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Transforaminal lumbar interbody fusion with cortical bone trajectory screws versus traditional pedicle screws fixation: a study protocol of randomised controlled trial

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ABSTRACT

Introduction Transforaminal lumbar interbody fusion (TLIF) has been widely used in the treatment of lumbar degenerative disc disorders and shows favourable clinical results. Recently, cortical bone trajectory (CBT) has become a new trajectory for screw insertion in the lumbar spine. Several biomechanical studies have demonstrated that the CBT technique achieves screw purchase and strength greater than the traditional method. Currently, the available data on the clinical effectiveness of the two performed surgeries, TLIF with CBT screws (CBT-TLIF) and TLIF with traditional pedicle screws (PS-TLIF), are insufficient. This is the first randomised study to compare CBT-TLIF against traditional PS fixation and will provide recommendations for treating patients with lumbar degenerative disc disorders.

Methods and analysis A blinded randomised controlled trial (blinding for the patient and statistician, rather than for the clinician and researcher) will be conducted. A total of 254 participants with lumbar disc degenerative disease who are candidates for TLIF surgery will be randomly allocated to either the CBT-TLIF group or the PS-TLIF group at a ratio of 1:1. The primary clinical outcome measures are the incidence of adjacent cranial facet joint violation, fusion rate and the screw loosening rate. Secondary clinical outcome measures are Visual Analogue Scale (VAS) of back pain, VAS of leg pain, Oswestry Disability Index, operative time, intraoperative blood loss and complications. These parameters will be evaluated on day 3, and then at 1, 3, 6, 12 and 24 months postoperatively.

Ethics and dissemination This study has been reviewed and approved by the Institutional Review Board of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University (batch: 2017–03). The results will be presented in peer-reviewed journals and an international spine-related meeting after completion of the study.

Trial registration number NCT03105167; Pre-results.

Strengths and limitations of this study

- This trial is designed to have a feasible, comparative effectiveness trial design that has similarities to common clinical situations.
- This study is the first randomised controlled trial to compare transforaminal lumbar interbody fusion with cortical bone trajectory screws against traditional pedicle screws.
- The size of the study sample limits the power of the observations.

INTRODUCTION

Along with growth in age, the occurrence of lumbar disc degenerative diseases is also growing.[1 2] Lumbar intervertebral fusion is the accepted method of surgery[3] if conservative treatment, including physiotherapy and drug therapy, of lumbar degenerative disease proves ineffective. These days, transforaminal lumbar interbody fusion (TLIF) is widely used in the therapy of lumbar disc disorders and shows favourable clinical results.[4 5]

Santoni *et al*[6] presented a fresh technique of pedicle screw (PS) insertion named the cortical bone trajectory (CBT) for lumbar screw, which has been proposed to be maximally in contact with the thread of this higher density bone surface. As an alternative, both cadaveric[7 8] and clinical studies[8] have proposed, or investigated the viability of, a novel CBT screw fixation technique whereby the screw follows a caudocephalad path and laterally directed path through the pedicle.

CBT screw fixation has evolved into an alternative to spinal instrumentation that can overcome some of the limitations of traditional PS fixation. Matsukawa *et al*[9] clarified that the incidence of adjacent cranial facet joint violation (FJV) caused by CBT screw fixation was lower than that of PS fixation. FJV was reported to be closely related to symptomatic adjacent segment disease,

which may affect the fusion rate (FR) after lumbar intervertebral fusion surgery.

Single-segment lumbar interbody fusion with CBT screws fixation demonstrates some advantages, such as lower rate of screw loosening, reduced loss of correction and is less invasive, compared with percutaneous PS fixation.[10] Kasukawa *et al*[11] examined the outcomes of TLIF with CBT screw fixation (CBT-TLIF) versus TLIF with traditional pedicle screw fixation (PS-TLIF). They showed that CBT-TLIF resulted in reduced blood loss and a shorter operation than PS-TLIF, and showed similar efficacy in the postoperative rates of bone union, maintenance of lordotic angles and accuracy of PS positions between the two groups. Chin *et al*[12] showed that the Visual Analogue Scale (VAS) and Oswestry Disability Index (ODI) scores of patients were significantly improved after lumbar fusion combined with CBT screws. However, the evidence was poor and limited by trials rated as having a high risk of bias and substantial clinical heterogeneity in controlled clinical trials (CCTs). Therefore, their conclusion could not prove that the efficacy of CBT-TLIF was better than that of PS-TLIF.

Compared with CCTs, randomised controlled trials (RCTs) have the superiority of controlling all possible variables because of the random sequence generation, in which confounding and bias may be more problematic. High-quality RCTs are often deemed to be the gold standard for investigating the consequence of an intervention. For all we know, no randomised controlled study of the clinical outcomes of CBT-TLIF versus PS-TLIF has been performed. In this study, we will perform an RCT to compare CBT-TLIF and traditional PS fixation.

