, 179). A study comparing seven different scales, including mJOA and EMS, found that they all detected significant improvement following surgery (180). Still, each scale had differing qualities of reliability, validity, and responsiveness. Lack of randomization is an obvious limitation. Follow-up exceeding one year may be warranted to detect the effect of surgery on the progression of symptoms. Some patients may have received physical therapy, but our study cannot assess the impact of such interventions.

Paper 4:

Our outcome in paper 4 is based on the medical benefit payment records provided by NAV, and a reduction in benefits is interpreted as an indirect measure of RTW. This method is commonly used in the RTW literature and is likely sufficient in our population (105, 181, 182). Second, we lack data on social factors, details on occupation, and a detailed psychological profile of each patient. Such information was not available in the data provided to us by NORspine and NAV, but we recommend that they are included in future studies. Third, missing data for PROMs in registry-based studies are a concern. We found no difference in RTW ratios between responders and non-responders in our study, which is consistent with previous studies indicating that non-responders do not bias evaluation of PROMs (174, 183, 184). Even so, we do not know the exact reasons for non-respondence, and

our results must be interpreted with this in mind. Fourth, all patients included in our study were selected for surgery and might not be representative for the total population of DCM patients. NORspine only includes patients that actually undergo surgery, and unfortunately, we do not have any information about patients who did not receive surgical treatment. Patient characteristics, indications, surgical strategies, and medical benefit systems may vary between countries, and results from our study might consequently differ from other clinical settings.

Future research

RTW remains a field with much yet undone. Our research group are currently examining RTW rates after surgery for LSS and LDH, which may yield important information for this growing patient group. More knowledge is needed about RTW as an outcome. Increasing RTW after surgical interventions will be increasingly important in the future.

Non-surgical management of LDH and LSS is still a source of much debate. More research is needed on the role of physical therapy for LDH and LSS. Management of patients who do not improve after surgery is also a much-debated topic. Our research group recently published a RCT comparing spinal cord stimulation with placebo and found no significant difference between the two (185). This study has received much international attention, and additional studies are needed.

As stated in this thesis, the optimal timing for surgical treatment for mild DCM remains uncertain. Additional observational studies or clinical trials should be encouraged to clarify the natural course of the disease and evaluate surgery and structured rehabilitation for patients with mild DCM.

Conclusions

- Lumbar microdiscectomy is an effective and safe treatment for patients with symptomatic LDH.

- A large proportion of patients that undergo surgery for LSS experience an improvement in pain during sexual activity at one year. Among the patients who reported pain during sexual activity prior to surgery, approximately 66% experienced an improvement at one year.

- Surgery for DCM is associated with significant improvement across a wide range of PROMs at one year.

- Surgical treatment cannot only arrest further progression of DCM, but also improve functional status, neurological outcomes, and quality of life.

- At 12 months following surgery for DCM, 65% had returned to work. At the end of the 36-month follow-up period, 75% had returned to work, 5 percentage points less than the working percentage in the beginning of the follow-up period.

- A large percentage of patients return to work after surgical treatment for DCM.

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Papers

Paper 1

Microdiscectomy for Lumbar Disc Herniation: A Single-Center Observational Study

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OBJECTIVE: **To examine outcomes and complications following first-time lumbar microdiscectomy.**

METHODS: **Prospective data for patients operated on between May 2007 and July 2016 were obtained from the Norwegian Registry for Spine Surgery. The primary outcome was change in Oswestry Disability Index (ODI) score at 1 year. Secondary endpoints were change in quality of life measured with EuroQol 5 Dimensions, back and leg pain measured with numeric rating scales, and perioperative complications within 3 months of surgery.**

RESULTS: **For all enrolled patients ($N = 1219$) enrolled, mean improvement in ODI at 1 year was 33.3 points (95% confidence interval [CI] 31.7 to 34.9, $P < 0.001$). Mean improvement in EuroQol 5 Dimensions at 1 year of 0.52 point (95% CI 0.49 to 0.55, $P < 0.001$) represents a large effect size (Cohen's $d = 1.6$). Mean improvements in back pain and leg pain numeric rating scales were 3.9 points (95% CI 3.6 to 4.1, $P < 0.001$) and 5.0 points (95% CI 4.8 to 5.2, $P < 0.001$), respectively. There were 18 surgical complications in 1219 patients and 63 medical complications in 846 patients. The most common complication was micturition problems at 3 months following surgery ($n = 25$, 2.1%). In multivariate analysis, ODI scores of 21–40 (hazard ratio [HR] 14.5, 95% CI 1.1 to 27.9, $P = 0.035$), 41–60 (HR 27.5, 95% CI 13.4 to 41.7, $P < 0.001$), 61–80 (HR 47.4, 95% CI 33.4 to 61.4, $P < 0.001$) and >81 (HR 66.7, 95% CI 51.1 to 82.2, $P < 0.001$) were identified as positive predictors for ODI improvement at 1 year, whereas age ≥65 (HR −0.9, 95% CI −0.3 to −1.5, $P = 0.004$) was identified as a negative predictor for ODI improvement.**

CONCLUSIONS: **Microdiscectomy for lumbar disc herniation is an effective and safe treatment.**

INTRODUCTION

Lumbar disc herniation (LDH) is the leading cause of sciatica.[1] If left untreated, most patients with LDH will have a favorable outcome. Surgery is typically offered to patients with persisting pain in the lower back radiating down the legs despite conservative treatment, intractable pain, or acute serious paresis including cauda equina syndrome.[1] For patients who require surgery, lumbar microdiscectomy is the most common surgical procedure.[2] Outcomes following lumbar microdiscectomy have been reported in both randomized trials and large registry-based studies[1–14]; we wanted to investigate outcomes from our own daily clinical practice. The aim of this study was to measure clinical outcomes at 1 year following first-time single-level lumbar microdiscectomy using data from St. Olavs University Hospital, Norway, retrieved through the Norwegian Registry for Spine Surgery (NORspine).

MATERIALS AND METHODS

Study Population

All patients were operated on at the Department of Neurosurgery, St. Olavs University Hospital, Trondheim, Norway. Data were

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

Abbreviations and Acronyms
BMI: Body mass index
CI: Confidence interval
EQ-5D: EuroQol 5 Dimensions
HR: Hazard ratio
LDH: Lumbar disc herniation
NORspine: Norwegian Registry for Spine Surgery
NRS: Numeric rating scale
ODI: Oswestry Disability Index
SPORT: Spine Patient Outcomes Research Trial

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Citation: World Neurosurg. (2020) 137:e577-e583.
https://doi.org/10.1016/j.wneu.2020.02.056

*Journal homepage: **www.journals.elsevier.com/world-neurosurgery***

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

1878-8750/$ - see front matter

prospectively collected through NORspine between May 2007 and July 2016. NORspine is a comprehensive clinical registry for research and quality control,[15] and currently all 40 centers performing lumbar spine surgery in Norway report to NORspine. Approximately 65% of all patients in Norway who undergo lumbar spine surgery are included in NORspine. Participation in NORspine by either providers or patients is not mandated, and participation is not required as a necessary condition for a patient to gain access to health care or for a provider to be eligible for payment for the health care service.

Follow-up time was 1 year from the date of the operation (baseline). A baseline questionnaire was administered to the patients on admission for surgery, which included questions about lifestyle issues and demographics as well as the primary and secondary outcome measures. Information about educational level, tobacco smoking, and body mass index (BMI) was available in NORspine.

During the hospital stay, using a standardized registration form, the surgeon recorded data on the diagnosis, previous lumbar spine surgery, comorbidity, American Society of Anesthesiologists grade, imaging, and surgical approach and procedure. The surgeons provided data on the following possible complications and adverse events to NORspine: intraoperative hemorrhage requiring blood replacement, postoperative hematoma requiring repeat 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: urinary tract infection, wound infection, micturition problems, pneumonia, pulmonary embolism, and deep vein 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 by regular mail. The patients who did not respond received a reminder with a new copy of the questionnaire without any assistance from the surgeon or other staff at the treating hospital.

We included all patients with a definitive diagnosis of symptomatic LDH who underwent a single-level lumbar microdiscectomy between January 2007 and July 2016. All patients were included in NORspine. Patients who had a history of lumbar spine surgery, extraforaminal LDH, or coexisting spinal degenerative spondylolisthesis and/or scoliosis were excluded.

The study was evaluated and approved by the regional committee for medical research 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 primary outcome measure was change of Oswestry Disability Index (ODI) from baseline to 1 year after surgery. NORspine uses version 2.0 of the ODI validated in Norwegian.[16,17] The ODI contains 10 questions on limitations of activities of daily living. Each variable is rated on a scale of 0–5 points, summarized, and converted into a percentage score. Scores range from 0 to 100, with lower scores indicating less severe pain and disability. Patients are asked to score questions regarding pain intensity; ability to care for oneself; lifting; ability to walk, sit, and stand; social life; sexual function; ability to travel; and quality of sleep.[16]

Secondary Outcome Measure

Changes in health-related quality of life were measured with the generic instrument EuroQol 5 Dimensions (EQ-5D) between baseline and 1-year follow-up.[18] The EQ-5D questionnaire evaluates 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 numeric 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. The NRSs for pain and the ODI have shown good validity and are frequently used in research on back pain.[17] We also evaluated the procedure duration, length of hospital stay, repeat surgery at the index level within 3 months of the initial surgery, and both surgeon- and patient-reported complications.

NORspine provided data on complications. In addition, a retrospective review of electronic medical records was performed in all included patients to detect complications not captured by NORspine and to identify causes of early reoperations.

Surgical Procedures

All patients underwent single-level lumbar microdiscectomy. The procedure involves preoperative fluoroscopy for detection of the target level, paramedian or median skin incision of approximately 3 cm, straight or curved opening of the paravertebral muscular fascia, and subperiosteal release of the paravertebral muscles from the spinous process and basal lamina above and occasionally below the target disc level. Self-retaining retractors (typically Caspar retractors) are introduced, and an operating microscope is used for magnification. Following flavectomy and required bony decompression (i.e., arcotomy and/or partial medial facetectomy), the dural sac and nerve root are carefully mobilized medially, and the herniated disc is evacuated. Removal of the disc herniation might involve entering the disc space or just removing a free sequestrated disc fragment (sequestrectomy).

