Minimally Invasive versus Open Lumbar Interbody Fusion Trial (MIOLIFT): a randomized controlled trial for surgical treatment of lumbar spondylolisthesis and foraminal stenosis

Published: 11-07-2023
Last updated: 07-04-2024

Currently, available literature on costs and clinical effectiveness of MITLIF compared to OTLIF for patients with lumbar spondylolisthesis and degenerative foraminal stenosis is not sufficient. With a steep increase in the number of instrumented...

Ethical review	Approved WMO
Status	Pending
Health condition type	Bone and joint therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON53233

Source
ToetsingOnline

Brief title
MIOLIFT

Condition

- Bone and joint therapeutic procedures

Synonym
spinal canal stenosis; nerve pain

Research involving
Human

Sponsors and support

Primary sponsor: Zuyderland Medisch Centrum
Source(s) of monetary or material Support: neuro-orthofonds (PAG)

Intervention

Keyword: Instrumented fusion, Minimally invasive, Spine, Spondylolisthesis

Outcome measures

Primary outcome

Change in quality-adjusted life years (QALY) measured with EQ-5D-5L.

Secondary outcome

Cost-effectiveness measured using the productivity related costs (iPCQ), informal care costs (limited iVICQ) and medical costs (iMCQ).

Quality of life measured using the following PROMs: Oswestry Disability Index (ODI), Short Form (36) Health Survey (SF-36), Visual Analogue Scale (VAS) score of back pain and leg pain and Hospital Anxiety Depression Scale (HADS).

Complications as a result of surgery, are defined as: dural tear, postoperative infection, deep venous thrombosis, hematoma, hardware failure, neurological deficits and other complications as pneumonia or urinary tract infection.

Care-related Quality of life measured using the CarerQol-7D and SRB, included in the limited Valuation of Informal Care Questionnaire (iVICQ).

Process evaluation will be performed according to the framework provided by

Saunders (19). Interviews will be held with randomly chosen patients and ICG, and the principal investigator to collect qualitative data.

Other study parameters

Other study parameters are: sex, age, BMI, smoking habits, occurrence of diabetes, diagnosis, level, grade of spondylolisthesis, previous back surgery and ASA classification.

Also, perioperative morbidity, assessed with: duration of surgery, intraoperative blood loss, duration of hospitalization.

Study description

Background summary

With the growing global healthcare expenses, economic evaluations are more important than ever. Due to the aging population, the number of surgical spine procedures is expected to increase, resulting in higher healthcare-related costs (1-3). Previous studies, concerning the national US bill for instrumented spine surgery, have shown a 7.9 fold increase between 1998 and 2008 and a 2.8 fold increase between 2004 and 2015 (4, 5). In the Netherlands, spine complaints are responsible for 25% of healthcare-related costs for musculoskeletal disease (6). To limit the increase of the healthcare-related costs of instrumented spine surgery in an aging population, medical practitioners should consider the most cost-effective surgical technique, especially when both techniques have comparable clinical outcomes (3, 7, 8). Common indications for instrumented lumbar spine surgery are lumbar spondylolisthesis and degenerative disc disease. Spondylolisthesis is a slippage of one vertebral body over another, mostly caused by one of the following three pathophysiological mechanisms; facet joint degeneration, lysis in the pars articularis, or postoperative changes after decompression surgery (3, 9). Degenerative disc disease can cause foraminal stenosis by a reduction in the available space for the exiting nerve root by osseus or ligamentous hypertrophy, thus leading to nerve root compression. Lumbar spondylolisthesis and degenerative foramen stenosis can cause back pain, neurogenic claudication, and lumbar radiculopathy (10). If conservative treatment fails, instrumented spine surgery can be performed to relieve complaints and restore spinal

stability. A widely used surgical technique is the open transforaminal lumbar interbody fusion (OTLIF). In OTLIF, a unilateral transforaminal approach with unilateral facetectomy is used to insert a single cage, combined with posterior pedicle-screw fixation (11). A newer, minimally invasive variation to this technique (MITLIF) is gaining popularity. In MITLIF, decompression and cage insertion are performed through tubular retractors, combined with percutaneous posterior pedicle-screw fixation. Previous literature generally describes comparable or improved clinical effectiveness for MITLIF compared to OTLIF. Furthermore, studies reported significantly less blood loss, less complications and shorter duration of hospitalization associated with MITLIF compared to OTLIF. It is hypothesized that these differences are a result from less iatrogenic damage associated with the minimally invasive approach (3, 12-16). There are no strict indications for using either technique, nor is literature in this matter conclusive. As a result, the choice for technique is greatly based on surgeon*s experience and preference.
Comparable clinical outcome, but less complications, less blood loss, shorter duration of hospitalization, lower pharmacy and laboratory costs, lower physical therapy costs could result in MITLIF being more cost-effective compared to OTLIF. However, prospective randomized studies directly comparing the cost-effectiveness of OTLIF and MITLIF from both hospital and societal perspectives are needed to obtain higher levels of evidence (3). In addition, process evaluation will be performed to improve care.

