SCIENTIFIC ARTICLE

New Cage for Posterior Minimally Invasive Lumbar Interbody Fusion: a Study *in Vitro* and *in Vivo*

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Objective: To design a new type of interbody fusion device made of nickel titanium NiTi shape memory alloy and to compare segmental stiffness after various posterior lumbar interbody fusion (PLIF) procedures *in vitro* and *in vivo*.

Methods: Twelve sheep lumbar functional spinal units were randomly allocated to four groups. One acted as controls (N); the other three were treated with autogenous iliac crest bone dowel graft (L), a threaded cylindrical titanium (KC) interbody fusion device (TFC) or a new type of interbody fusion device made of NiTi shape memory alloy (NT) containing autogenous iliac crest graft. In addition, 15 sheep were allocated to three groups; one served as controls and the other two underwent TFC (KC) or NiTi-FC (NT). Nondestructive mechanical tests were performed in pure compression, extension, lateral bending and torsion. The operated spines were photographed regularly to assess changes in interbody height and degree of fusion. The animals were killed at 6 months for histologic testing.

Results: Biomechanical tests showed both the strength and axial stiffness of the NT and KC groups were significantly higher than those of the control group and L group ($P < 0.05$). When the mechanical performance in torque and torsion of each group were compared, the same results could be obtained. The maximal destructive load of the NiTi-TFC was 11 200 N and the safety coefficient was above 1.2. Radiological observations revealed that the bone callus around the interbody fusion device were gradually increased postoperatively (2 months, no obvious; 4 months, poorly define; 6 months, dense). The KC and NT group had lost 16% and 16.5% of their postoperative height but remained well above normal disc height ($P < 0.05$). Histologic examination showed new trabeculation connected with that of the host.

Conclusion: The mechanical characteristics of the NiTi-TFC are excellent and it is safe and reliable.

Key words: Biomechanics; Interbody fusion device; NiTi shape memory alloy

Introduction

The benefits of minimal access were first recognized with the widespread adoption of laparoscopic cholecystectomy. Since then, increasingly complex intraabdominal procedures have been carried out using laparoscopic techniques¹. However, minimal access surgery has only recently entered the field of spinal surgery². Review of published laparoscopic series shows that the laparoscopic approach has infrequently been employed for exposure of levels cephalad to the L₅/S₁ disc space. Mahvi and Zdeblick reported a single case of L₄₋₅ fusion and commented that it was extremely difficult². In addition, it did not allow adequate decompression of the nerve root.

The procedure of minimally invasive posterior lumbar interbody fusion (PLIF) is becoming more and more popular with many advantages. Using minimally invasive techniques to complete PLIF procedure is safe and effectively and potentially reduce the pain and morbidity associated with traditional open techniques. Several studies found that minimally invasive PLIF had similar good long-term clinical outcomes of standard open TLIF procedure, with high fusion rates and the additional favorable outcomes in the aspects of less blood loss, less transfusion need, less initial postoperative pain, early rehabilitation, shorter hospitalization and fewer complications.

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Fig. 1 Photograph of lumbar interbody fusion device, the NiTi-TFC.

As in the standard open interbody fusion procedure, biomechanics in the minimally invasive spine surgery is a crucial factor which may greatly influenced the operation efficacy. Tencer *et al.* found that posterior placement of an insert can compromise the facet and lamina structures by reducing torsional stiffness, two inserts reduces this even more³. They interpreted these data as indicating that it is better to use a single insert than use two.

As to clinical studies, we were unable to find any reports of the design and use of new types of interbody fusion device for posterior minimally invasive endoscopic discectomy. Our study aimed to create a new type of interbody fusion device (TFC) made of nickel titanium (NiTi) shape memory alloy and to explore its characteristics impact on segmental stiffness. *In vitro* study, biomechanical features including strength and stiffness were compared between different groups. And *in vivo* study, we evaluated the effectiveness of the interbody fusion procedures radiographically and histologically.