Statistics

All statistical analyses were performed with IBM SPSS Version 24.0 (IBM Corporation, 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. We used the χ^2 test for categorical variables. Baseline and 1-year scores were compared with 1-sample t test. We also performed a mixed linear model analysis owing to missing data. The fixed effect was time (with levels baseline and 1 year), and the covariance structure of the 2 outcomes on each patient was taken as unstructured owing to apparent heterogeneity of variance across time.

A multivariate linear regression model was applied with the difference in ODI score at 1 year as the outcome. The selection of predictors included in the final model was based on their clinical importance and association with the dependent variable.[9,11] The multiple linear regression analysis included variables that might affect clinical outcomes, including age, BMI, sex, preoperative ODI score, smoking, and depression and/or anxiety.[4,6,9-11]

In the final regression model, patients were categorized according to their BMI as normal (<25 kg/m^2, reference value), overweight (25–29.9 kg/m^2), class I obesity (30–34.9 kg/m^2), or

class II/III obesity (>35 kg/m²) (i.e., as dummy variables). Owing to a strong nonlinear relationship between preoperative ODI and the dependent variable, patients were categorized (i.e., as dummy variables) according to the preoperative ODI score: 0–20 (minimal disability, reference value), 21–40 (moderate disability), 41–60 (severe disability), 61–80 (crippled), or 81–100 (bed-bound).[16]

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 analysis on longitudinal data.[19]

RESULTS

Study Population

The study enrolled 1219 patients. The 1-year follow-up with ODI was completed by 852 patients (69.9%). Baseline characteristics, surgical treatments, and comorbidities are summarized in Table 1. The mean patient age at baseline was 46.7 ± 15.0 years, and 42.7% were female.

Primary Outcome

Changes in ODI between baseline and 1 year after surgery are presented in Table 2. There was a significant improvement in the cohort between mean preoperative ODI and mean ODI at the 1-year follow-up (33.3 points; 95% confidence interval [CI], 31.7 to 34.9; $P < 0.001$). We performed a complete case analysis of the group that completed the 1-year follow-up (Figure 1). Among 852 patients with complete 1-year ODI follow-up, 591 (69.4%) had an ODI score of ≤20 at 12 months compared with 85 of 1219 patients (7%) at baseline. Of the patients who completed the 1-year follow-up, 26 (3.1%) experienced a deterioration of ≥8 points in ODI 1 year after surgery. A deterioration of ≥8 points is commonly defined as a clinically significant worsening in ODI between baseline and 1-year follow-up.[11]

Table 1. Demographics

Variable	Value
Age at surgery, years, mean ± SD	46.7 ± 15
Female sex, %	42.7
ASA >2, %	10.3
BMI, kg/m², mean ± SD	26.8 ± 4.4
Obesity, BMI ≥30, %	20.5
College education, %	37.5
Daily tobacco smoking, %	27.4
Preoperative ODI, mean ± SD	48.1 ± 19.7
Preoperative EQ-5D, mean ± SD	0.23 ± 0.36
Preoperative leg pain NRS, mean ± SD	6.6 ± 2.4
Preoperative back pain NRS, mean ± SD	7.1 ± 2.2
Spine level of surgery ($n = 1211$)	
L2-L3	29 (2.4%)
L3-L4	104 (8.6%)
L4-L5	553 (45.7%)
L5-S1	525 (43.4%)

ASA, American Society of Anesthesiologists; BMI, body mass index; ODI, Oswestry Disability Index; EQ-5D, EuroQol 5 Dimensions; NRS, numeric rating scale.

Secondary Outcomes

Changes in EQ-5D, back pain NRS, and leg pain NRS at 1 year are presented in Table 2. There was a significant difference between mean preoperative EQ-5D score and mean EQ-5D score at 1 year (0.52 point, 95% CI 0.55 to 0.49, $P < 0.001$). A large effect size was found for change in EQ-5D at 1 year (Cohen's $d > 0.8$), indicating a large difference between the 2 groups.

The mean difference between the mean baseline value and 1-year value in back pain NRS was 3.9 points (95% CI 3.6 to 4.1, $P < 0.001$). Among patients who completed the follow-up, 74% experienced a clinically significant improvement, defined as improvement of ≥2 points.[20] The mean difference between the mean baseline value and 1-year value in leg pain NRS was 5.0 points (95% CI 4.8 to 5.2, $P < 0.001$); 82.2% of the patients experienced a clinically significant improvement (≥2 points).

Complications are presented in Table 3. Of the 1219 included patients, 18 (1.5%) experienced perioperative complications, with unintentional durotomy as the most common complication (8 cases; 0.7% in total). Of the 846 patients who completed the 3-month follow-up period, 63 (5.2%) experienced postoperative complications following hospital discharge, with micturition problems as the most common complication (2.1%).

Reoperations after the initial procedure were performed in 176 (14.4%) patients, and 57 of the reoperations (4.7%) occurred within 90 days after the initial procedure. Recurrent and residual LDH were the most common causes of reoperations (51/176 cases; 4.2%). Among the 57 patients who underwent a reoperation within 90 days, the reason for repeat surgery was postoperative hematoma in 4 (7.0%).

Multivariate Regression Analysis

A multiple regression analysis with change in ODI as the dependent variable was performed. A positive value in the outcome corresponds to less disability related to low back pain. The effect estimates are presented in Table 4 (367 observations were deleted owing to missing data [30.1%]). In a multivariate analysis, ODI scores of 21–40 (hazard ratio [HR] 14.5, 95% CI 1.1 to 27.9, $P = 0.035$), 41–60 (HR 27.5, 95% CI 13.4 to 41.7, $P < 0.001$), 61–80 (HR 47.4, 95% CI 33.4 to 61.4, $P < 0.001$), and >81 (HR 66.7, 95% CI 51.1 to 82.2, $P < 0.001$) were identified as positive predictors for ODI improvement at 1 year, whereas age ≥65 (HR −0.9, 95% CI −0.3 to −1.5, $P = 0.004$) was identified as a negative predictor for ODI improvement. Mixed linear model analyses showed similar results for all patient-reported outcomes.

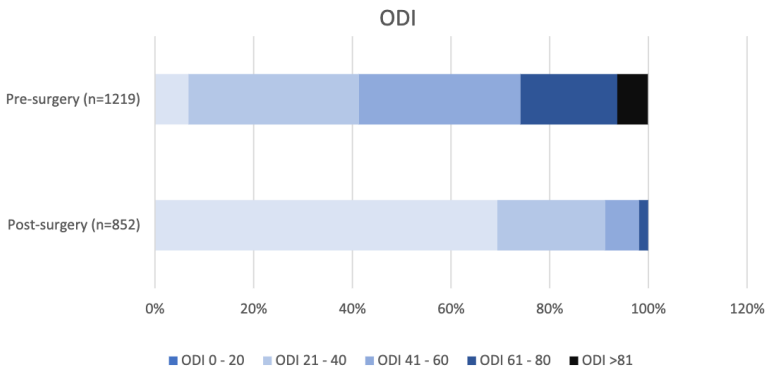
Table 2. Patient-Reported Outcome Measures Following Lumbar Microdiscectomy

Variable	Baseline	1-Year	Mean Change	95% CI	*P* Value
ODI	48.1	15.4	33.3	31.7 to 34.9	<0.001
EQ-5D	0.23	0.75	−0.52	−0.55 to −0.49	<0.001
Leg pain NRS	7.1	2.1	5.0	4.8 to 5.2	<0.001
Back pain NRS	6.6	2.7	3.9	3.6 to 4.1	<0.001
Mixed Linear Models					
ODI	47.7	15.4	32.3	14.3 to 31.3	<0.001
EQ-5D	0.23	0.75	−0.52	−0.55 to −0.49	<0.001
Leg pain NRS	7.1	2.1	5.0	4.8 to 5.2	<0.001
Back pain NRS	6.6	2.7	3.9	3.7 to 4.1	<0.001

CI, confidence interval; ODI, Oswestry disability index; EQ-5D, EuroQol 5 Dimensions; NRS, numeric rating scale.

DISCUSSION

This study adds to an increasing amount of evidence that lumbar microdiscectomy is an effective and safe treatment for patients with symptomatic LDH, although there is still room for improvements. Among the patients with complete follow-up, 69% experienced no or minimal disability at 1 year (i.e., ODI score between 0 and 20). There were 26 (3.1%) patients who experienced a clinically significant deterioration in ODI 1 year after surgery. Increasing ODI score at baseline was identified as the most important positive predictor for ODI improvement. This is in line with findings from multiple studies demonstrating that a high baseline ODI score before



	ODI 0-20	ODI 21-40	ODI 41-60	ODI 61-80	ODI > 81
ODI Pre-surgery (n=1219)	83	421	400	240	75
ODI Post-surgery (n=852)	591	186	59	16	0

Figure 1. Case analysis of the group that completed 1-year follow-up. Data are presented in a stacked bar plot and table. ODI, Oswestry Disability Index.

Table 3. Complications

Complication	Number (%)
Perioperative complications	18 (1.5)
Unintentional durotomy	8 (0.7)
Nerve injury	1 (0.1)
Blood replacement	3 (0.2)
Cardiovascular complications	2 (0.2)
Anaphylactic reaction	1 (0.1)
Wrong-level surgery	1 (0.1)
Respiratory complications	1 (0.1)
Complications within 3 months ($n = 846$)	63 (5.2)
Wound infection	16 (1.3)
Urinary tract infection	24 (2)
Pneumonia	7 (0.6)
Pulmonary embolism	1 (0.1)
Deep vein thrombosis	2 (0.2)
Micturition problems	25 (2.1)
Reoperations	176 (14.4)
Within 90 days	57 (4.7)
After 90 days	119 (9.8)

surgery will result in a large improvement in mean ODI score after surgery.[8-10]

Obesity has previously been reported as a negative predictor in terms of improvement following spine surgery.[8,9,21] In the Spine Patient Outcomes Research Trial (SPORT) study, BMI <30 was associated with greater improvement in ODI after surgery. Obese patients were also found to have significantly worse outcomes after surgery than nonobese patients.[12] We were unable to confirm high BMI as a negative predictor for ODI improvement. Moreover, a recent study from NORspine demonstrated similar patient-reported outcomes for obese and nonobese patients after surgery for LDH, although obese patients (BMI ≥30) had slightly longer hospital stays and increased risk of minor complications.