In summary, the hypothesis of this randomized controlled trial study is that MITLIF is the preferred technique in patients with neurogenic claudication or lumbar radiculopathy caused by single level lumbar spondylolisthesis or degenerative foraminal stenosis for the following reasons: 1) Clinical and patient*s outcome following MITLIF is not inferior compared to OTLIF; 2) Direct healthcare-related costs of MITLIF are lower; 3) Indirect costs of MITLIF are lower; 4) MITLIF is more cost-effective compared to OTLIF.

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Study objective

Currently, available literature on costs and clinical effectiveness of MITLIF compared to OTLIF for patients with lumbar spondylolisthesis and degenerative foraminal stenosis is not sufficient. With a steep increase in the number of

instrumented spinal fusion procedures, the expected further increase in the future, and the associated costs, there is a need for comparative data to develop evidence-based treatment recommendations.

Primary objective:
To determine whether the MITLIF procedure is not inferior to the OTLIF procedure, in increasing quality of life, measured as the amount of change on the EQ-5D-5L, in patients with degenerative, iatrogenic, or isthmic single level lumbar spondylolisthesis or degenerative foraminal stenosis.

Secondary objectives:
1. To determine whether the MITLIF procedure is cost-effective (measured with productivity related costs (iPCQ), informal costs (limited iVICQ), medical costs (iMCQ), EQ-5D-5L and Short Form (36) Health Survey) compared to the OTLIF procedure.

2. To determine whether the MITLIF procedure is associated with increased quality of life (measured with: Oswestry Disability Index (ODI), Short Form (36) Health Survey, Visual Analogue Scale (VAS) score of back pain and leg pain, Hospital Anxiety Depression Scale (HADS)) than the OTLIF procedure.

3. To determine whether the MITLIF procedure is associated with less complications (defined as: dural tear, postoperative infection, deep venous thrombosis, hematoma, hardware failure, neurological deficits, medical other complications as pneumonia or urinary tract infection) than the OTLIF procedure.

4. To determine whether the MITLIF procedure is associated with lower/higher scores postoperatively on Care-related Quality of Life (measured with CarerQol-7D, SRB) than preoperatively.

5. To evaluate the experiences and opinions of patients, ICG and professionals regarding MITLIF and OTLIF processes.

Study design

Prospective, Randomized Controlled non-inferiority Trial (RCT; blinding for the statistician, not for the patient, the clinician and the researcher). The study includes patients with single level symptomatic lumbar degenerative foraminal stenosis or spondylolisthesis of degenerative, iatrogenic, or isthmic order. Neurogenic claudication or radicular leg pain are caused by a central spinal canal stenosis or uni-, or bilateral foraminal stenosis. Preferred surgical therapy is single level LIF (lumbar interbody fusion) surgery with decompression of the symptomatic neural structures, combined with pedicle screw fixation. Patients eligible for inclusion and interested in our study will be referred to the researchers. The researchers will inform the patient, and when they are willing to participate and meet the inclusion criteria, include them. These patients are randomly divided into two parallel groups (1) MITLIF and (2)

OTLIF. The study inclusion period will be approximately two years. Follow-up period requires two years, which results in a total study duration of four years.
Treatment is performed by an experienced orthopaedic surgeon and neurosurgeon, who possesses adequate knowledge of both treatment methods.
To study the quality of life and burden of ICG before and after MITLIF or OTLIF surgery, ICG of participating patients will be informed and asked for informed consent.

Intervention

Investigational treatment

A. MITLIF group. After receiving antibiotic prophylaxis, the patient is brought under general anaesthesia and positioned in prone position. Tubular retractors are used to access the posterior elements, allowing decompression. The retractor is seated against the posterior elements. In case of spinal canal stenosis, the central part of the spinal canal is decompressed by laminectomy. Unilateral exposure to the intervertebral disc is assured by total unilateral facetectomy, decompressing the descending and leaving roots. In case of bilateral symptomatic leg pain, the side of the unilateral approach is free of choice for the surgeon. Unilateral facetectomy is performed to gain access to the intervertebral disc. Endplate cartilage is prepared to provide a host bed of bleeding subchondral bone for placement of the cage. The TLIF cage size is determined by a trial cage and fluoroscopy. The definitive cage is filled with autologous bone or allograft and is tamped into place. Its position is checked radiological. After placement of the TLIF cage, the remainder of the disc space is filled with autologous bone, obtained from the decompression. Pedicle-screws will be placed percutaneously. A titanium rod interconnects the screws on each side. The retractors are removed and the wounds are thoroughly irrigated and closed in several layers without suction drainage.