METHODS AND DESIGN

This study conforms to the Declaration of Helsinki and is approved by the Institutional Ethics Review Board of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. All participants will be asked to sign an informed consent form. This trial has been registered at the US National Institutes of Health Clinical Trials Registry: NCT03105167. The protocol conforms to the Standard Protocol Items Recommendations for Interventional Trials.[13] Figure 1 provides the chart of the trial design.

Participants

This study is a parallel group RCT conducted at the Orthopaedic Hospital, Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University.

Randomisation and blinding

Participants will be equally randomised to either the CBT-TLIF group or the PS-TLIF group based on a permuted blocks randomisation scheme. Using a block size of four in a scheduled computer-generated randomisation program, the final group assignments will be sealed in opaque envelops. In order to ensure the proper management of the randomisation procedure, the sequence numbers will be marked on the opaque envelope, and the group assignment will be sealed inside. All envelopes will be numbered sequentially. The envelops will be delivered according to patients' sequence numbers, and the surgeon will be informed of the random numbers and group assignments by either telephone or email. Patients will remain blinded for the allocation until the last questionnaires have been completed. At the final follow-up period, the blind can be released to the patient's request. In addition, the assessor will also be blinded.

Inclusion criteria

1. age of at least 18 years
2. chronic lower back pain alone or associated with neurological symptoms of the lower limbs after receiving failed conservative treatment for a period of more than 3 months
3. indication for monosegmental TLIF due to degenerative disc disease (including spondylolisthesis, foraminal stenosis, spinal stenosis lumbar disc herniation and painful disc degeneration).

Exclusion criteria

1. spinal scoliosis with a Cobb angle of more than 10° in the index level
2. previous failed fusion at the same level
3. pregnancy
4. active infection or surgical site of the previous infection
5. planned (e)migration abroad within 2 years after inclusion
6. metabolic bone disease
7. spondylolisthesis according to Meyerding grades III and IV
8. patients with glucocorticoid or immunosuppressants therapy.

Interventions

CBT-TLIF group

After using antibiotics 30 min before the operation, a posterior midline skin incision was made at the fused level identified using fluoroscopy, and a pilot hole of the CBT screws was created with the drill according to Matsukawa *et al*.[14] After the trajectory was created by a pedicle probe from the starting point, screws were placed bilaterally along the trajectories. Appropriate screw length and tap size are critical to prevent pars or pedicle fracture. A thorough posterior decompression including unilateral facetectomy and total discectomy was carried out. The endplate cartilage was ready to offer a bleeding subchondral bone to place a cage. The disc space was filled with autogenous bone obtained from the decompression and its position was checked