Materials and Methods

New Nickel Titanium Interbody Fusion Device

The new type of NiTi minimally invasive lumbar interbody fusion device is made of NiTi shape memory alloy (components Ti-50.5–51.5%Ni). The thickness is 1.5–2.0 mm, it is 9 mm in diameter and the length is 20 mm. It has a placket on one side and an agnail extrudes from the body to prevent protrusion and rotation (Fig. 1). Its martensitic transformation temperature is 4–7 °C and the restoration temperature is 37 °C.

Animals

Nineteen sheep (4–6 years old, body weight 45–60 kg) from local Academy of Agricultural Sciences were used for this study, 4 for *vitro* and 15 for *vivo*. So the influences of these multi-factors were minimized.

In Vitro Biomechanical Tests

Four sheep were sacrificed and twelve sheep lumbar functional spinal units were obtained. The units were randomly allocated to four groups. One acted as controls (N); the other three were treated either with autogenous iliac crest bone dowel graft (L); Sofamor (Minneapolis, MN, USA) TFC (KC) or the new NiTi-TFC (NT). When the specimens were obtained they were stored at –20 °C until used. The neutral axis of each fringe sensor unit (FSU) was located on a lateral radiograph to eliminate abnormalities, fractures and severe degeneration. Before testing, the specimens were thawed at room temperature and then cleaned carefully of musculature and vessels, leaving the osteo-ligamentous tissues intact. Each segment consisted of two vertebrae with intact disc, facets, and ligamentous connections, comprising an FSU. During the thawing process and the time between tests, the specimens were wrapped in saline-soaked gauze to keep the FSU moist. After discectomy of the nucleus and preparation of the sites for each kind of fusion device, all fusion devices were placed in the prepared sites for subsequent nondestructive mechanical testing. After insertion of the fusion devices, the upper and lower sides of the specimens were fixed with bone cement, parallel to both sides with a gradient $\leq 1^\circ$ to insure precision.

- 1 Nondestructive tests were conducted using a material testing machine (omnipotent experimental machine, WD-5; Xieqiang, Shanghai, China) with the specimen mounted in an apparatus so that it was oriented perpendicular to the axis of actuation. One end of the specimen was fixed, whereas the other was free to move. Tests consisted of pure compression, extension, flexion, left and right lateral bending, and left and right torsion. For each test, 20 s cycles of preconditioning were run, followed by five data collection cycles that simulated every type of lumbar physical exercise. Stiffness was calculated as the slope of the force versus angular displacement curve in all groups.
- 2 For pure compression, extension, flexion and lateral bending, each FSU underwent a ramp load input from 0 to 300 for each cycle, the velocity of the load being 1.5 mm/s. For torsion, 50 N of compression was statically applied under torsion control with the materials testing system. After each test, there was a short rest followed by a recycle load.

In Vivo Study

Fifteen sheep weighing 45–60 kg were randomly allocated to three groups; one was a control group, the other two were treated with either with Sofamor TFC (KC) or NiTi-TFC (NT). After induction of anesthesia with pentobarbital sodium (Sigma, Santa clara, CA, USA), a 3 cm midline incision was made over the spine under sterile conditions. One side of the paravertebral muscles was then split and retracted laterally to the outer edge of the facet joint, exposing the lamina and facet joint. Then a tube for minimally invasive surgery was inserted to the lamina. Inferior hemilaminectomy was then performed, followed by unilateral facetectomy. Next, the entire nerve root and intervertebral space were exposed

Fig. 2 Load and strain changes in the sheep lumbar spines. Note: KC, Sofamor TFC; L, autogenous iliac crest bone dowel graft; N, controls; NT, new NiTi-TFC.

simultaneous with achieving adequate decompression. The dura and nerve root were displaced medially and laterally. A drill tube was inserted obliquely to prepare the fusion site for the cage. The NiTi-TFC was pre-cooled, curved and then inserted into the prepared fusion sites, after which it was re-warmed to allow it to resume its former shape. Finally, the bone graft was performed.

