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Clinical evaluation of percutaneous transforaminal endoscopic discectomy (PTED) and paraspinal minitubular microdiscectomy (PMTM) for lumbar disc herniation: study protocol for a randomised controlled trial

Ze Yan Liang, Yuan Dong Zhuang, Chun Mei Chen , Rui Wang

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ZYL and YDZ contributed equally.

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Neurosurgery, Fujian Medical University Union Hospital, Fuzhou, Fujian, China

Correspondence to
Dr Chun Mei Chen;
cmchen2009@sina.com

ABSTRACT

Introduction For sciatica caused by lumbar disc herniation (LDH), the standard surgical technique is conventional microdiscectomy. In recent years, minimally invasive techniques (eg, percutaneous transforaminal endoscopic discectomy (PTED), paraspinal minitubular microdiscectomy (PMTM)) have gained increasing interest. PTED and PMTM are considered alternative minimally invasive techniques for the treatment of LDH. Due to insufficient evidence, the differences in efficacy between PTED and PMTM have been debated. A pragmatic, multicentre, non-inferiority, randomised controlled trial has been designed to determine the efficacy and cost-effectiveness of PTED versus PMTM for the treatment of LDH.

Methods and analysis A total of 280 patients (18–70 years) presenting with significant symptoms of sciatica and failure after 3 months of conservative treatment will be recruited. Patients must have an indication for surgery based on MRI demonstrating LDH with nerve root compression. Patients will be randomised to PTED or PMTM treatment. The primary outcome is Oswestry Disability Index scores. Secondary outcomes include Visual Analogue Scale scores, Short Form 36 health survey scores, physical examination, length of hospital stay, costs and complications. Outcomes will be measured the day following surgery, at 1 week, and at 1, 3, 6, 12 and 24 months after surgical treatment. Physical examination will be conducted at 1 week, 1 month and 12 months after surgery. The non-inferiority margin for the primary outcome is 5.

Ethics and dissemination Ethical approval has been granted by the Ethics Committee of Fujian Medical University Union Hospital, Fuzhou, China (2018YF010-02). Results of the research will be published in an international peer-reviewed scientific journal and disseminated through presentation at scientific conferences.

Trial registration number ChiCTR1800015727; Pre-results.

Strengths and limitations of this study

- Large, multicentre, pragmatic, randomised controlled trial designed to evaluate the efficacy and cost-effectiveness of percutaneous transforaminal endoscopic discectomy versus paraspinal minitubular microdiscectomy for the treatment of lumbar disc herniation.
- Use of standardised and validated outcomes instruments.
- Potential performance bias due to the lack of participant blinding.

INTRODUCTION

Surgery is recommended when patients with sciatica caused by lumbar disc herniation (LDH) are refractory to conservative treatment or have been associated with progressive neurological deficits.[1 2] In 1934, Mixter and Barr[3] reported the first successful LDH operation. Subsequently, Yasargil[4] and Caspar[5 6] performed conventional microdiscectomy (CMD) with the advent of the microscope, which redefined the surgical treatment of LDH. To date, CMD remains the standard surgical technique for the treatment of LDH.[7 8]

In 1997, Foley[9] and Smith[10] introduced microendoscopic discectomy (MED) for the treatment of LDH. In 2002, Greiner-Perth R *et al*[11] demonstrated that the use of tubular retractors and trocar systems combined with microscopy could overcome the disadvantage of the two dimensionality of the endoscopic image obtained during traditional CMD. Since then, the results of multiple randomised controlled trials (RCTs) and systematic reviews[12–15] comparing the efficacy of tubular microdiscectomy (TMD) and CMD have revealed no significant difference between the two. Recently, Zhuang *et al* and Chunmei *et al*[16 17] improved on the tubular retractors

and trocar systems and introduced the paraspinal minitubular microdiscectomy system (PMTM). PMTM is characterised by a smaller tubular diameter which can achieve bilateral decompression based on the surgical approach from one side. Another more recently developed technique is percutaneous transforaminal endoscopic discectomy (PTED). With the advent of the transforaminal endoscopic spine system (TESS) developed by Hoogland *et al*,[18 19] PTED has become more mature and complete. Based on recent work,[20–23] PTED is a safe and minimally invasive alternative technique for the removal of a lumbar disc herniation.