Age >65 was also identified as a negative predictor in our study population. However, in a recent NORspine study it was clearly shown that patients >65 years of age experienced similar improvement as younger patients, but with a slightly elevated risk of minor complications and longer hospital stays.[10] The HR for age >65 was also notably weak, indicating this as a weak negative predictor in our study.

Smoking, female sex, and American Society of Anesthesiologists grade >2 were not established as negative predictors in our study. However, these factors have been identified as negative predictors in similar studies.[9,21] Given that this is a single-center study, our sample size is limited compared with many studies, which might explain why we were not able to establish smoking, female sex, and American Society of Anesthesiologists >2 as negative predictors.

Our patient group achieved a mean ODI improvement of 33.3 points, which is slightly less than the improvement found in large multicenter studies (i.e., the SPORT study showed a mean improvement −35.7). This might be due to patient characteristics and selection, especially in the SPORT study where higher preoperative ODI values provide larger room for improvement following surgery.[21] Although minimally invasive procedures, such as lumbar microdiscectomy and microdecompression, may not impact long-term outcomes compared with open procedures, the benefits in terms of rapid recovery following surgery, early

Table 4. Multivariate Regression Analysis

Variable	Parameter Estimate (β)	95% CI	*P* Value
ODI score 21–40, presurgery	14.5	1.1 to 27.9	0.035
ODI score 41–60, presurgery	27.5	13.4 to 41.7	<0.001
ODI score 61–80, presurgery	47.4	33.4 to 61.4	<0.001
ODI score >81, presurgery	66.7	51.1 to 82.2	<0.001
Age ≥65	−0.9	−1.5 to −0.3	0.004
ASA grade >2	−2.1	−8.9 to 4.8	0.552
Depression and/or anxiety	28.4	−7.1 to 63.9	0.115
Female sex	−3.0	−9.5 to 3.5	0.366
BMI 25–29.99 kg/m^2	−1.4	−8.0 to 5.3	0.686
BMI 30–34.99 kg/m^2	−11.0	−22.0 to 0.1	0.051
BMI ≥35 kg/m^2	−25.7	−61.8 to 10.3	0.16
Smoker	−2.6	−11.5 to 6.3	0.563

CI, confidence interval; ODI, Oswestry Disability Index; ASA, American Society of Anesthesiologists; BMI, body mass index.

mobilization, and shorter hospital stays are obvious.[15,22] Furthermore, in selected patients without serious comorbidities, hospital discharge on the day of surgery appears to be safe.[23]

Strengths and Limitations

Our study is strengthened by the large number of patients, high external validity, prospective data collection, and widely applied and validated outcome measures.[16-20] The main limitation of this study is the relatively high loss to follow-up at 1 year for the primary outcome measure. Although nonresponders received reminders, loss to follow-up at 1 year was 30.1% in our study. Missing data in spine registries remain a concern and may introduce bias.[24] Efforts must be made to reduce loss to follow-up, and researchers should be encouraged to use appropriate statistical analyses to address this problem. However, a previous study from NORspine in a similar study population with 22% nonresponders found no difference between responders and nonresponders on long-term follow-up.[25] Moreover, it seems that NORspine participants >65 years of age are more likely to complete 1-year follow-up.[10]

This study set out to examine outcome after only 1 year, and a longer follow-up period could possibly provide more information on long-term outcomes for lumbar microdiscectomy. Other studies examining outcomes after surgery for lumbar disc herniation have reported longer follow-up times.[3,7,13] A study examining long-term results in the SPORT study concluded that improvement after surgery seemed to peak at 6 months following treatment and persisted through an 8-year follow-up period.[7]

This study included only patients who received operative treatment. We did not have a conservative treatment group with which to compare, and there is no information in NORspine regarding conservative management before surgery. Future studies comparing surgical interventions with well-defined nonsurgical interventions are warranted.

CONCLUSIONS

Microdiscectomy for LDH is an effective and safe treatment, although there is still room for improvements.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Vetle Vangen-Lønne: Conceptualization, Methodology, Visualization, Writing - original draft, Writing - review & editing, Formal analysis. **Mattis A. Madsbu:** Writing - review & editing. **Øyvind Salvesen:** Writing - review & editing, Formal analysis. **Øystein P. Nygaard:** Writing - review & editing. **Tore K. Solberg:** Writing - review & editing. **Sasha Gulati:** Conceptualization, Data curation, Methodology, Project administration, Writing - review & editing, Formal analysis, Funding acquisition, Resources, Validation.

ACKNOWLEDGMENTS

We thank all patients and surgeons who participated in the Norwegian Registry for Spine Surgery.

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Conflict of interest statement: Study data were obtained from the Norwegian Registry for Spine Surgery, which receives funding from the University of Northern Norway and Norwegian health authorities.

Received 20 January 2020; accepted 8 February 2020

Citation: World Neurosurg. (2020) 137:e577-e583. https://doi.org/10.1016/j.wneu.2020.02.056

Journal homepage: ***www.journals.elsevier.com/world-neurosurgery***

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

Paper 2

Holmberg, Siril Therese; Vangen-Lønne, Vetle; Gulati, Agnete Malm; Nygaard, Øystein P; Solberg, Tore K.; Salvesen, Øyvind; Gulati, Sasha. Pain During Sex Before and After Decompressive Surgery for Lumbar Spinal Stenosis: A Multicenter Observational Study. Spine 2021 ;Volum 46.(19) s. 1354-1361

Paper 3

Surgery for Degenerative Cervical Myelopathy: A Nationwide Registry-Based Observational Study With Patient-Reported Outcomes

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Received, February 11, 2021.
Accepted, May 16, 2021.
Published Online, July 29, 2021.

BACKGROUND: Indications and optimal timing for surgical treatment of degenerative cervical myelopathy (DCM) remain unclear, and data from daily clinical practice are warranted.

OBJECTIVE: To investigate clinical outcomes following decompressive surgery for DCM.

METHODS: Data were obtained from the Norwegian Registry for Spine Surgery. The primary outcome was change in the neck disability index (NDI) 1 yr after surgery. Secondary endpoints were the European myelopathy score (EMS), quality of life (EuroQoL 5D [EQ-5D]), numeric rating scales (NRS) for headache, neck pain, and arm pain, complications, and perceived benefit of surgery assessed by the Global Perceived Effect (GPE) scale.

RESULTS: We included 905 patients operated between January 2012 and June 2018. There were significant improvements in all patient-reported outcome measures (PROMs) including NDI (mean −10.0, 95% CI −11.5 to −8.4, $P < .001$), EMS (mean 1.0, 95% CI 0.8-1.1, $P < .001$), EQ-5D index score (mean 0.16, 95% CI 0.13-0.19, $P < .001$), EQ-5D visual analogue scale (mean 13.8, 95% CI 11.7-15.9, $P < .001$), headache NRS (mean −1.1, 95% CI −1.4 to −0.8, $P < .001$), neck pain NRS (mean −1.8, 95% CI −2.0 to −1.5, $P < .001$), and arm pain NRS (mean −1.7, 95% CI −1.9 to −1.4, $P < .001$). According to GPE scale assessments, 229/513 patients (44.6%) experienced "complete recovery" or felt "much better" at 1 yr. There were significant improvements in all PROMs for both mild and moderate-to-severe DCM. A total of 251 patients (27.7%) experienced adverse effects within 3 mo.

CONCLUSION: Surgery for DCM is associated with significant and clinically meaningful improvement across a wide range of PROMs.

KEY WORDS: Cervical spine, Decompressive surgery, Degenerative, Degenerative cervical myelopathy, Observational study, Spine disorder, Spine surgery

Neurosurgery 89:704–711, 2021 https://doi.org/10.1093/neuros/nyab259 www.neurosurgery-online.com

Degenerative cervical myelopathy (DCM) is a progressive spine disorder and the most common cause of spinal cord impairment in adults over 55 yr.[1-4] The cervical spine is prone to degenerative changes such as disk herniation, ligament hypertrophy or ossification, and osteophyte formation that may lead to spinal cord compression and dysfunction.[4,5] DCM should be considered in patients >50 yr with progressive neurological symptoms, such as pain and stiffness in the neck, pain and numbness in limbs, poor coordination, imbalance, loss of dexterity, frequent falls, and bowel and/or urinary incontinence.[6,7] As nonspecific and subtle initial early features of DCM overlap with other neurological conditions, it is frequently challenging to catch the diagnosis early. Lack of awareness and incomplete neurological assessments can also delay diagnosis,[8] and this may also increase patients' risk of developing life-long disability and impaired quality of life.[9,10] Magnetic resonance imaging (MRI) is the investigation of choice to detect spinal cord compression with

ABBREVIATIONS: DCM, degenerative cervical myelopathy; **EMS,** European myelopathy score; **EQ-5D,** EuroQoL-5D; **GPE,** Global Perceived Effect; **MCIC,** minimal clinically important change; **mJOA,** modified Japanese Orthopedic Association; **NDI,** neck disability index; **NORspine,** Norwegian Registry for Spine Surgery; **NRS,** numeric rating scales; **PROM,** patient-reported outcome measure

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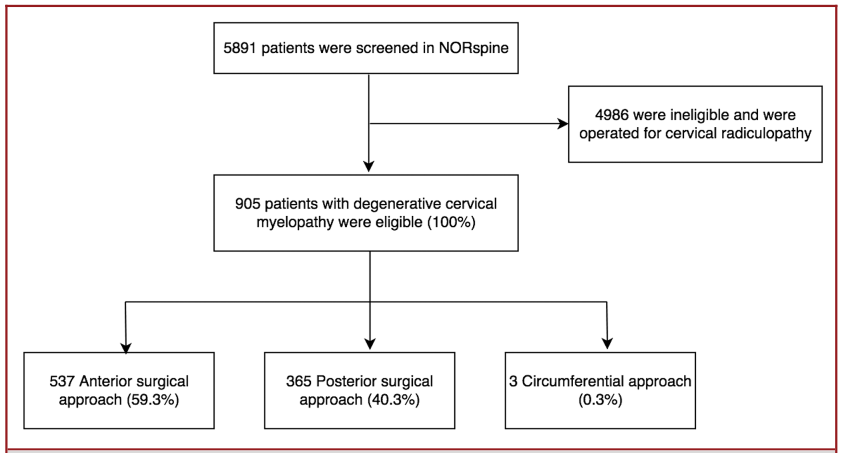


FIGURE 1. *Flow diagram with study enrolment and surgical treatment.*

or without intramedullary signal abnormalities and electrophysiologic testing can sometimes help exclude alternative diagnoses.[7,11] Incidental degenerative changes in the cervical spine with spinal cord compression are commonly encountered on MRI and do not correlate well with the severity of symptoms.[4] As the oldest sector of the population continues to grow and wishes to remain active, physicians will be required to manage an increasing number of patients with degenerative changes in the spine and DCM.[4,12]

Indications and optimal timing for surgical treatment of DCM remain unclear, and additional high-quality data from daily clinical practice including all disease severities are warranted. According to current guidelines, surgery is recommended for moderate-to-severe or progressive DCM to prevent further deterioration.[5] Two prospective multicenter AOSpine studies showed that decompressive surgery in selected patients can halt disease progression and achieve meaningful, albeit limited, recovery in pain, function, and quality of life.[13,14] These 2 large studies were instrumental in driving the development of the 2017 AOSpine and Cervical Spine Research Society guidelines for management of DCM.[5] Still, it is a common perception among healthcare providers that chances of clinically relevant improvement following surgery for DCM are slim.