All sheep were killed 6 months postoperatively. Anteroposterior and lateral X-ray films were taken immediately preoperatively and 2, 4 and 6 months postoperatively, the last being taken 3 days before killing. Tetracycline (50 mg/kg, i.m)

was used for fluorescent labeling. The “interbody height index” (IB index) was calculated to reflect interbody distraction. The FSU units were then harvested. The central parts of the fusion sites with the fusion devices were resected, decalcified, cleared and embedded in wax, and then sliced into 100 μ m thick sections, stained with toluidine and examined microscopically.

The local Animal Ethics Committee approved this study and all animals were kept under the approved conditions.

Statistical Analysis

Analysis of variance was used to assess mechanical measures of stiffness for each plane of motion, the measures being grouped according to type of implant. The untreated spine units were grouped as a separate condition (control). All data were inputted with statistical software SPSS 7.0. Statistical significance was set at $P < 0.05$.

Results

Biomechanical Tests

These tests included use of a strain gauge (for vertebral strength), a displacement gauge (for vertebral rigidity), mechanical performance for torque and compression performance of the NiTi-TFC. We found the strength of the FSU with NT or KC surpassed that of the control group (Figs. 2, 3; Table 1); however, there was no difference between the NT and KC groups ($P > 0.05$). Changes in displacement and axial

Fig. 3 The strength of sheep lumbar spine on compression, extension, flexion, left and right lateral bending.

TABLE 1 The strength of sheep lumbar spine (mean $\pm$ s.d., MPa)

Group	Compression	Flexion	Extension	Lateral bending
N (n = 3)	3.03 $\pm$ 0.26	1.24 $\pm$ 0.12	3.52 $\pm$ 0.30	3.30 $\pm$ 0.31
L (n = 3)	3.20 $\pm$ 0.28	0.83 $\pm$ 0.08	3.23 $\pm$ 0.28	2.88 $\pm$ 0.28
NT (n = 3)	3.37 $\pm$ 0.31	1.93 $\pm$ 0.14	3.87 $\pm$ 0.32	3.77 $\pm$ 0.36
KC (n = 3)	3.52 $\pm$ 0.29	3.23 $\pm$ 0.16	3.53 $\pm$ 0.31	4.08 $\pm$ 0.41

Fig. 4 Load-displacement changes in the lumbar spines. Note: KC, Sofamor TFC; L, autogenous iliac crest bone dowel graft; N, controls; NT, new NiTi-TFC.

rigidity were similar to those for strength (Fig. 4). Strength and displacement in the L group (autogenous iliac crest bone dowel graft) differed significantly from that in the other two groups ($P < 0.05$). Assessment of mechanical performance showed that the changes in the three groups in torque and torsion rigidity were similar to those for strength and rigidity (Fig. 5). The maximum destruction load of the NiTi-TFC was 11 200 N and the safety coefficient was above 1.2 (Fig. 6).

Radiological Observations

Radiological results are shown in Fig. 7. There was no obvious bone callus 2 months postoperatively. Poorly defined bone callus was found 4 months postoperatively and dense bone callus 6 months postoperatively, when macroscopic bone trabeculae were visible across the inter-vertebral space.

According to the IB index (Table 2), in the first two months there was loss of intervertebral height in all three groups (KC, 19%; NT, 19.9%; control group 75.7%). The heights in the test groups were clearly greater than in the control group at all time points. Compared to the initial height, the percentage by which the intervertebral height decreased in the test groups was significantly less than in the control group ($P < 0.05$).

Fig. 5 Torsion mechanical characteristics of the lumbar spines. Note: KC, Sofamor TFC; L, autogenous iliac crest bone dowel graft; N, controls; NT, new NiTi-TFC.

Fig. 6 Compression testing of the NiTi-TFC.

Histological Findings

Sections ($n = 5$ for each group) were stained with toluidine and examined microscopically, revealing varying destruction of the cartilage under the end-plate and exposure of the cancellous bone under it in the NT group. This kind of destruction also appeared in the KC group but not obvious in the control group, indicating a beneficial injury which may induce interbody fusion by exposing the cancellous bone. In addition, new bone trabeculae had formed and connected with those of the host to varying degrees (Fig. 8). Histologically, the NiTi-TFC (NT) could get an encouraging result as well as the commonly used Sofamor TFC (KC).