PMTM and PTED are considered minimally invasive alternatives for the treatment of LDH.[24 25] Nevertheless, there are some significantly different characteristics.[25] For example, PMTM is performed under general anaesthesia and with a direct view of the herniated disc. The latter is conducted under local anaesthesia and with an indirect endoscopic view. According to the current literature,[26] possible advantages of PTED versus PMTM are the following: (1) decreased medical costs due to local versus general anaesthesia; (2) to the feasibility of removing intraforaminal and extraforaminal herniated discs and (3) shorter operation time. Recently, Seiger *et al*[27] reported an ongoing, multicentre, high-quality PTED-related RCT study, but this study compared the efficacy of PTED and OM for LDH. Hence, there currently exists no high-quality, prospective study to examine the difference in the efficacy between the two approaches.

To date, the differences in efficacy and cost-effectiveness between PMTM and PTED remain controversial. Therefore, this study protocol was designed for a forthcoming, prospective RCT. This study used a non-inferiority design, assuming that PTED is not less efficacious nor less cost-effectiveness compared with PMTM in patients with sciatica and LDH.

METHODS AND ANALYSIS

Study description

This study protocol describes a pragmatic, multicentre, non-inferiority RCT comparing the efficacy and cost-effectiveness of PMTM and PTED using parallel controls. The follow-up period will last 2 years. After patients sign a written informed consent to participate, they will be randomised to one of two groups: the A group will receive PMTM treatment and the B group will receive PTED treatment. The primary outcome measure is Oswestry Disability Index (ODI).[28] Secondary outcomes include Visual Analogue Scale (VAS)[29] and the Short Form 36 (SF-36) health survey,[29] physical examination, length of hospital stay, costs and complications. The timing of screening, randomisation, treatment allocation and assessment is summarised in table 1.

Participant recruitment and eligibility

All patients will be between 18 and 70 years of age. Patients should present significant symptoms of sciatica

Table 1 Flow chart visits and case report forms

Visits and case report forms	Intake +baseline	Surgery	1 week following treatment	1 month following treatment	3 months following treatment	6 months following treatment	12 months following treatment	24 months following treatment
Eligibility screen	✓							
Informed consent	✓							
Randomisation	✓							
Operation		✓						
ODI	✓		✓	✓	✓	✓	✓	✓
VAS of leg pain and back pain	✓		✓	✓	✓	✓	✓	✓
SF-36	✓		✓	✓	✓	✓	✓	✓
Physical examination	✓			✓		✓	✓	
Costs		✓	✓	✓	✓	✓	✓	✓
Surgical data		✓						
Reoperation and complications	With occurrence							

ODI, Oswestry Disability Index; SF-36, Short Form 36; VAS, Visual Analogue Scale.

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Box 1 Selection criteria for trial eligibility

Inclusion criteria
- Aged 18–70 years.
- Persistent radicular pain lasting more than 3 months.
- Indication for surgery.
- Disc herniation with nerve compression with or without concomitant spinal or lateral recess stenosis or sequestration confirmed. MRI.
- Informed consent.
- Sufficient knowledge of the Chinese language to complete forms and follow instructions independently.

Exclusion criteria
- Previous surgery on the same or adjacent disc level.
- Cauda equina syndrome.
- Spondylytic or degenerative spondylolisthesis.
- Pregnancy.
- Severe somatic or psychiatric illness.
- Excessive obesity.

caused by disc herniation, as confirmed by MRI. Patients should also meet the criteria of failure to improve after 3 months of conservative treatment. Detailed inclusion and exclusion criteria are listed in box 1.

Eligible patients with LDH will be referred by participating surgeons following a formal outpatient assessment. To recruit sufficient patients, a multicentre design is necessary. This study follows the informed consent principle; thus, it is necessary for each patient to provide a written informed consent prior to group randomisation.

