Fusion capacity after the implantation of interspinous fusion device - a biomechanical analysis and preliminary histological evaluation in pigs

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Research article

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Abstract

Background

The interspinous fusion device (ISFD) was widely used in the degenerative lumbar diseases. Previous clinical studies have demonstrated favorable efficacy. To further explore interspinous fusion capacity after ISFD implantation, we performed biomechanical analysis and preliminary histological evaluation.

Methods

Twelve experimental pigs were selected and accepted a simulated operation of ISFD implantation. The animals were grouped into six groups based on different procedures: sham surgery; unilateral laminotomy (UL); bilateral laminotomy (BL); ISFD + intact; ISFD + UL; ISFD + BL. The graft-bed site was filled with purified bone graft material without any autograft bone. After six months feeding, all experimental animals were sacrificed and the corresponding lumbar vertebrae were obtained. The samples were fixed on the spinal test system and the motion range of flexion-extension, lateral bending and rotation were tested through a multiaxial robotic system. The samples were prepared to cut using a hard tissue-slicing machine. Then, tissue sections stained with hematoxylin-eosin (HE) and toluidine blue were observed to evaluate the new-bone formation.

Results

Laminotomy increased lumbar mobility in comparison with intact model, especially for BL. The implantation of ISFD can reduce the range of motion in all motion directions. Well-defined bone tissue can be observed in the histological images after 6 months. In the histological part of toluidine blue staining, the area of newly formed bone accounted for 8.721%. The hyperchromatic osteoblasts cells and dense bone tissue can be observed in HE staining slides.

Conclusions

The interspinous osteogenesis in histology confirmed the possibility of interspinous fusion. Moreover, the implantation of ISFD provides the necessary stabilization for promoting fusion.

Introduction

Lumbar degenerative disease is one of the most common diseases in elderly patients, which could cause severe lower back pain and influence the quality of life(1). Conservative treatment is preferred during the early symptom stage. If conservative management fails, surgical intervention should be considered. Posterior lumbar interbody fusion (PLIF) is considered as gold standard (2). In recent years, with the development of minimally invasive technology, all variety of interspinous fusion devices begin to be explored in the treatment of lumbar degenerative diseases. Several studies reported the usage of interspinous fixation device (ISFD) to stabilize the intervertebral fusion segment(3, 4). However, some literatures began to explore the application of ISFD as a stand-alone device in lumbar degenerative disease, and reported good clinical efficacy(5–7).

ISFD can be fixed into the spinous process through locking mechanism, which can provide certain stability after decompression. Moreover, the designed cavity of ISFD is filled with the mixture of the autogenous bone and bone graft material to promote interspinous fusion. It is vital to achieve interspinous fusion for long-term clinical

efficacy. If bone fusion cannot be achieved, the instrument will be fail in the long term(8). This is a general rule that stability provided by internal fixation is temporary and long term stability depends on bony fusion. Otherwise, it is easy to occur spinous process fracture and instrument failure, which further lead to symptom recurrence. At present, only a clinical study reported 84% interspinous fusion in patients with Grade I degenerative spondylolisthesis through the CT evaluation at 34.4 months after surgery(9). However, it is still difficult to judge whether true fusion can be achieved through radiological evaluation because of metal artifacts interference from ISDF. The interspinous fusion after the implantation of ISDF was still understudied area. Cunningham performed a biomechanical and histologic evaluation experiment to explore the osteogenesis capacity of a new bone graft substitute in sheep PLF model(10). Therefore, we conducted an larger-bodied animal trial to explore interspinous fusion capacity after the implantation of ISDF through biomechanical analysis and preliminary histological evaluation.

Materials And Methods

The interspinous fusion device applied in our study was BacFuse (Pioneer Surgical Technology Inc Marquette, MI, US) which including a rigid barrel and staggered spike on the lateral plate to optimize fixation (Fig. 1, A). The device applied for animal was custom-made and was available in 8mm and 10 mm height. The bone graft material (Hydroxyapatite/collagen) used was originated from Beijing Allgens Medical Science & Technology Co Ltd.

1.Preparation and grouping of specimens

Twelves experimental pigs were randomly grouped into six groups and then accepted different surgical operations. Group A: sham surgery; Group B: unilateral laminotomy (UL); Group C: bilateral laminotomy (BL); Group D: ISFD; Group E: ISFD + UL; Group F: ISFD + BL.