B. OTLIF group. After receiving antibiotic prophylaxis, the patient brought under general anaesthesia and positioned in prone position. A midline approach is performed, exposing the posterior lumbar elements including the facet joints. Pedicle screws are placed bilaterally, using fluoroscopic guidance or navigation, depending on preference of the surgeon. In case of spinal canal stenosis, the central part of the spinal canal is decompressed by laminectomy. Unilateral exposure to the intervertebral disc is assured by total unilateral facetectomy, decompressing the descending and leaving roots. In the case of bilateral symptomatic leg pain, the side of the unilateral approach is free of choice for the surgeon. Unilateral facetectomy is performed to gain access to the intervertebral disc. Endplate cartilage is prepared to provide a host bed of bleeding subchondral bone for placement of the cage. The TLIF cage size is determined by a trial cage and fluoroscopy. The definitive cage is filled with autologous bone or allograft and is tamped into place. Its position is checked radiological. After placement of the TLIF cage, the remainder of the disc space

is filled with autologous bone, obtained from the decompression. A titanium rod interconnects the screws on each side. The spreader is removed and the wound is thoroughly irrigated and closed in several layers without suction drainage.

Use of co-intervention
Both groups receive the same perioperative protocol. This includes:
- pre-operative Cefazolin (two grams intravenous, 30 minutes before incision, or adequate alternative whenever a patient is allergic);
- post-operative pain management based on local hospital protocol;
- standard physical therapy during hospitalization for mobilization instructions;
- no mandatory physical therapy at home for the first six to eight weeks postoperatively;
- deep venous thrombosis prophylaxis according to local hospital protocol;
- the position of the implants will be checked by the means of lumbar spine X-ray (AP and lateral);
- Partially (web based) follow-up at 3, 6, 12 and 24 months postoperatively.

Study burden and risks

MITLIF and OTLIF are currently standard care for patients with symptomatic single level lumbar degenerative, iatrogenic, or isthmic spondylolisthesis or degenerative foraminal stenosis. The choice of technique is mainly based on surgeon*s experience and preference. For patients who are eligible for TLIF surgery through a posterior approach, participating in this study does not pose any extra risks.
The burden for patients and ICG participating in this trial is low. Patients are asked to fill out paper or online questionnaires concerning Patient Related Outcome Measurements (PROMS) (HADS, ODI, EQ-5D-5L, SF-36, VAS) at five fixed time-points (pre-operatively, and 3, 6, 12 and 24 months postoperatively). To determine cost-effectiveness, productivity related costs (iPCQ) and medical costs (iMCQ)) are recorded additionally at the five time-points. There are no extra visits to the outpatient clinic. There are no benefits in participating in this study compared to care as usual. ICG are asked to fill out the paper or online questionnaire concerning the CarerQol-7D, SRB, the intensity of caregiving and informal care costs (limited-iVICQ) at 3 fixed time-points (preoperatively, and 3 and 6 months postoperatively).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Indication for MITLIF (minimal invasive transforaminal lumbar interbody fusion) or OTLIF (open transforaminal lumbar interbody fusion) surgery.
- Clinical mono uni- or bilateral lumbar radiculopathy or intermittent neurogenic claudication caused by a single level degenerative foraminal stenosis or isthmic, iatrogenic, or degenerative spondylolisthesis gr I or II according to Meyerding classification at level L3L4, L4L5 or L5S1.
- Age over 18 years.
- Single level degenerative foraminal stenosis or isthmic, iatrogenic, or degenerative spondylolisthesis causing central stenosis on MRI (or CT), of which the anatomical level is corresponding to the clinical syndrome.
- Psychosocially, mentally, and physically able to fully comply with this study protocol.
- Informed consent prior to this study.

Exclusion criteria

- Previous radiotherapy at the intended surgical level.
- (Progressive) motor failure and/or anal sphincter disorders which urges

instant intervention.
- Active spinal infection.
- Immature bone (on-going growth).
- Active malignancy.
- Pregnancy.
- Symptomatic osteoporosis (Current or previous use of bisphosphonates).
- Contra-indications for anaesthesia or surgery.
- Inadequate command of the Dutch language.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2023
Enrollment:	198
Type:	Anticipated

Ethics review

Approved WMO

Date:	11-07-2023
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL83923.096.23