In this nationwide study with prospectively collected data from the Norwegian Registry for Spine Surgery (NORspine), we investigated clinical outcomes in patients undergoing decompressive surgery for DCM.

TABLE 1. Personal Characteristics, Coexisting Illnesses, and Measures of Health

Variables	
Age, years (standard deviation [SD])	57.5 (+/−12.4)
Female	365 (40.3)
Married or partner	627 (69.3)
Current tobacco user	324 (35.8)
College education	281 (31.0)
Prior cervical spine surgery	102 (11.3%)
Body mass index (SD)	27.2 (+/−4.8)
Comorbidity	508 (56.1)
American Society of Anesthesiologists grade > 2	190 (21.0)
Ranawat grade 3A or 3B	339 (37.5)
Symptoms >1 yr	183 (20.2)
Preoperative EMS (SD)	14.3 (+/−2.4)
Preoperative NDI (SD)	34.9 (+/−16.8)
Preoperative EQ-5D (SD)	0.45 (+/−0.33)
Preoperative diagnostic imaging:	
MRI	885 (97.8)
Computed tomography	112 (13.5)
Myelography	2 (0.2)
Electrophysiologic testing	5 (0.6)

Values are numbers (percentages) unless stated otherwise.

METHODS

Reporting is consistent with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.[15] The Regional Committee for Medical Research Ethics approved the study (2016/840), and all participants provided written informed consent.

Study Population

NORspine is a comprehensive registry for quality control and research and includes all eight centers performing cervical spine surgery in Norway.[16,17] Currently, approximately 81% of patients who undergo

surgery in the cervical spine in Norway are included in NORspine. The inclusion rate for DCM surgery is probably higher as these procedures typically are scheduled. NORspine participation was not a requirement for patients to gain access to treatment or for a provider to be eligible for reimbursement and payment. Patients were eligible if they were ≥18 yr, underwent decompressive surgery for DCM between January 1, 2012 and June 15, 2018, had a preoperative European myelopathy score (EMS) <18 points, and were registered in NORspine.

Surgical Procedures

All patients underwent decompressive surgery of the cervical spine. The surgical approach, the number of operated levels, and the use and type of instrumentation were performed at the surgeons' discretion.

Outcome Measures

The primary outcome was change in the neck disability index (NDI) between baseline and 1 yr. Secondary outcome measures were changes at 1 yr in EMS, EuroQoL-5D (EQ-5D), and numeric rating scales (NRS) for headache, neck pain, and arm pain. In addition, we report complications occurring within 3 mo and patients' perceived benefit of surgery assessed by the Global Perceived Effect (GPE) scale at 1 yr.

The NDI is a self-rated questionnaire developed for patients with neck disability.[18] The questionnaire is composed of 10 items: 7 related to activities of daily living, 2 to pain, and 1 to concentration. The sum of the 10 items is recalculated into a percentage NDI score from 0 to 100 (no to maximum disability). The minimal clinically important change (MCIC) is approximately 7.5 percentage points.[19,20]

The EMS has 5 subscores obtained by patient questionnaires to evaluate the 4 major neural systems, the impairment of which contributes to the clinical picture of DCM: (a) the upper motor neuron with signs of spasticity as well as bladder and bowel disturbances; (b) the lower motor neuron with impairment of hand function; (c) the posterior roots with upper limb radicular deficits and paresthesias; and (d) the posterior columns with proprioceptive sensory loss, disturbed coordination, and ataxia.[21,22] The total score ranges between 5 and 18, and the lower the score, the more severe the deficits. Scores ≥13 were classified as mild DCM and scores between 5 and 12 points were classified as moderate-to-severe DCM.[21] There is no consensus of the MCIC for EMS, but even a small change in severe DCM might be considered important in daily function.

Changes in health-related quality of life were measured with EQ-5D.[23] An index value for health status is generated for each patient. Scores range from −0.6 to 1, in which 1 corresponds to perfect health. Effect size estimations were used to evaluate the magnitude of changes.[24] EQ-5D also contains a vertical visual analogue scale, ranging from 0 to 100 (lower scores indicate poorer health).

Intensities of headache, neck pain, and arm pain were assessed on 0 to 10 NRS, with response options ranging from 0 (no pain) to 10 (worst imaginable pain). The MCIC for NRS is approximately 1.5 points.[25]

The GPE has 7 response categories: (1) complete recovery, (2) much better, (3) slightly better, (4) unchanged, (5) slightly worse, (6) much worse, and (7) worse than ever.[26]

Surgeons provided the following data on perioperative complications: unintentional durotomy, nerve root injury, wrong level surgery, misplacement of implant, intraoperative hemorrhage requiring blood replacement, respiratory complications, anaphylactic reaction, spinal cord injury, esophageal injury, major vessel injury, cardiovascular complications, and other nerve injury. Patients reported the following complications if occurring within 3 mo: wound infection, urinary tract infection, pneumonia, pulmonary embolism, deep vein thrombosis, dysphagia, dysphonia, and new-onset arm or leg weakness.

Data Collection

On admission for surgery, the patients completed a self-administered questionnaire, which included questions about demographics, personal characteristics, and patient-reported outcome measures (PROMs). Using a standard registration form, surgeons recorded data on diagnosis, severity of DCM according to the Ranawat[27] classification of myelopathy, comorbidity, American Society of Anesthesiologists grade, image findings, and surgical procedure. NORspine distributed self-administered questionnaires to the patients by mail 3 and 12 mo after surgery. Nonresponders received 1 reminder with a new copy of the questionnaire.

Statistical Analysis

Statistical analyses were performed with SPSS (IBM Corp) version 26.0 and Software R (R Foundation for Statistical Computing) version 3.6.3. For statistical comparison tests, we defined the significance level as $P \leq .05$. Frequencies were used for demographic variables at baseline, and changes in PROMs were compared with paired-sample *T*-test.

Missing data were managed with mixed linear model analyses. Previous studies have shown that imputations are not required before performing a mixed model analysis on longitudinal data.[28,29] Patients were not excluded from mixed model analyses if a variable was missing at some, but not all, time points following baseline.

Patient and Public Involvement

A member from The Norwegian Back Pain Association reviewed the study protocol and provided feedback concerning the study design.

RESULTS

Figure 1 shows the inclusion and exclusion process leading to 905 eligible patients. Baseline characteristics are presented in Table 1. Participants underwent surgery at 8 neurosurgical departments. The mean age was 57.5 +/−12.4 yr, 365 (40.3%) were female, and 163 patients (18.0%) had moderate-to-severe DCM at baseline. In total, 697 participants (77%) provided patient reported outcome measures at 3 and/or 12 mo. The only differences in baseline characteristics between responders and non-responders were tobacco use (32.1% vs 47.6%, $P < .001$), age (58.3 vs 54.9 yr, $P < .001$), and life partner (73.1% vs 59.1%, $P < .001$). Preoperative EMS was missing in 89 patients (9.8%).

Primary Outcome

The mean NDI score at baseline was 35.1 and at 1-yr follow-up was 25.1 (difference −10.0, 95% CI −11.5 to −8.4, $P < .001$). In patients with mild DCM, the mean NDI score at baseline was 32.2 and at 1-yr follow-up was 22.7 (difference −9.5, 95% CI −11.7 to −7.9, $P < .001$). In patients with moderate-to-severe DCM, the mean NDI score at baseline was 48.7 and at 1-yr follow-up was 34.9 (difference −13.8, 95% CI −19.0 to −8.6, $P < .001$). The mean change in NDI exceeded the MCIC of 7.5 points for all DCM severities.