2.Surgery

All pigs were operated on with general anesthesia by professional animal anesthesiologist. The pigs were placed in the prone position on the operative table. After confirmation of the target segment, a skin incision was made along the midline. Keep the supraspinous ligament in the intact condition. The fascia and paraspinal muscle were stripped gradually, exposing L3/4 spinous processes and lamina. Bone decompression was performed based on requirement of different groups. Remove the lower part of L3 lamina and upper of L4 lamina to imitate laminotomy. The lateral half part of facet joint should be retained in the procedure of laminotomy as much as possible. The different size bone files were inserted into interspinous space to expand and polish the adjacent spinous processes. The cavity of ISDF was filled with purified bone graft material without any autograft bone (Fig. 1, A). Implant suitable size instrument according to the tension of supraspinous ligament. The instrument was placed in the base part of interspinous processes. The compressive clamp was used to clamp tightly spinous processes, and the entire system was locked by screwdriver (Fig. 1, B). Then, the incision was then closed. After surgery, all pigs were prescribed with oral anti-bacterial drug. The next 2 weeks all pigs were observed closely and keep the incision in dry condition.

After six months feeding, all miniature pigs were sacrificed and corresponding spinal segment (L3/4) was obtained. All samples were performed X-ray fluoroscopy (Fig. 2). All muscle tissue were removed and a intact

spinal motion element was retained, such as vertebral bodies, discs, facet joints and all ligamentous structure. The cranial and caudal of samples were potted in polymethacrylate in a metal fixture for subsequent spinal mechanical tests.

2. Biomechanical test

The specimens embedded with polymethacrylate were installed in the spinal test system (MH5S, Yaskawa electric corporation, Kitakyushu, Japan). The L4 vertebral body was fixed on the base and the cranial of L3 vertebral body was connected to a robotic arm. Make sure the spinal segment was in neutral position and the L3/4 disc was horizontal. Markers were placed on each vertebral segments, the displacement of these markers was captured by the photoelectric camera system (Optotrak; Northern Digital Inc., Waterloo, Ontario, Canada). The motion range of flexion-extension, lateral bending and rotation were calculated by the computer system (Fig. 3A, B). The force-moment sensor was applied to measure the applied load and provided feedback to the robot. The sensor can measure axial forces and torque and provide feedback to ensure that pure torque was applied along the main axis of motion of the spine. First, the biomechanical machine run in the speed of $1.0^{\circ}/s$ with 3.0 NM moments in the intact model to get a series of standard angle. Subsequently, each of the test constructs was subjected to six load-unload cycles in each of the physiologic planes, generating flexion, extension, left /right lateral bending, and left /right axial rotation load–displacement curves. The construct was sprayed frequently with normal saline to keep sample in a moist condition. The coordinate system for each vertebra and a set of adjacent vertebrae was based on the international community biomechanics 2002 revised standard(11). In order to reduce the influence of spinal viscoelasticity, the mean value of the results of the last three times was taken for data analysis.

3. Histological experiment

The bone tissues including ISDF were obtained and submerged into ethylene diamine tetraacetic acid (EDTA) to decalcify. The tissues were cut to satisfy requirement and further dehydrate in the tissue dehydration liquid. Then, the tissues were deal with paraffin immersion and embedding. Tissue slices were made by using a hard tissue-slicing machine (German EXAKT-300CP) to cut 4 microns thick slices (Fig. 3C). After slicing specimens, the slices were stained with toluidine blue and hematoxylin-eosin. Then the ready-made paraffin sections were observed and analyzed under electronic microscope.

Data Analysis

All the data were measured and evaluated by an external third party. Statisticians do not participate in entire decision-making process. The normal distribution and continuity of test data are based on Kolmogorov-Smirnov test. The range of motions of each group were compared using a repeated measures ANOVA. SPSS 20.0 and GraphPad Prism 6.0 were used for statistical analyses, $P < 0.05$ was statistically significant.

Results

1. Biomechanical evaluation

The range of motion (ROM) angles for each group in each direction was presented in Table 1. Compared with Group A, the ROM of Group B and Group C increased significantly in the movement of inflexion, extension,

left/right lateral bending and left/right rotation ($P < 0.05$, vs group B, $P < 0.05$ vs. Group C). The ROM of Group C in any movements significantly increased comparing with that of Group B ($P < 0.05$).

The ROM of Group D, E, F with the implantation of ISDF was significant less than that of Group A, B, C in any motion models, respectively ($P < 0.05$).

1.1 Extension and Flexion

As can be seen from Table 1, the ROM of flexion in group B increased by 60.95% and that in group C increased by 97.16%. After applying the ISFD, the ROM of group D decreased significantly compared with group A ($P < 0.05$), a decrease of about 21.43%. Group E and F showed a decrease in ROM compared with group B and C ($P < 0.05$), about 39.98% and 34.53%, respectively.

The extension ROM in group B increased by 42.61% compared with that in group A, and that in group C increased by 76.52%. After the implantation of ISFD, the ROM of group D significantly decreased compared with group A ($P < 0.05$), a decrease of about 26.70%. Group E and F showed a decrease in ROM compared with group B and C ($P < 0.05$), by 22.07% and 21.76%, respectively.