Discussion

Posterior lumbar interbody fusion (PLIF) for achieving lumbar interbody fusion and neural decompression was first introduced by Cloward⁴. The posterior approach permits interbody fusion and transpedicular instrumentation through a single incision. The autogenous or allogeneic interbody bone grafts used lack initial mechanical strength and frequently collapse, displace or extrude⁵. Also, there is donor site morbidity occurs in up to 30% of cases⁶. Some authors have found the use of femoral ring allograft struts to be superior to tricortical iliac crest autograft wedges because of the improved compressive strength of the constructs⁷. It is widely accepted that disadvantages of structural allografts, include relatively slow graft incorporation and long-term evidence of resorption.

Potential complexities and the desire for rigid axial mechanical support led to the development of metal and carbon fiber interbody implants or cages⁸. New versions of these implants, such as threaded interbody fusion devices, are designed specifically according to the anatomy of the interior of discs. These fusion devices provide superior mechanical support and improve the three-dimensional stability of bone housed within and around the device. Donor site complications are minimized because the bone needed to fill the device can be acquired locally⁹. Recently, various types of interbody fusion devices have been developed and shown to produce good clinical outcomes^{8,10}. Most of these devices are hollow, allowing the cages to be filled with bone graft. The holes in the sides of the cages allow ingrowth of vasculature and

Fig. 7 Radiological examination postoperatively (2, 4, 6 months). There was no obvious bone callus 2 months postoperatively. Poorly defined bone callus was found 4 months postoperatively and dense bone callus 6 months postoperatively. Note: The white arrows indicate the interbody fusion devices and the bone calluses around.

remodeling of the bone graft, thus facilitating fusion between adjacent vertebral bodies. Cages vary with respect to size, shape, composition, flexibility, and size and distribution of openings¹¹.

However, PLIF also has disadvantages. For example, the procedure involves trauma to paraspinal muscles and extensive removal of laminae, facet joints and spinal processes bilaterally.

TABLE 2 Interbody height index at 0, 2, 4 and 6 months according to group

	0 m	2 m	4 m	6 m
NT group	0.205	0.164	0.133	0.157
	0.203	0.0161	0.132	0.155
	0.202	0.160	0.130	0.154
	0.195	0.159	0.130	0.153
	0.196	0.157	0.129	0.151
Mean	0.200	0.160	0.131	0.154
KC group	0.214	0.173	0.146	0.163
	0.212	0.172	0.145	0.161
	0.210	0.170	0.141	0.160
	0.209	0.169	0.140	0.157
	0.207	0.167	0.139	0.156
Mean	0.210	0.170	0.142	0.159
Control group	0.073	0.018	0.002	-0.002
	0.071	0.017	0.002	-0.002
	0.071	0.017	0.002	-0.002
	0.068	0.017	0.002	-0.002
	0.067	0.017	0.002	-0.002
Mean	0.070	0.017	0.002	-0.002

The lumbar spine's biomechanical stiffness decreases immediately after surgery, especially in flexion and torsion because the facet joints are very important to flexion and torsion. In addition, insertion of the fusion device requires extensive retraction of the cauda equina, with attendant risk of damage to the cauda equina and nerve roots.

Zhao *et al.* found that torsional stiffness is significantly greater with one-cage than with the two-cage constructs when the single-cage construct is 15 mm × 36 mm and the two-cage constructs 15 mm × 24 mm¹². They also found greater differences for pure compression, flexion, and left and right bending, but these differences were not significant. Use of a single posterolateral cage in PLIF requires unilateral

Fig. 8 Photomicrograph showing the edge of the NiTi-TFC (black opacity) and the connecting trabeculation (the arrows show). Toluidine stain ×400.

facetectomy and hemilaminectomy. Large parts of the posterior constructs are preserved, including the counter-side facet joint, lamina and spinous process. Thus, these constructs produce greater stiffness in flexion and torsion than PLIF with two cages.