TABLE 2. Complete Case Analysis and Mixed Linear Model Analysis for Outcomes at 1 yr in Patients With DCM

Variable	Baseline	1 yr	Mean change	95% CI	*P*-value
Complete case analyses:					
All categories					
NDI (N = 385)	35.1	25.1	−10.0	−11.5 to −8.4	<.001
EMS (N = 416)	14.3	15.2	1.0	0.8 to 1.1	<.001
EQ-5D summary score (N = 453)	0.45	0.61	0.16	0.13 to 0.19	<.001
EQ-5D VAS (N = 470)	49.1	62.9	13.8	11.7 to 15.9	<.001
Headache NRS (N = 435)	3.3	2.2	−1.1	−1.4 to −0.8	<.001
Neck pain NRS (N = 457)	4.8	3.0	−1.8	−2.0 to −1.5	<.001
Arm pain NRS (N = 459)	5.1	3.5	−1.7	−1.9 to −1.4	<.001
Mild myelopathy					
NDI (N = 298)	32.2	22.7	−9.5	−11.7 to −7.9	<.001
EMS (N = 330)	15.3	15.8	0.5	0.4 to 0.7	<.001
EQ-5D summary score (N = 338)	0.52	0.66	0.14	0.11 to 0.18	<.001
EQ-5D VAS (N = 345)	52.8	65.5	12.7	10.3 to 15.1	<.001
Headache NRS (N = 314)	3.1	2.1	−1.0	−1.4 to −0.7	<.001
Neck pain NRS (N = 332)	4.6	2.9	−1.7	−2.0 to −1.4	<.001
Arm pain NRS (N = 336)	4.8	3.2	−1.6	−1.9 to −1.3	<.001
Moderate-to-severemyelopathy					
NDI (N = 64)	48.7	34.9	−13.8	−19.0 to −8.6	<.001
EMS (N = 86)	10.4	13.0	2.6	2.0 to 3.2	<.001
EQ-5D summary score (N = 83)	0.18	0.44	0.26	0.16 to 0.36	<.001
EQ-5D VAS (N = 86)	35.3	53.1	17.8	12.0 to 23.5	<.001
Headache NRS (N = 83)	3.7	2.8	−0.9	−1.6 to −0.2	.009
Neck pain NRS (N = 83)	5.3	3.4	−1.9	−2.6 to −1.3	<.001
Arm pain NRS (N = 82)	5.8	4.1	−1.7	−2.5 to −0.9	<.001
Mixed linear model analyses					
All categories					
NDI (N = 854)	35.1	25.8	−9.4	−10.6 to −8.1	<.001
EMS (N = 880)	14.3	15.2	0.9	0.7 to 1.0	<.001
EQ-5D summary score (N = 887)	0.44	0.60	0.16	0.14 to 0.19	<.001
EQ-5D VAS (N = 884)	49.1	62.5	13.4	11.6 to 15.2	<.001
Headache NRS (N = 870)	3.2	2.1	−1.0	−1.3 to −0.8	<.001
Neck pain NRS (N = 882)	4.8	3.0	−1.7	−2.0 to −1.5	<.001
Arm pain NRS (N = 882)	5.0	3.4	−1.6	−1.9 to −1.4	<.001
Mild myelopathy					
NDI (N = 633)	32.3	23.1	−9.2	−10.6 to −7.8	<.001
EMS (N = 653)	15.3	15.8	0.5	0.3 to 0.6	<.001
EQ-5D Summary score (N = 647)	0.52	0.66	0.14	0.11 to 0.17	<.001
EQ-5D VAS (N = 645)	52.8	65.5	12.7	10.7 to 14.8	<.001
Headache NRS (N = 633)	3.0	2.0	−1.0	−1.3 to −0.7	<.001
Neck pain NRS (N = 642)	4.6	2.9	−1.7	−2.0 to −1.4	<.001
Arm pain NRS (N = 642)	4.8	3.2	−1.6	−1.9 to −1.3	<.001
Moderate-to-severe myelopathy					
NDI (N = 144)	48.8	35.3	−13.5	−17.3 to −9.7	<.001
EMS (N = 163)	10.4	13.0	−2.6	−2.1 to −3.0	<.001
EQ-5D Summary score (N = 162)	0.14	0.43	0.29	0.21 to 0.36	<.001
EQ-5D VAS (N = 159)	36.0	53.6	17.6	12.8 to 22.3	<.001
Headache NRS (N = 156)	3.5	2.6	−0.9	−1.5 to −0.4	<.001
Neck pain NRS (N = 158)	5.5	3.4	−2.1	−2.6 to −1.5	<.001
Arm pain NRS (N = 157)	5.8	4.0	−1.8	−2.4 to −1.1	<.001

Secondary Outcomes

PROMs are presented in Table 2. There were significant improvements in all PROMs at 1 yr including EMS (mean 1.0, 95% CI 0.8–1.1, $P < .001$), EQ-5D index score (mean 0.16, 95% CI 0.13–0.19, $P < .001$), EQ-5D visual analogue scale (mean 13.8, 95% CI 11.7–15.9, $P < .001$), headache NRS (mean −1.1, 95% CI −1.4 to −0.8, $P < .001$), neck pain NRS (mean −1.8, 95% CI −2.0 to −1.5, $P < .001$), and arm pain NRS (mean −1.7, 95% CI −1.9 to −1.4, $P < .001$).

The change in EQ-5D index score represents a moderate clinical change, with an effect size of 0.51. Further, there were significant improvements in all PROMs for both mild and moderate-to-severe DCM. The mean changes in neck and arm pain NRS exceeded the MCIC of 1.5 points. Mixed linear model analyses showed similar results for all PROMs

Patients' perceived benefit of surgery assessed by the GPE at 3 mo and 1 yr is presented in Figure 2A and 2B, respectively. According to GPE assessments, 229 out of 513 patients (44.6%) reported complete recovery or feeling much better at 1 yr. In total, 81 out of 513 patients (15.8%) reported feeling "slightly worse," "much worse," or "worse than ever" at 1 yr.

Table 3 provides details of surgical treatments and complications. There were no deaths within 30 d of surgery. In total, 251 patients (27.7%) experienced complications or adverse effects within 3 mo.

DISCUSSION

This nationwide study shows that surgery for DCM is associated with significant and clinically relevant improvements across the whole range of PROMs at 1 yr. Favorable outcomes were observed for both mild and moderate-to-severe DCM, with the largest effects observed in the latter more severely disabled group. Our study adds to the evidence from previous observational studies that surgical treatment cannot only arrest further progression of myelopathy, but also improve functional status, neurological outcomes, and quality of life.[13,14,30] Although >70% of responders perceived a benefit from surgery, a substantial placebo effect cannot be ruled out following such complex treatment.[31] Risk associated with surgery for DCM is not negligible and should be clearly communicated to patients prior to surgery. Patients should also be informed that complete resolution of symptoms is unlikely following surgery. Life-threatening complications and early reoperations are fortunately rare. In our study, 27.7% of responders experienced adverse effects or complications within 3 mo and 15.8% perceived a clinical worsening.

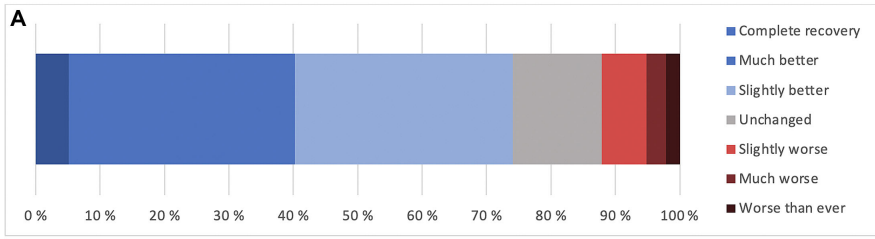
The epidemiology of DCM is poorly understood, and exact numbers of prevalence or incidence are not known. The prevalence of surgically treated DCM in Europe has been estimated between 1.6 and 4.7 per 100 000 inhabitants.[32,33] It is important to refer patients with suspected DCM promptly to MRI and a specialist for consideration of decompressive surgery, as delayed diagnosis and treatment can lead to unnecessary residual symptoms and worsening of disability. For nonmyelopathic patients without radiculopathy and only radiological evidence of cervical cord compression, prophylactic surgery is not recommended.[5,6] These patients should be followed clinically if feasible and counseled as to potential risks of progression and advised to seek medical attention if symptoms should develop.

Until recently, there has been limited evidence to guide clinical management of mild DCM.[5] In a large and recent prospective study on mild DCM with 2 yr follow-up, significant gains in a wide range of PROMs were observed following surgery.[34] Two small randomized trials in patients with mild-to-moderate DCM found no differences in neurological outcomes at 2 yr between those who received conservative vs surgical treatment.[35,36] Still, the majority of patients in our study had mild DCM and significant improvements were observed for all PROMs. However, these improvements were smaller compared to patients with moderate-to-severe DCM. Although we have detailed clinical data at the time of surgery, little is known about the dynamics of symptoms, disability, and neurological functioning preceding surgery. A recent study showed that machine learning algorithms might become useful to identify patients with mild DCM that will benefit from surgery.[37] The phenotype of mild DCM needs to be acknowledged, and a recent study reported that neck pain, motor symptoms, and female gender were associated with greater impairment of quality of life and greater response to surgery.[38] Additional observational studies or clinical trials should be encouraged to clarify the natural course of the disease and evaluate surgery and structured rehabilitation for patients with mild DCM.

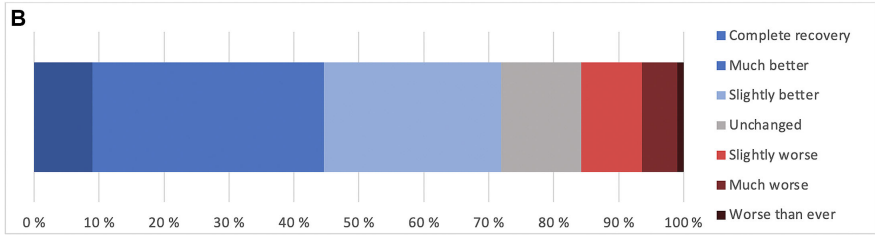
There are no randomized trials comparing surgical and nonsurgical management of patients with moderate-to-severe DCM. In a recent trial, adjuvant treatment perioperatively with riluzole (Aventis Pharma) did not improve functional recovery beyond decompressive surgery in patients with moderate-to-severe DCM.[39] Age-related degeneration of the cervical spine encompasses a complex set of anatomical changes that can result in DCM.[4] Spine surgeons can draw from a repertoire of different operations to treat DCM, and the surgical strategy is typically based on patient specific factors and preferences of the surgeon. An interesting topic is the comparative efficacy and effectiveness of different surgical treatments.[30,40-42] Unfortunately, this is beyond the scope of our study as we did not have detailed enough information in order to compare the effectiveness of different surgical procedures. Interestingly, a recent trial showed that an anterior surgical approach did not significantly improve outcomes compared with a posterior surgical approach.[43]

Limitations

The modified Japanese Orthopedic Association (mJOA) scale is currently the recommended disease-specific PROM. The use



	Complete recovery	Much better	Slightly better	Unchanged	Slightly worse	Much worse	Worse than ever
Perceived benefit after three months, N=601 (%)	31 (5.2)	211 (35.1)	203 (33.7)	83 (13.8)	42 (7.0)	18 (3.0)	13 (2.2)



	Complete recovery	Much better	Slightly better	Unchanged	Slightly worse	Much worse	Worse than ever
Perceived benefit after twelve months, N=513 (%)	46 (9.0)	183 (35.6)	140 (27.3)	63 (12.3)	48 (9.4)	28 (5.5)	5 (0.9)

FIGURE 2. **A**, *Patients' perceived benefit of surgery for DCM after 3 mo.* **B**, *Patients' perceived benefit of surgery for DCM after 1 yr.*

of the EMS might make it more challenging to compare results across more recent studies. This is to some extent alleviated by the use of the NDI and EQ-5D, which are included in recent studies on DCM. NORspine started including patients several years prior to the current practice guidelines.[5] Solely assessing the myelopathy is likely insufficient to fully understand clinical outcome in its totality, and combinations of questionnaires are recommended.[38,44,45] A study comparing 7 different scales, including mJOA and EMS, found that all of them detected significant improvement following surgery.[46] Still, each scale had differing qualities of reliability, validity, and responsiveness. Lack of randomization is an obvious limitation. Loss to follow-up is another concern, but a previous NORspine study showed no difference in outcomes between responders and nonresponders.[47] Follow-up exceeding 1 yr may be warranted to detect the effect of surgery on progression of symptoms. Some patients may have received physical therapy, but our study cannot assess the impact of such interventions.