Patient and public involvement statement

The patients and the public were not (or will not) be involved in the design, conduct, reporting or dissemination of the research.

Randomisation and blinding

Once written informed consent has been obtained, patients are to be randomised to receive either PMTM or PTED treatment at a ratio of 1:1. Participants will be randomised by using a block randomisation model (block size 6). Computer-generated, random-number tables will be prepared by an experienced statistician. After obtaining baseline data and a physical examination, allocation of treatment will be performed by the computer system, and results of allocation will be provided to the surgeon in a concealed envelope the day before surgery. Due to the noticeable differences between the PMTM and PTED procedures, blinding of the patients will not be strictly required. However, all researchers and data analysts will be blinded as to the allocated intervention during the follow-up period of 2 years.

Treatment

Patients will be randomised into either PMTM or PTED treatment. Verification of the affected disc level will be performed by a mobile image intensifier with fluoroscopy (anteroposterior and lateral view). PMTM will be performed under general anaesthesia, whereas PTED will be operated under local anaesthesia. All patients will be placed in the standard prone position. The surgeons involved in this study have extensive experience in both procedures.

Intervention: PMTM

A small paraspinal incision (1.5–1.8 cm) will be made and the skin will be retracted laterally. The trocar and sequential tubular retractors will be placed paraspinally under fluoroscopic control. Subsequently, the lumbar fascia and muscles will be bluntly separated step by step. After exposure of the interlaminar space, the working tubular retractor will be fixed through a flexible arm. If necessary, a minimal interlaminar fenestration will be performed by use of drills. With the aid of the operative microscope (Carl Zeiss), further surgery, including a unilateral flavectomy and discectomy, will be performed. After the removal of all fragments, a pulsation of the nerve root will be visible. Following removal of the working tubular retractor, the wound will be closed in layers.

Intervention: PTED

PTED will be performed using a standardised transforaminal approach and 'outside-in' surgical technique using the TESS.[18] A skin incision measuring 0.8–1.0 cm in length will be made above the dorsolateral side of the pelvis and 10–14 cm from the midline.[18]The puncture needle will be inserted from the incision to the superior articular process of the lower involved vertebrae. After checking the position of the puncture needle under fluoroscopic control, a guidewire will be set. Next, the sequential straight guide rods and a drill/reamer will be placed along the guidewire or rods. After enlarging the intervertebral foramen, the working cannula and the endoscope will be introduced. Following removal of the herniated disc, the pulsation of the nerve root and/or dural sac should be visible in most cases.[18] Subsequently, removal of the working cannula and the endoscope will be performed.

Baseline assessment

Baseline records will include demographics, employment status, smoking history, history of lower back pain, family history of sciatica, results of a physical examination, body mass index, herniated disc level, VAS scores, ODI scores and SF-36 scores. Data are to be collected prior to randomisation.

Outcomes assessment

The outcome parameters will be assessed by following validated questionnaires and by physical examination. Data from questionnaires will be collected at 1 week and at 1, 3, 6, 12 and 24 months following surgery by the research nurse. The physical examination will be performed at 1, 6 and 12 months following surgery (table 1).

Primary outcome measure

Oswestry Disable Index

The ODI 2.1a will be used to measure functional status within 10 domains of daily activity including pain

intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life and travel. The total score of ODI ranges from 0 to 100, with higher scores indicating greater disability.

Secondary outcome measures

VAS of leg and back pain

The parameter will measure perceived pain intensity by VAS score (scale ranging from 0 (no pain) to 100 mm (the worst pain imaginable)). Because some patients experience lower back pain, both the extent of leg pain and lower back pain will be assessed.

Short Form 36

Several generic quality-of-life outcome measures have been identified. Among these, the SF-36 has been found to be sensitive to quality of life changes in the chronic lower back pain population.[29] The questionnaire is subdivided in eight domains: (1) physical functioning, (2) physical role limitations, (3) emotional role limitations, (4) social functioning, (5) physical pain, (6) general mental health, (7) vitality and (8) general health perception. A higher score reflects a better health condition.