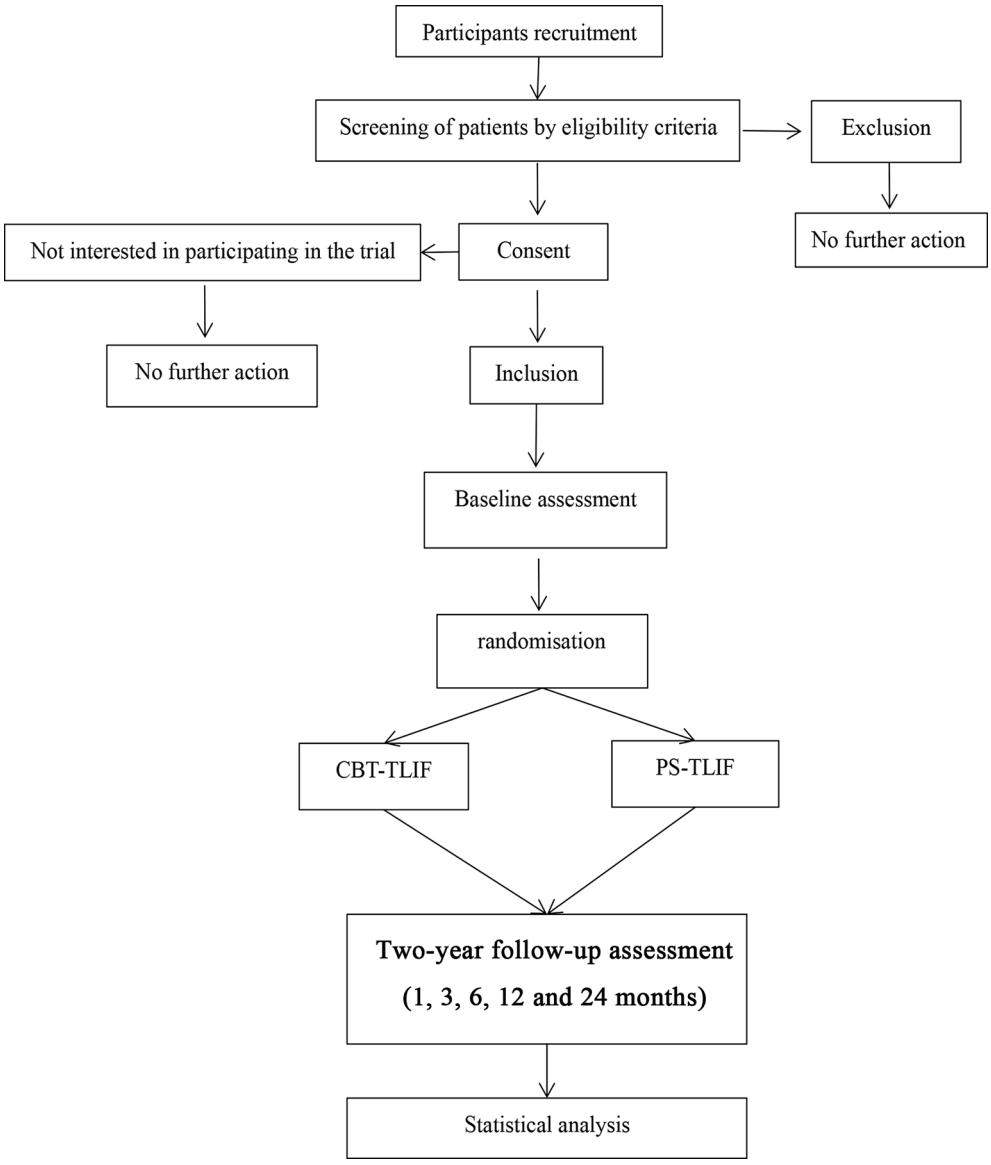

Figure 1 Flow chart showing the steps in participant recruitment, treatment and analysis. CBT-TLIF, transforaminal lumbar interbody fusion with cortical bone trajectory screws; PS-TLIF, Transforaminal lumbar interbody fusion with traditional pedicle screws.

radiologically. Two rods were used to connect with screws on either side.

PS-TLIF group

After using antibiotics 30 min before the operation, patients were placed under general anaesthesia in the prone position. A posterior small incision was made at the indexed segment and a starting point of PS was drilled. A pilot hole of the PS screws was created with the drill. Screws were inserted along the trajectory of PS screw. A thorough posterior decompression including unilateral facetectomy and total discectomy was carried out in response to patients' pathological conditions. Afterwards, preparation of endplate cartilage was performed. Transforaminal placement of an intervertebral cage filled with autogenous bone obtained from the decompression within the disc space was performed. Besides, two rods were used to connect with screws on either side.

Outcome measurements

Primary outcomes

1. The incidence of adjacent cranial FJV. FJV will be evaluated by using two-dimensional CT reconstruction at 3 days and 6 months, and at 1 and 2 years postoperatively.
2. Fusion rate. FR will be evaluated by using two-dimensional CT reconstruction at 6 months postoperatively. If not fused, it will be evaluated at 1-year postoperatively once again.
3. Screw loosening rate (SLR). SLR will be evaluated at 3 and 6 months, and at 1 and 2 years postoperatively.

Table 1 Time of data collection

	Baseline	Operation	Follow-up					
Measures	Perioperation	Duration	3 days	1 month	3 months	6 months	12 months	24 months
Screening for inclusion/exclusion criteria	√							
Informed consent	√							
Assignment to two groups	√							
Baseline demographics	√							
Operative time		√						
Blood loss		√						
Complications		√	√	√	√	√	√	√
FR						√	X or √	
FJV			√			√	√	√
SLR				√	√	√	√	√
VAS of back pain	√		√	√	√	√	√	√
VAS of leg pain	√		√	√	√	√	√	√
ODI	√		√	√	√	√	√	√
JOA	√		√	√	√	√	√	√
X-ray	√		√	√	√	√	√	√

FJV, adjacent cranial facet joint violation; FR, fusion rate; JOA, Japanese Orthopaedic Association; ODI, Oswestry Disability Index; SLR, screw loosening rate; VAS of back pain: Visual Analogue Scale of back pain; VAS of leg pain, Visual Analogue Scale of leg pain.