TABLE 3. Surgical Treatment, Complications, and Events

Variables	
Emergency surgery	137 (15.1)
Surgical approach	
Anterior	537 (59.3)
Posterior	365 (40.3)
Instrumented fusion	17 (1.9)
Circumferential	3 (0.3)
Number of levels decompressed, median (range)	2 (1-6)
Spine level of surgery	
C0-C1	3 (0.3)
C1-C2	4 (0.4)
C2-C3	54 (6.0)
C3-C4	258 (28.5)
C4-C5	389 (43.0)
C5-C6	580 (64.1)
C6-C7	327 (36.1)
C7-TH1	35 (3.9)
Operation time, min (SD)	92.5 (+/−42.7)
Number of days in hospital (SD)	1.7 (+/−1.8)
Reoperation within 90 d	5 (0.6)
Patients with complications	251 (27.7)
Perioperative complications	13 (1.4)
Unintentional durotomy	4 (0.4)
Nerve root injury	0
Iatrogenic spinal cord injury	2 (0.2)
Wrong level surgery	0
Postoperative hematoma	2 (0.2)
Misplacement of implant	0
Esophageal injury	0
Major blood vessel injury	0
Cardiovascular complications	1 (0.1%)
Respiratory complications	1 (0.1)
Anaphylactic reaction	0
Other complications	5 (0.6%)
Complications within 3 mo	244 (27.0)
Deep wound infection	9 (1.0%)
Superficial wound infection	35 (3.9%)
Urinary tract infection	41 (4.5%)
Pneumonia	12 (1.3%)
Pulmonary embolism	5 (0.6%)
Deep venous thrombosis	7 (0.8%)
New-onset arm or leg weakness	120 (13.3%)
Dysphagia	72 (8.0%)
Dysphonia	62 (6.9%)

Values are numbers (percentages) of participants unless stated otherwise.

CONCLUSION

Surgery for DCM is associated with significant improvements across the whole range of PROMs. Favorable outcomes were observed at 1 yr for both mild and moderate-to-severe DCM. Surgical treatment cannot only arrest further progression of myelopathy but also improve functional status, neurological outcomes, and quality of life.

Funding

This study did not receive any funding or financial support.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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Acknowledgments

This work is in memory of Stein Andresen, former user representative in NORspine. The authors thank NORspine and are greatly indebted to all patients and spine surgeons who participated in NORspine registration.

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Paper 4

Acta Neurochirurgica (2023) 165:779–787
https://doi.org/10.1007/s00701-023-05521-w

ORIGINAL ARTICLE - SPINE DEGENERATIVE

Return to work after surgery for degenerative cervical myelopathy: a nationwide registry-based observational study

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Received: 7 December 2022 / Accepted: 1 February 2023 / Published online: 16 February 2023

Abstract

Background Few studies of high quality exist on return to work (RTW) rate after surgery for degenerative cervical myelopathy (DCM). This study aims to examine the RTW rate in patients undergoing surgery for DCM.

Methods Nationwide prospectively collected data were obtained from the Norwegian Registry for Spine Surgery and the Norwegian Labour and Welfare Administration. The primary outcome was return to work, defined as being at work at a given time postoperatively without any medical income-compensation benefits. Secondary endpoints included the neck disability index (NDI) and quality of life measured by EuroQol-5D (EQ-5D).

Results Among 439 patients operated for DCM between 2012 and 2018, 20% of the patients received a medical income-compensation benefit one year before surgery. This number increased steadily towards the operation at which timepoint 100% received benefits. By 12 months after surgery, 65% had returned to work. By 36 months, 75% had returned to work. Patients that returned to work were more likely to be non-smokers and to have a college education. They had less comorbidity, more were without benefit 1-year pre-surgery, and significantly more patients were employed at operation date. Average days of sick leave in the year before surgery were significantly less in the RTW group, and they had a significantly lower baseline NDI and EQ-5D All PROMs reached statistical significance at 12 months, in favor of the group that achieved RTW.

Conclusion At 12 months following surgery, 65% had returned to work. At the end of the 36-month follow-up period, 75% had returned to work, 5% less than the working percentage in the beginning of the follow-up period. This study demonstrates that a large percentage of patients return to work after surgical treatment for DCM.

Keywords Return to work · Degenerative cervical myelopathy · Spine surgery · Cervical

Abbreviations

DCM	Degenerative cervical myelopathy
RTW	Return to work
NDI	Neck disability index
EMS	European myelopathy scale
EQ-5D	EuroQol-5D
NRS	Numeric rating scale
GPE	Global perceived effect scale
PROMs	Patient-reported outcome measures

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

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NORspine The Norwegian Registry for Spine Surgery
NAV The Norwegian Labour and Welfare Administration

Introduction

Degenerative cervical myelopathy (DCM) is a progressive spine disorder and the most common cause of spinal cord impairment in adults over 55 years [18, 23, 26, 37]. Degenerative changes in the cervical spine such as disk herniation, ligament hypertrophy or ossification, and osteophyte formation may lead to compression and dysfunction of the spinal cord [9, 26]. Symptoms of DCM include pain and stiffness in the neck, pain and numbness in limbs, poor coordination, imbalance, frequent falls, loss of dexterity, and incontinence [4, 38]. Several symptoms of DCM are non-specific and subtle and overlap with other neurological conditions, which makes early diagnosis a challenge. Lack of awareness and incomplete neurological assessment can also delay diagnosis, which may increase patients' risk of developing life-long disability and impaired quality of life [3, 27, 36].

Neck and back pain are leading causes of absence from work [24, 42]. Recent studies examining outcomes after surgery for DCM found significant improvement for both mild, moderate, and severe DCM measured with several different patient-reported outcome measures (PROMs) [12, 17]. Due to the high relevance for the individual and society, return to work (RTW) has become an important outcome measure in recent years [5]. Few studies of high quality exist on RTW after surgery for DCM [13, 20]. As the working population continues to grow older and wishes to stay active and working, knowledge about RTW for patients with DCM is paramount. Further, there are few established predictors for RTW after undergoing surgery for DCM. This study aims to examine the RTW rate in patients undergoing decompressive surgery for DCM.

Materials and methods

Reporting is consistent with the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) statement [40]. The Regional Committee for Medical Research Ethics in Central Norway approved the study (No. 2016/840), and all participants provided written informed consent. Data from the Norwegian Registry for Spine Surgery (NORspine) and the Norwegian Labour and Welfare Administration (NAV) were linked individually for each participant. This research group recently published a study examining RTW after surgery for cervical radiculopathy, using a similar approach [13].

Study population

We collected data from patients who underwent decompressive surgery for DCM between January 1, 2012, and June 15, 2018. Patients were considered eligible if they were between the age of 18 to 60 years old, diagnosed with cervical myelopathy, included in NORspine, and received a temporary medical benefit (any grade of sickness benefit or work assessment allowance) on the day of surgery. Patients who did not receive a temporary benefit on the day of surgery (i.e., students, homemakers, retired, recipients of full disability benefit) were excluded. Patients over the age of 60 were excluded, as retirement pension in Norway can be taken out at the age of 62 at the earliest, and we wanted to examine a group that were in working age following surgery.

Surgical procedures

All patients underwent decompressive surgery of the cervical spine. The surgical approach, the number of operated levels, and the use and type of instrumentation were determined at the surgeons' discretion.

NORspine

Norwegian Registry for Spine Surgery (NORspine) is a comprehensive clinical registry for research and quality control [25]. It provides data on demographics, lifestyle, comorbidity, diagnoses, clinical and radiological findings, surgical procedures, and complications, as well as PROMs before and after spinal surgery [25, 34]. Currently, all 40 centers performing lumbar spine surgery in Norway report to NORspine, and approximately 81% of patients who undergo surgery on the cervical spine are included in NORspine. The inclusion rate for DCM surgery is probably higher as these procedures typically are scheduled and rarely performed as emergency surgery [35]. NORspine participation was not a requirement for patients to gain access to treatment or for a provider to be eligible for reimbursement and payment. On admission for surgery (baseline), the patients completed the self-administered baseline questionnaire. During the hospital stay, the surgeon recorded relevant data using a standard registration form. Follow-up questionnaires were distributed to patients by regular mail at three months and one year after surgery, completed at home by the patients and returned. The patients who did not respond received one reminder with a new copy of the questionnaire. The patients completed all the questionnaires without any assistance from the surgeon or other staff from the treating hospital.

Norwegian Labour and Welfare Administration (NAV)

Norway has a comprehensive national insurance scheme administered by the Norwegian Labour and Welfare Service (NAV). Economic loss due to sickness and injury is generously compensated. Medical benefits issued by NAV are summarized as follows:

- Sickness benefit (temporary and short-term: partial or full): Every member of the society who has worked in Norway continuously for six weeks is entitled to a sickness benefit for the first 12 months of sick leave. This compensates previous salary with 100% coverage, with some limitations regarding size of the salary.

- Work assessment allowance (temporary and long-term: partial or full): Persons who cannot resume work after this period and are under ongoing medical treatment or with a possibility of improving may apply for a benefit termed work assessment allowance for the next 36 months. This compensates on average about 66% of the income. In addition, persons may be entitled to work assessment allowance without working experience if their ability to work is impaired due to illness or injury (e.g., students, handicapped, refugees with health problems). Sickness benefits and work assessment allowance are mutually exclusive.