1.2 Lateral bending

The ROM of left lateral bending in group B increased by 34.20% and that in group C increased by 78.67%. After applying the ISFD, the ROM of group D decreased significantly compared with group A ($P < 0.05$), a decrease of about 19.32%. Group E and F had significantly decreased in motion compared with group B and C ($P < 0.05$), about 28.05% and 27.30%, respectively.

The ROM of right lateral bending in group B increased by 26.56% and that in group C increased by 66.30%. After applying the ISFD, the ROM of group D decreased significantly compared with group A ($P < 0.05$), a decrease of about 21.45%. Group E and F had significantly decreased in motion compared with group B and C ($P < 0.05$), about 21.49% and 25.44%, respectively.

1.3 Axial rotation

The ROM of left rotation in group B increased by 88.20% and that in group C increased by 175.85%. After the implantation of ISFD, the ROM of group D decreased significantly compared with group A ($P < 0.05$), a decrease of about 49.25%. Group E and F had significantly decreased in motion compared with group B and C ($P < 0.05$), about 24.97% and 18.67%, respectively.

The ROM of right lateral bending in group B increased by 108.60% and that in group C increased by 212.21%. After the implantation of ISFD, the ROM of group D decreased significantly compared with group A ($P < 0.05$), a decrease of about 33.77%. Group E and F had significantly decreased in motion compared with group B and C ($P < 0.05$), about 17.21% and 21.59%, respectively.

Table 1
ROM of specimens in different directions (X ± SD)

	A	B	C	D	E	F
FI	2.707(0.0376)	4.357(0.1204)	5.337(0.3320)	2.127(0.0687)	2.615(0.0594)	3.494(0.3173)
Ex	1.929(0.0240)	2.751(0.0484)	3.405(0.1741)	1.414(0.2695)	2.144(0.1258)	2.664(0.2560)
L- LB	4.482(0.7696)	6.015(0.3980)	8.008(0.4543)	3.616(0.3199)	4.328(0.4294)	5.822(0.3309)
R- LB	4.695(0.3964)	5.942(0.5724)	7.808(0.5761)	3.688(0.1894)	4.665(0.8230)	5.822(0.3820)
L- Ar	1.466(0.0641)	2.759(0.3103)	4.044(0.2883)	0.744(0.218)	2.070(0.2017)	3.289(0.0904)
R- Ar	1.359(0.2704)	2.835(0.1095)	4.243(0.3170)	0.900(0.173)	2.347(0.3655)	3.327(0.1884)
FL: Flexion; EX :Extension; LB: Lateral bending; AR: Axial rotation. A, Intact; B. Unilateral laminotomy (UL); C. Bilateral laminotomy (BL); D, ISFD + intact; E. ISFD + UL; F. ISFD + BL.						

2. Histological evaluation

2.1 Toluidine blue staining

The toluidine blue staining results were shown in Fig.4. The blue part represented the new formation bone and the black was the precursor condition of new bone formation. Most of the area was filled with precursor condition of bone tissue. The new formation bone area took account of 8.71% through OsteoMeasure 64 software analysis.

Figure 4. The results of hematoxylin-eosin staining. The blue part represented the new formation bone and the black was the precursor condition of new bone formation.

2.2 HE staining

As described in Fig. 5, the cavity of ISFD was occupied with osteoblast cells and bone tissues. The surround black part was metal frame. The red staining part indicated new bone formation which was constituted with osteoblast cells and bone tissues. The brown part was the precursor condition of new bone formation. The blank part was caused of tissue exfoliation.

Discussion

Several studies reported the application of ISFD alone in lumbar degenerative diseases with good clinic efficacy(6, 7, 12). According to the initial design philosophy, final interspinous process fusion was an expected goal(13). However, whether this fusion device can provide enough stability after decompression and meet the requirement of fusion needed to be studied.

At present, most of related biomechanical literature focused to analyze the application of ISFD as an adjunct to stabilize intervertebral fusion(3, 4, 14). Techy demonstrated that ISFD provided similar stability in the flexion-

extension motion and inferior stability in the lateral bending and rotation comparing with bilateral pedicle screws and rods system(3). Karahalios and Gonzalez et al. reported that ISFD as an adjunctive construct with anterior lumbar interbody fusion provided equivalent stability with bilateral pedicle screws and rods(4, 14). In this present study, we investigated the stability of lumbar motion unit with ISFD stand-alone in the fresh animal samples. The results indicated that ROM of lumbar motion unit in the intact model significantly decreased after ISFD implantation in all directions. Similarly to our results, Karahalios reported that ISFD alone limited flexion-extension 75% ROM and reduced lateral bending and rotation 29% ROM when it was used in an intact cadaveric sample(4). Differ from traditional interspinous distraction devices, ISFD can be gripped and fixed to the spinous process through medial plates spikes, which limit spinal motion and provide stability.