Physical examination

Physical examination will be conducted 1, 6 and 12 months after surgery. This will include straight leg raising test, crossed straight leg raising test, patellar and Achilles tendon reflex assessment and strength measurement of the quadriceps femoris and triceps surae. Muscle strength of the quadriceps femoris and triceps surae will be measured from a sitting position. Muscle strength will be scored on a scale are ranging from 0 (no contraction) to 5 (normal muscle strength).[30]

Costs

The primary costs of treatment will include the cost of hospital admission, surgery, medication, rehabilitation and other healthcare utilisations. The details of these charges will be registered in a diary.

Length of hospital stay

Patients achieving off-bed activity with no complications will be discharged.

Complications

Immediately following operation, a systematic assessment of complications (including cerebrospinal fluid leakage, venous thromboembolism, wound infection, urinary tract infection, haematoma, progressive neurological deficit) will be conducted by the surgeon and research nurse until patient discharge.

Others

Surgical data

Surgical data will include intraoperative dural tear, nerve root injury, operative time and intraoperative blood loss.

Table 2 Non-Inferiority margins

Outcome measurements	Expected differences	Non-inferiority margin
ODI	<5	5
VAS	<5	5
SF-36	<5	5
Straight leg raising test	<5	5
Crossed straight leg raising	<5	5

ODI, Oswestry Disability Index; SF-36, Short Form 36; VAS, Visual Analogue Scale.

Sample size

The sample size for this study was calculated based on the ODI scores. Across studies, the mean difference and SD for the ODI used in the sample size calculation was: mean 3.2, SD 8.5.[20] Sample size for non-inferiority trials was calculated using: (1) significance level (alpha) of 0.05; (2) power (beta) of 90%. The margin of non-inferiority was listed in table 2.[21] We estimated that 116 patients would need to be included in each group. Accounting for 10% attrition and the actual situation of each participating centre, 280 patients will be recruited in total. We intend to complete the recruitment of patients within 2 years. Recruitment for the study has begun as of September 2018.

Statistical analysis

All data will be analysed according to the 'intention-to-treat principle'.[31–33] Baseline data will be compared and analysed by descriptive statistics (means (SD), proportion or median (range)) to determine whether balanced groups are obtained after randomisation. The Student's t-test or the Mann-Whitney U test will be used to compare continuous variables. Categorical variables will be compared using the χ^2 tests or Fisher's exact test. Furthermore, an exploratory subgroup analysis will be carried out to investigate whether the treatment effect varied over a specific subgroup of patients (box 2). All comparative analyses will be reported with point estimates (means (SD) or ORs), 95% CIs and p values. A $p<0.05$ is set for significance. Non-inferiority margins are set and listed in table 2. Statistical analysis will be performed using appropriate statistical software (eg, SPSS version 22.0 or Stata).

Box 2 Selected prognostic variables for subgroup analysis

Demographic variables:
Age <40 years versus >40 years.

Radiological variables:
Median versus mediolateral and lateral disc herniation.
High versus low height of disc level.

ETHICS AND DISSEMINATION

This article describes a protocol for a prospective, non-inferiority randomised controlled trial to examine the efficacy and cost-effectiveness of PTED versus PMTM in the treatment of LDH. Informed consent will be obtained prior to randomisation from all eligible participants (see online supplementary appendix 1). Results of the research will be published in an international peer-reviewed scientific journal and disseminated through presentation at scientific conferences.

Contributors CC, YZ, ZL and RW are the principal investigators and have coordinated all the phases of trial design, statistical analysis plan and drafting of the protocol. ZL and YZ wrote the manuscript. All authors contributed to refinement of the study protocol and approval of the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethical approval has been granted by the Ethics Committee of Fujian Medical University Union Hospital, Fuzhou, China (2018YF010-02).

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ORCID iD

Chun Mei Chen http://orcid.org/0000-0002-4483-7465

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