The benefits of minimal access surgery were first recognized with the widespread adoption of laparoscopic cholecystectomy. Since then, increasingly complex intra-abdominal procedures have been carried out using laparoscopic techniques¹. However, minimal access surgery has only recently entered the field of spinal surgery^{13,14}. Initially, endoscopic spine procedures appeared to offer theoretical advantages over traditional surgery. However, despite their theoretical attractiveness, it has not yet been proven that these procedures offer advantages over open procedures for degenerative disease. The most important question is whether anterior-lumbar interbody fusion for disc degeneration improves functional outcomes.

Currently, 40%–70% of patients with lumbar disc degeneration undergo posterior microendoscopic discectomy to achieve nerve roots decompression. However, is there a means of achieving lumbar interbody fusion without additional inter-fixation during annulus discectomy? Whether it is possible to perform minimal lumbar interbody fusion during annulus discectomy is still uncertain. Most importantly, there are no published reports of a minimally invasive lumbar interbody fusion device that can change in shape. Therefore, in this study we discuss the design, manufacture and implementation of a new type of NiTi-TFC.

NiTi shape memory alloy has unique advantages. First, the alloy can remember its own shape. When it is at 0 °C–10 °C it is soft and can be deformed. When it reaches human body temperature, it recovers the original shape that has been specifically designed. Second, the alloy retains strength in the human body and remains super-elastic for a long time, thus providing orthopedic and supportive functions. Third, the alloy strongly resists corrosion. Fourth, many compatibility tests have suggested that standard of the alloy is adequate for medical use. In addition, the elastic modulus of the NiTi shape memory alloy is 54.18 GPa at +37 °C, which is close to the elastic modulus of bone. This suggests that the stress-shielding of the alloy is small, increasing compressive stress in the fixed area and promoting reconstruction of vascularity and bone fusion.

The sheep model is useful anatomically because virgin lumbar disc-to-vertebral height ratios are consistent between sheep and between levels within individual sheep. This is important when assessing distraction or subsidence after treatment by measuring the IB index.

We found that the maximal destructive load of the NiTi-TFC is 11200 N and the safety coefficient above 1.2, which is adequate for safety. In the NiTi-TFC and Sofamor TFC groups, the strengths of the segments were similar (difference 7.6%, not statistically significant, $P > 0.05$) and both were greater than in the control group. The difference in stiffness between the NiTi-TFC and Sofamor TFC groups was also similar, at 5.6% (not statistically significant, $P > 0.05$). The strength of the segments of the autogenous iliac crest bone dowel graft group was significantly different from those of the NiTi-TFC and Sofamor TFC groups, 22% and 28%, respectively ($P < 0.05$). The stiffness of the autogenous iliac crest bone dowel graft group was also significantly different from those of the NiTi-TFC and Sofamor TFC groups, 15% and 10%, respectively ($P < 0.05$). The changes in torque and torsion stiffness in these groups were similar to the changes in strength and stiffness. Thus, it is clear that the immediate stabilization by NiTi-TFC of the lumbar spine was adequate. After inter-fixation with the NiTi-TFC, the anti-compressive capacity of the lumbar spine was stronger than it was preoperatively. The anti-deformation capacity of the NiTi-TFC was also significantly superior to that of the autogenous iliac crest bone dowel graft.

The findings concerning the NiTi-TFC of the *in vitro* part of our study were confirmed by the subsequent animal tests, radiological and histological examination showing adequate distraction and fusion 6 months postoperatively. We are planning a series of scientific tests to determine whether this device is indeed safe, reliable and easy to install micro-endoscopically. Then, using appropriate devices, we will attempt to perform posterior minimally invasive lumbar interbody fusion simultaneously with nucleus discectomy and to implant the NiTi-TFC micro-endoscopically without additional inter-fixation. Thus, we hope to establish a better theoretic foundation for the development and popularization of this new technique. As described above, the new type of NiTi-TFC has unique superior features and is safe and effective.

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