- Disability benefit: Disability benefits may be warranted for those permanently disabled to work, either partially or fully. Patients with partial disability benefits are considered actively working, albeit with a reduced work capacity.

Primary outcome measure

RTW

Our primary outcome was return to work (RTW), defined as being at work at a given time postoperatively without a medical income-compensation benefit from NAV. We calculated the grades of received benefits (partial or full sick leave, partial or full work assessment allowance, partial or full disability benefit) for each day from 1 year before to 3 years after surgery. The benefits were then grouped into five categories: no medical benefit, partial medical benefit of any kind, full sickness benefit, full work assessment allowance, and full disability benefit. We then examined the data on a group level and explored the trends in sick leave and RTW for our patient group.

Secondary outcome measures

PROMs

The neck disability index (NDI) is a self-rated questionnaire developed for patients with neck disabilities [16]. The questionnaire is composed of 10 items: 7 related to activities of daily living, 2 to pain, and 1 to concentration. The sum of the 10 items is recalculated into a percentage NDI score from 0 to 100 (no to maximum disability). The minimal clinically important change (MCIC) is 4.3 percentage points [21, 22, 43].

The European myelopathy score (EMS) is a questionnaire with 5 subscores designed to evaluate the 4 major neural systems, the impairment of which contributes to the clinical picture of DCM: (a) the upper motor neuron with signs of spasticity, bladder and bowel disturbances; (b) the lower motor neuron with impairment of hand function; (c) the posterior roots with upper limb radicular deficits and paresthesias; and (d) the posterior columns with proprioceptive sensory loss, disturbed coordination, and ataxia [2, 39]. The total score ranges between 5 and 18, and the lower the score, the more severe the deficits. Scores $\geq$13 were classified as mild DCM and scores between 5 and 12 points were classified as moderate-to-severe DCM [39]. There is no consensus on the MCIC for EMS, but even a small change in severe DCM might be considered important in daily function.

Changes in health-related quality of life were measured with EQ-5D [32]. An index value for health status is generated for each patient. Scores range from − 0.6 to 1, in which 1 corresponds to perfect health. Effect size estimations were used to evaluate the magnitude of changes [6]. EQ-5D also contains a vertical visual analog scale, ranging from 0 to 100 (lower scores indicate poorer health).

Headache, and neck and arm pain were assessed with a numeric rating scale (NRS) from 0 to 10, with response options ranging from 0 (no pain) to 10 (worst imaginable pain). The MCIC for NRS is approximately 1.5 points [6].

The Global Perceived Effect (GPE) scale has seven response categories: (1) complete recovery, (2) much better, (3) slightly better, (4) unchanged, (5) slightly worse, (6) much worse, and (7) worse than ever [19].

Statistics

Statistical analyses were performed with STATA 16.1 and 17.0 (StataCorp., College Station, TX) and SPSS version 27 (IBM Corporation, IL). The population was divided into two groups, the group that successfully returned to work at 2 years after surgery and the group that did not. We compared the groups for the available variables using a two-sample *t*-test for the continuous variables and Pearson's χ^2 test for the categorical variables.

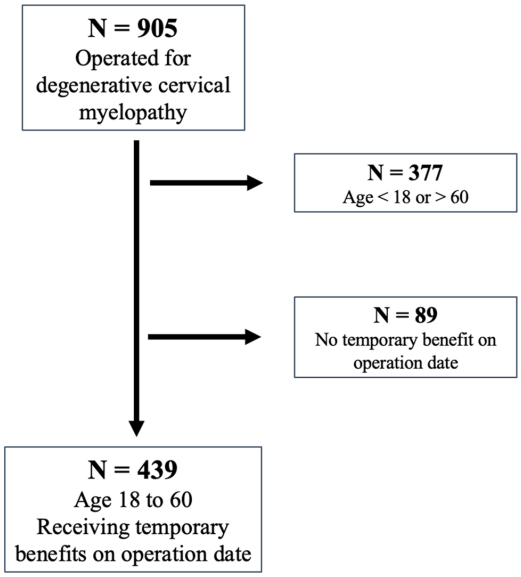

Fig. 1 Patients included

Logistic regression analyses were performed with "achieved RTW two years after surgery" as the dependent variable. Variables with a p value < 0.05 in a two-sample t-test or Pearson's χ^2 test were selected for a multivariable regression analysis if also considered clinically relevant. All selected variables were analyzed in one single model, with odds ratios calculated from it.

Missing data

Patients were excluded if they were younger than 18 or older than 60 years old, or if they did not receive a temporary benefit on the day of operation. When examining all longitudinal data from NAV, we found occasional gaps in longer sick leave periods. If the gaps were 28 days or less, they were replaced with the last registered value under the assumption that the gap was due to a temporary work trial, missing registration, or planned vacation. Gaps longer than 28 days were left untouched and treated as "periods without medical benefit." Twelve-month PROMs data was used as standard. If 12-month data were missing (due to loss to follow-up), 3-month data were used if available.

Table 1 Demographic and clinical characteristics

Variable	Return to work at 2 years		p value
	No, $n = 130$	Yes, $n = 309$	
Mean age at surgery (±SD)	48.8 (7.3)	48.1 (8.1)	0.42
Gender (female)	63 (48.4%)	120 (38.8%)	0.062
Any college education	30 (23.1%)	133 (43%)	<0.001
Employed at operation date	89 (68.4%)	267 (86.4%)	<0.001
Work assessment allowance at operation date	27 (20.8%)	20 (6.5%)	<0.001
No benefit 1-year pre-surgery	88 (67.7%)	263 (85.1%)	<0.001
Smoker	55 (42.3%)	93 (30.1%)	0.025
Obesity (BMI ≥ 30)	43 (33.1%)	81 (26.2%)	0.188
Comorbidity	67 (51.5%)	110 (35.6%)	0.002
Hypertension	15 (11.5%)	28 (9.1%)	0.425
Cardiovascular disease	16 (5.2%)	2 (0.5%)	0.079
Diabetes mellitus	6 (4.6%)	15 (4.9%)	0.915
Chronic neurological disease	2 (1.5%)	6 (1.9%)	0.773
Anxiety/depression	7 (5.4%)	4 (1.3%)	0.012
Rheumatoid arthritis	4 (3.1%)	0 (0%)	0.02
ASA ≥ 3	10 (7.7%)	17 (5.5%)	0.588
Pain > 1 year	29 (22.3%)	66 (21.4%)	0.589
Mild DCM pre-surgery	107 (82.3%)	264 (85.4%)	0.646
Moderate DCM pre-surgery	14 (10.8%)	24 (7.8%)	0.574
Severe DCM pre-surgery	0 (0%)	1 (0.3%)	0.799
Sick days the year before surgery	183.1 (± 128.1)	100.9 (± 116.0)	<0.001
≤ 90	43 (33.1%)	189 (61.2%)	< 0.001
90–180	25 (19.2%)	52 (16.8%)	0.546
180–270	21 (16.2%)	22 (7.1%)	0.004
> 270	41 (31.5%)	46 (14.9%)	< 0.001

Results

Among 906 patients operated for cervical myelopathy, 439 were eligible for our study (Fig. 1). Baseline characteristics are presented in Table 1. Mean age for all included patients was 48 years and 42% were women.

Primary outcome

Changes in sick leave benefits throughout the follow-up period are displayed in Fig. 2. One year before surgery, 20% of the patients received any kind of benefit from NAV. This number increased towards the operation date, the main reason being increases in full sickness benefit or partial benefits of any kind. By 1 week before surgery, 66% received some sort of medical benefit. Following surgery, the number of recipients rapidly decreased. The percentage of patients who received full sickness benefit decreased the fastest. By 5 months, 50% had returned to work. The rapid rate of patients returning to work gradually slowed down and flattened out at approximately 12 months, by which time 65% of the patients had returned to work. The percentage of patients receiving full work assessment allowance increases during the first year, peaking at around 12 months. The percentage of patients who received full disability benefit gradually increased from a few months after surgery all the way to the end of the follow-up period, where 10% received full disability benefit. By the end of the follow-up period at 36 months, 75% had returned to work, while 25% still received some sort of benefit. The working percentage decreased by 5%, from 80% at the beginning of the follow-up period to 75% at the end of the follow-up period.

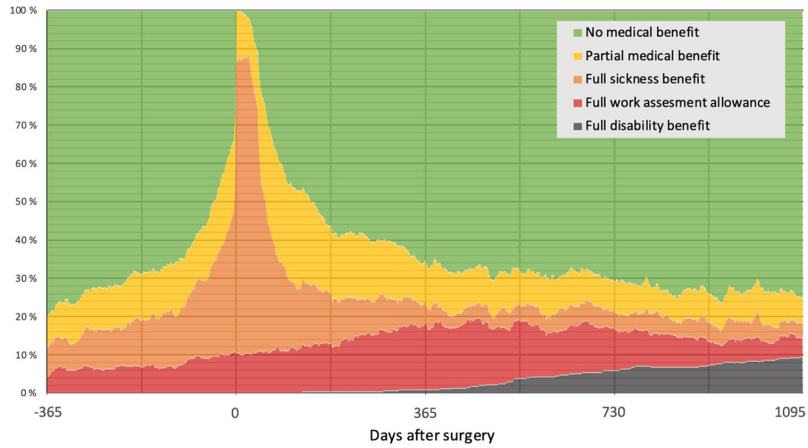

Fig. 2 Trends of sick leave benefits from 1 year before to 3 years after surgery

Table 2 Patient reported outcome measures

Baseline mean values	Returned to work at 2 years		*p* value
	No, *n* = 130	Yes, *n* = 309	
Neck disability index (SD)	39.8 (16.3)	32.5 (15.7)	< 0.001
European myelopathy score (SD)	14.9 (2.0)	15.3 (1.9)	0.057
EQ-5D (SD)	0.42 (0.33)	0.50 (0.31)	0.018
Arm pain numerical rating scale (SD)	5.2 (2.8)	4.8 (2.9)	0.186
Neck pain numerical rating scale (SD)	5.4 (2.8)	4.6 (2.9)	0.008
Headache numerical rating scale (SD)	5.2 (2.8)	4.8 (2.8)	< 0.001
Mean values at 12 months*			
Neck disability index (SD)	33.6 (16.7)	21.3 (17.3)	< 0.001
European myelopathy score (SD)	15.5 (2.0)	16.3 (1.6)	< 0.001
EQ-5D (SD)	0.48 (0.34)	0.71 (0.26)	< 0.001
Arm pain numerical rating scale (SD)	3.9 (2.9)	2.9 (2.7)	0.003
Neck pain numerical rating scale (SD)	4.1 (2.7)	3.0 (2.7)	0.002
Headache numerical rating scale (SD)	3.0 (2.9)	1.98 (2.6)	0.004

*Three-month values were used if 12-month data were not available

Secondary outcomes

The patients were divided into two groups: those who achieved RTW at 2 years and those who did not (Table 1). Patients that returned to work were more likely to be non-smokers and to have a college education. They also had less comorbidity overall and were less likely to suffer from anxiety and depression. Work assessment allowance at operation date was more common among the non-RTW group than the RTW group (20.8% vs. 6.5%, $p < 0.001$). Significantly more patients were employed at operation date in the RTW group (86.4% vs. 68.4%, $p < 0.001$), and more were without benefit 1-year pre-surgery (85.1% vs. 67.7%, $p < 0.001$). Average days of sick leave in the year before surgery were significantly less in the RTW group.