Laminectomy/laminotomy seems to be effectively ease the neurological symptom in clinic. However, bone decompression may influence lumbar stability which can prompt the degeneration progress. In this study, the ROM in flexion-extension, lateral bending and rotation significantly increased in the laminotomy groups, especially for BL. This may be one reason some patients experienced decompression alone occurred to symptom recurrence after several years(15, 16). The implantation of ISFD after laminotomy not only stabilize spine but also prevent degeneration when true interspinous fusion has been achieved. Gonzalez et al concluded that the ISFD may be a suitable device to provide immediate flexion-extension balance after a UL, but the bilateral screw and rods system provides greater stability in lateral bending and axial rotation motions. Anyhow, the implantation of ISFD can provide certain stability which may be required for interspinous fusion.

When it comes to interspinous fusion, several studies have reported related contents(4, 13, 17, 18). It is vital important for implanting ISFD to achieve interspinous bone fusion. Spadea S resected the L3 spinous process and implanted it as a bone implant substitute in L4/5 interspinous space in lumbar disc herniation patients. After several years, interspinous bone fusion can be observed directly in several revision patients(17). Tian reported a case of lumbar spinal stenosis with Coflex implantation after decompression. His symptoms were completely relieved postoperatively. After 4.5 years follow-up, X-ray examination showed definite bone fusion between the spinous processes in the Coflex implantation segment. The author thought that it was a phenomenon of heterotopic ossification, but it did confirm the possibility of interspinous fusion(18). Karahali performed the biomechanical study of anterior lumbar interbody fusion combined with posterior interspinous fixation. From postoperative imaging, it was found that interspinous fusion was achieved between upper and lower spinous processes through bone graft groove(4). In our study, we implanted the bone graft material without any autograft bone in the barrel. However, well-defined bone tissue can be observed in the histological images after 6 months. Previous literature has reported this kind of bone graft material used in the tibial bone defect model of rabbit. Bone defects can be repaired at 2 months and bone graft material can be fully resorbed at 3 months(19). In our study, we first report the usage of bone graft material in the ISFD without any autograft bone and observed effective bone formation, which provide strong evidence to support interspinous fusion theory.

However, this study also has several shortcomings. First, the experimental model used in the study were non-upright animals, which spinal anatomy and motion pattern may be different with human beings. Moreover, we just presented histological pictures at 6 months after surgery. In the further study, the histological pictures at different time points will be presented to demonstrate entirely osteogenetic process more truer.

Conclusion

The histological interspinous osteogenesis confirmed the possibility of interspinous fusion. Moreover, the implantation of ISFD provide the necessary stabilization for promoting fusion.

Abbreviations

ISFD: interspinous fusion device; UL: unilateral laminotomy; BL, bilateral laminotomy. HE: hematoxylin-eosin; PLIF: posterior lumbar interbody fusion; EDTA, ethylene diamine tetraacetic acid; ROM, range of motion.

Declarations

Ethics approval and consent to participate

This study was approved by life ethics committee of Beijing Friendship Hospital.

Consent for publication

Not applicable

Availability of data and materials

Related data and materials can be obtained.

Competing interests

All authors declare that they have no conflict of interest.

Funding

No

Authors' contributions

TH and CMM designed the research. BL, JX and SQC performed related experiments. BL and CMM analyzed the extractable data and wrote the first draft of the paper. BL searched the literature, extracted and analyzed the data. TH was responsible for the statistical analysis and reviewed the manuscript and had the primary responsibility for the paper's final content.

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Figures

Figure 1

A. The ISFD was filled with purified bone without bone autograft. B. The image of the implantation of ISFD. (ISFD, interspinous fusion device)

Figure 2

The spinal segment obtained were performed X-ray fluoroscopy. A. anterior-posterior image. B. lateral image.

Figure 3

Biomechanical test and hard tissue slice. A. Spinal biomechanical test system. B. The cranial and caudal of samples were potted in polymethacrylate in a metal fixture for spinal mechanical tests. C. The presentation of sample cut with hard tissue machine.

Figure 4

The results of hematoxylin-eosin staining. The blue part represented the new formation bone and the black was the precursor condition of new bone formation.

Figure 5

The results of toluidine blue staining. The surround black part was metal frame. The red staining part indicated new bone formation which was constituted with osteoblast cells and bone tissues. The brown part was the precursor condition of new bone formation. The blank part was caused of tissue exfoliation.