Secondary outcomes

1. The pain degree of back and lower limb during follow-up will be assessed by the VAS of back pain and VAS of leg pain.[15] The scores of VAS of back pain and VAS of leg pain will be recorded preoperatively, at 3 days, at 1, 3 and 6 months, and at 1 and 2 years postoperatively.
2. The ODI will be recorded both preoperatively and postoperatively.[16] The ODI scores will be recorded preoperatively, at 3 days, at 1, 3 and 6 months, and at 1 and 2 years postoperatively.
3. The Japanese Orthopaedic Association (JOA) scores will be recorded both preoperatively and postoperatively including 3 days, 1, 3 and 6 months, and 1 and 2 years. Functional improvement is expressed by the rate of recovery of the JOA score.[17]
4. The parameters of intervertebral height (including anterior and posterior height of intervertebral), intervertebral foramen height and kyphosis angle will be measured in X-ray fluorescence preoperatively, at 3 days, at 1, 3 and 6 months, and at 1 and 2 years postoperatively.
5. Operative time, intraoperative blood loss.
6. Complications including pedicle fracture, intraoperative pars fracture, postoperative infection, deep venous thrombosis, nerve injury, and any other direct and indirect surgical complications will be recorded.

Table 1 presents the data collection times.

Baseline demographics

Sex, age, body mass index, smoking habit, diagnosis, level and occurrence of diabetes will be recorded.

Follow-up

Follow-up will be conducted at 3 days, and at 1, 3, 6, 12 and 24 months postoperatively.

Monitoring

All investigators who have completed good clinical practice training will independently collect the data and assess the clinical outcomes of the treatments. Safety and data monitoring will be performed periodically during the study. Only the principal investigator (WFN) will have access to the final trial data set. All paper and electronic versions of the case reports will be stored for 10 years in the secure research archives at the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University with restricted access.

Sample size calculation

As there has been no previous similar trial that has used our RCT design, we carried out a power analysis to assess the required sample size to show safety with a type I error probability of 5% and an 80% probability of avoiding a type II error. According to the related study,[9] the proportion of the control group was 11.8%, and the proportion of intervention group was 27%. We carried out a two independent proportions power analysis on PASS software

(Power Analysis and Sample Size), and the results was 106. We propose to enrol 254 participants (127 randomised to each arm) and allow for a dropout rate of 20% for an effective sample size of 212.

Statistical analysis

Data from the trial will be calculated using the SPSS V.19.0 software. Differences in the operative time and intraoperative blood loss, FR, FJV and other complications between the CBT-TLIF and PS-TLIF groups will be analysed by two independent-samples t-tests with a type I error probability of 5%. Preoperative VAS of back pain, VAS of leg pain and ODI scores, and scores taken immediately postoperation, and at postoperative 1, 3, 6 and 24 months, will be analysed by a repeated-measures analysis of variance. Changes in the data between different follow-up time points and the baseline will also be calculated, and the changes in data between the CBT-TLIF and PS-TLIF groups will be assessed by two independent-samples t-tests.

DISCUSSION

CBT screw fixation is reported as a minimally invasive technique,[18 14] and biomechanical comparisons with PS fixation have noted its biomechanical superiority.[19 20] This paper describes the rationale and protocol for conducting an RCT in China that will investigate the efficacy of CBT screws with TLIF in treating lumbar disc degenerative diseases such as lumbar spinal canal stenosis that require spinal interbody fusion surgery. In this trial, we designed a PS-TLIF group as a controlled comparison group to identify the clinical outcomes of TLIF with CBT screw fixation. The demand for spinal interbody fusion surgery has risen steeply over the last 10 years and is expected to increase even further in the near future. It is hypothesised that CBT-TLIF, compared with PS-TLIF, is superior in reducing disability and thus has a better clinical outcome.

This study is the first RCT to compare TLIF with CBT against traditional PS. An RCT has the superiority of controlling all possible variables because of the random sequence generation, in which confounding and bias may be more problematic. High-quality RCTs are often deemed to be the gold standard for investigating the consequence of an intervention.

Randomised trials that compare surgery with non-surgical treatments have several features that are distinctly different from drug trials and can lead to serious limitations. Moreover, compared with drug trials, surgery has many irreversible features.

In the case that our hypothesis is confirmed, our consequences will have an important value in the schedule and development of treatment options in spinal interbody fusion surgery. We anticipate that the results will provide more reliable evidence and clarify the value of CBT with TLIF as a treatment for patients with lumbar disc degenerative diseases.

Contributors ZHF helped to conceive and design the trial and wrote the manuscript. XBL helped to conceive of and design the trial. QT helped to conceive the trial and revised the manuscript. CGW and WHZ will recruit the patients and conduct the trial. HZ planned the statistical analysis. A-MW and NFT will supervise the trial. YSW and WFN helped to conceive and design the study and critically revised the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient consent Obtained.

Ethics approval The study had been reviewed and approved by the ethics committee of the Second Affiliated Hospital of the Wenzhou Medical University, Wenzhou, China (batch: 2017-03).

Provenance and peer review Not commissioned; externally peer reviewed.

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