The group that achieved RTW at 2 years had a significantly lower average baseline disability measured by NDI (32.5 ± 15.7 vs. 39.8 ± 16.3, $p < 0.001$) and EQ-5D (0.50 ± 0.31 vs. 0.42 ± 0.33, $p = 0.018$) (Table 2). Difference in neck pain and headache at baseline also reached statistical significance (mean NRS neck 4.6 ± 2.9 vs 5.4 ± 2.8, $p = 0.008$, mean NRS headache 4.8 ± 2.8 vs 5.2 ± 2.8, $p < 0.001$). The difference in mean EMS and NRS arm pain did not reach statistical significance at baseline. The difference in perceived benefit according to the GPE scale (presented in Fig. 3) was statistically significant, with 90% in the RTW group reporting "unchanged" perceived benefit or better (vs 78%, $p = 0.008$). All PROMs reached statistical significance at 12 months, in favor of the group that achieved RTW.

The results of the regression analyses are presented in Table 3. College education (OR 3.5, CI 1.76–6.96), less than 90 sick days in the year before surgery (OR 1.99, CI 1.03–3.85) and increasing NRS neck pain (OR 1.28, CI 1.04–1.58) were associated with increased chance of RTW at 2 years. Female sex (OR 0.44, CI 0.23–0.82), increasing NDI (OR 0.95, CI 0.92–0.99), and decreasing EQ-5D (OR 13.1, CI 2.35 – 73.29) were associated with less chance of RTW at 2 years.

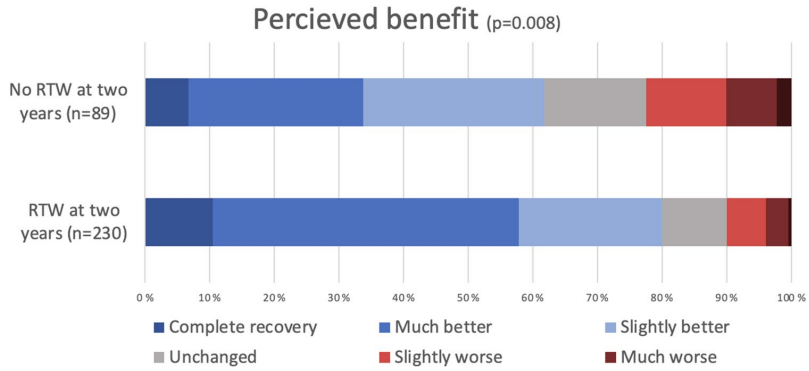

Fig. 3 Global perceived effect at one year following surgery for degenerative cervical myelopathy in patients with and without return to work (RTW) at 2 years

Table 3 Multivariable logistic regression

Variable	OR	Lower 95% CI	Upper 95% CI	*p* value
Age	0.98	0.94	1.02	0.323
Female sex	0.44	0.23	0.82	0.011
College education	3.50	1.76	6.96	< 0.001
Smoker	0.99	0.51	1.91	0.976
Employed at operation date	1.52	0.60	3.87	0.378
AAP at operation date	1.44	0.45	4.60	0.538
≤ 90 sick days in the year before surgery	1.99	1.03	3.85	0.042
PROMs, mean values at 12 months*				
Neck disability index	0.95	0.92	0.99	0.012
European myelopathy scale	0.83	0.64	1.07	0.141
EQ-5D	13.1	2.35	73.29	0.003
Arm pain numerical rating scale	1.15	0.99	1.35	0.075
Neck pain numerical rating scale	1.28	1.04	1.58	0.023
Headache numerical rating scale	1.12	0.95	1.32	0.189
Global perceived effect scale	0.78	0.58	1.05	0.098

*Three-month values were used if 12-month data were not available

Discussion

This study examined patterns for returning to work after surgery for DCM as well as predictors for achieving RTW. In total, 50% of the patients returned to work after 5 months, and by 12 months 65% of the patients had returned to work. At the end of the follow-up period at 36 months, 75% had returned to work, 5% less than the working percentage in the beginning of the follow-up period.

In addition to pain, physical disability, and health related quality of life, RTW is increasingly acknowledged as a core outcome measure in spine surgery [5, 41]. Recent studies have shown considerable improved physical function after surgery for DCM which may provide new opportunities to patients who were previously unable to work [8, 12, 17]. Although surgery for DCM results in statistical and clinical meaningful improvement, this is not a guarantee for returning to work. Even so, larger percentage of patients operated on for DCM achieved RTW than in a similar study examining RTW after surgery for cervical radiculopathy [13].

To our knowledge, this is the largest study to date examining RTW after surgery for DCM. Direct comparison with other studies examining RTW-rate after surgery for DCM is challenging [5, 10, 31]. Differences in cohort selections, welfare systems, authors definition of RTW and health care policies in individual countries contributes to this. A study examining RTW for 102 non-retired patients found that 58.8% of the total population achieved RTW at 1 year, while 75.9% of the population who were working pre-surgery achieved RTW [31]. Like our study, working pre-surgery was associated with RTW. This study did, however, include all patients who were considered "non-retired" and had a smaller sample size than our study. A study from 2018 examining RTW after cervical spine surgery found that 82% achieved RTW after three months [5]. They found that patients who achieved RTW were more likely to have higher education, 100% employment, and lower NDI at baseline and three months. However, this study included patients operated on for both cervical myelopathy and radiculopathy and included only patients who were working pre-surgery. A study from 2020 examined RTW, among other outcomes, in 219 patients operated for cervical myelopathy [10]. They found that 96% of patients with mild DCM 100% of patients with moderate DCM and 84% of patients with severe DCM achieved RTW. They did not, however, define RTW clearly in their study, and only reported it as a secondary outcome.

College education, female sex, and less than 90 days of sick leave in the year before surgery, as well as NDI and EQ-5D at 12 months, had the strongest effect on RTW in this study. A study from 2021 examining work ability measured with the Work Ability Index score (WAI) after surgery for cervical radiculopathy found that thoughts of being able to work within the next 6 months, NDI score and work-related neck load explained 59% of the variance in WAI after 2 years of follow-up [29]. A study from 2021 identified occupational profile as a predictor for RTW after surgery for DCM, with manual laborers having the lowest RTW rate [28]. We did not have access to specific occupation in this study, and more research is needed to establish the relationship between occupational factors and RTW rate after surgery for DCM. A study from 2013 examining prognostic factors for RTW in patients with sciatica found that less sciatica bothersomeness at baseline and duration less than 3 months predicted faster RTW [11]. Less than 90 days of sick leave in the year before surgery were associated with higher chances of RTW in our study, indicating that both manageable symptoms and a shorter symptom duration before surgery might contribute to achieving RTW.

In addition to being less likely to have a college education and employment, the patients that did not return to work were more likely to receive some sort of benefit 1 year pre-surgery and had more comorbidity overall. This group might benefit from counseling from primary care providers, employers, or local labor offices. Identifying individuals at risk for not returning to work remains a challenge for all health care providers, and more research is required to help as many as possible return to work after surgery.

Limitations

This study has several limitations. First, our outcome is based on the medical benefit payment records provided by NAV, and a reduction in benefits is interpreted as an indirect measure of RTW. This method is commonly used in the RTW literature and is likely sufficient in our population [1, 13, 30]. Second, we lack data on social factors, details on occupation, and a detailed psychological profile of each patient. Such information was not available in the data provided to us by NORspine and NAV, but we recommend that they are included in future studies. Third, missing data for PROMs in registry-based studies are a concern. However, a NORspine study showed no difference in outcomes between responders and non-responders [33]. We found no difference in RTW ratios between responders and non-responders in our study, which is consistent with previous studies indicating that non-responders do not bias evaluation of PROMs [7, 14, 15]. Even so, we do not know the exact reasons for non-respondence, and our results must be interpreted with this in mind. Fourth, all patients included in our study were selected for surgery and might not be representative for the total population of DCM patients. NORspine only includes patients that actually undergo surgery, and unfortunately,

we do not have any information about patients who did not receive surgical treatment. Patient characteristics, indications, surgical strategies, and medical benefit systems may vary between countries, and results from our study might consequently differ from other clinical settings.

Conclusion

At 12 months following surgery, 65% had returned to work. At the end of the 36-month follow-up period, 75% had returned to work, 5% less than the working percentage in the beginning of the follow-up period. This study demonstrates that a large percentage of patients return to work after surgical treatment for DCM.

Acknowledgements The authors wish to sincerely thank all the patients participating in this study, without whom this research would be impossible.

Funding Open access funding provided by NTNU Norwegian University of Science and Technology (incl St. Olavs Hospital - Trondheim University Hospital) The Norwegian Registry for Spine Surgery receives funding from the University of Northern Norway and Norwegian health authorities

Declarations

Conflicts of interest The authors declare no competing interests.

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The manuscript submitted does not contain information about medical device(s)/drug(s).

ISBN 978-82-326-7054-3 (printed ver.)
ISBN 978-82-326-7053-6 (electronic ver.)
ISSN 1503-8181 (printed ver.)
ISSN 2703-8084 (online ver.)

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