The implantation of a Nickel-Titanium shape memory alloy ameliorates vertebral body compression fractures: a cadaveric study

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Abstract: Objective: To evaluate the effect of a Nickel-Titanium (Ni-Ti) shape memory alloy in the treatment of vertebral body compression fractures. Methods: The experimental thoracic-lumbar fracture units were made with adult human fresh-frozen vertebral specimens. A total of 30 fresh-frozen vertebral units were randomly assigned to 3 experimental groups: control group, percutaneous kyphoplasty group (PKP group), and percutaneous Ni-Ti shape memory alloys implant group (Ni-Ti implant group). Vertebral height and ultimate compression load of the vertebral body before and after procedures were measured to determine the restoration of vertebral heights and compressive strength, respectively. Results: The Ni-Ti implant group achieved a vertebral endplate reduction effect comparable to the PKP group. The vertebral height of the PKP group was restored from 2.01±0.21 cm to 2.27±0.18 cm after procedure, whereas that of the Ni-Ti implant group was restored from 2.00±0.18 cm to 2.31±0.17 cm. The ultimate loads of the vertebrae body of the PKP and the Ni-Ti implant groups were 2880.75±126.17 N and 2888.00±144.69 N, respectively, both of which were statistically significantly higher than that of the control group (2017.17±163.71 N). There was no significant difference in ultimate compression load of vertebrae body between the Ni-Ti implant and PKP groups. Conclusions: The implantation of Ni-Ti shape memory alloys of vertebral body induced effective endplate reduction, restored vertebral height, and provided immediate biomechanical spinal stability.

Keywords: Osteoporosis, Ni-Ti shape memory alloys, ultimate load, endplate reduction

Introduction

Osteoporosis-associated vertebral compression fractures have become increasingly common among elderly patients in an aging society. Osteoporosis is a common skeletal disease characterized by bone mass loss and bone micro-fracture. In osteoporotic patients, vertebral compression fracture is one of the major clinical consequences that also lead to high morbidity and mortality [1].

Although percutaneous vertebral augmentation, such as percutaneous vertebroplasty and percutaneous kyphoplasty, can improve patients' quality of life by effectively restoring vertebral height, adjusting spinal array, and relieving pain [2], the outcome of such treatments heavily depends on the efficacy of perfusion of bone cement (polymethylmethacrylate, PMMA) [3, 4]. The side effects of vertebroplasty and kyphoplasty limit their further application. Short-term complications, predominantly due to extravasation of the cement, include increased pain and damage by heat or pressure to the spinal cord or nerve roots [5] and poor cement embolization [6]. The potential long-term complications include local acceleration of bone reabsorption caused by the treatment itself or by foreign body reaction at the cement bone interface, and increased risk of fracture in treated or adjacent vertebrae due to changes in mechanical forces. Furthermore, PMMA cement is not as bio-inert as initially believed and has been associated with bone necrosis surrounded by fibrotic tissue, foreign body reaction, and...
neovascularization [7]. The cement reaction might also lead to new fractures in adjacent vertebrae. Alternative treatments for vertebral compression fractures have been proposed in order to provide better clinical outcome [8-12].

Currently, there are three major advancements in minimally invasive vertebral augmentation techniques: (1) adopting a Vessel-X design with bone cement permanently implanted into the closed balloon; (2) replacing PMMA with bone grafts that have osteoinduction and osteoconduct; (3) using a metallic vertebral reduction device with a special shape.

Vessel-X-type close dilation balloons can prevent the reoccurrence of endplate collapse when the balloon is withdrawn, and significantly reduce the side-effects caused by the leakage of bone cement [8]. However, several in vitro studies using human vertebral body specimens have raised questions about whether this type of bone filling container system can prevent the leakage of small particles of bone cement during the augmentation procedure and reduce complications. The clinical efficacy of Vessel-X close dilation balloons remains uncertain [8].

Rauschmann [13] and Grafe, [14] et al. used calcium sulphate hydroxyapatite and calcium phosphate (CaP) cement as a biologic bone graft to replace PMMA for vertebral augmentation. The results showed that these biologic bone grafts could effectively provide early vertebral stability. Bone reconstruction took place over the long term due to its osteoinduction and osteoconduction capability. However, its treatment efficacy is still questionable due to possible failure to restore biomechanical stability in unstable vertebral endplate fractures. In addition, the leakage of biological bone grafts and its effects on adjacent vertebral segments require further investigated.

Based on the defects of these techniques and the series of studies by Verlaan [15] and Oner [16] on how the local balance of the spine is affected by endplate change with vertebral fracture, metal vertebral reduction devices gained increasing attention. This is because of their better efficacy in reducing endplate collapse and providing immediate biomechanical spinal stability independent of bone cement. Meanwhile, the application of a metal vertebral reduction device significantly avoids the various side effects of bone cement leakage.

Rotter, et al. [11] designed a process named “vertebral body stenting (VBS)”. They found that, in comparison with balloon kyphoplasty, VBS could reduce the reoccurrence of endplate collapse when the balloon is removed after the formation of vertebral body cavities. In addition, VBS could reduce the volume of bone cement needed and thus reduce its side effects. Schmoelz, et al. [10] compared the biomechanics of self-locking hexagonal metal implants and vertebral augmentation with PMMA (Percutaneous vertebroplasty or Percutaneous kyphoplasty), and found that the metal implants without bone cement can achieve similar biomechanical spinal stability compared to vertebroplasty with bone cement. Upasani, et al. [9] reported that the replacement of cement by a titanium mesh implant can stabilize vertebral compression fractures. Another study by Ghofrani [17] showed that titanium mesh implants without cement can effectively achieve endplate reduction, but also can acquire enough biomechanical spinal stability to be effective.

Compared to other currently available metal materials that are vertebral body reduction implants, Nickel-Titanium (Ni-Ti) shape memory alloys have unique temperature and shape memory characteristics. Reduction implants can be customized to different dimensions and “temperature-shape memory degrees” according to the anatomic morphology of the vertebra and reduction force. The design of the implant allows increases in contact surface area between the leaflets of the implant and the vertebral endplate, and in supportive force of the implant in vertebral fracture reduction by increasing the stretching force of the memory alloys when they are extended. A distraction rod at the end of the implant allows operators to apply extra reduction power by taking advantage of the “hyper elasticity” property of Ni-Ti shape memory alloys, which can increase reliability of the procedure. In addition, the symmetrical design of the implant improved manipulation efficiency during the procedure.

Although their wide application in orthopedics, however, the implantation of Ni-Ti shape memory alloys in the treatment of human adult vertebral body compression fractures have not been studied experimentally.

In this study, we designed a Ni-Ti shape memory alloy of vertebral body reduction implant
which substitutes dilated balloon in PKP to ensure the spinal stability for effective endplate reduction. The implant was placed in the human adult fresh-frozen fractured spine specimen. Endplate reduction and ultimate load of the experimental vertebra were measured. The experiment demonstrates that, without using bone cement, the Ni-Ti shape memory alloy can achieve similar therapeutic effects in the treatment of human vertebral body compression fractures in comparison with conventional percutaneous kyphoplasty.

**Materials and methods**

*Nickel-Titanium (Ni-Ti) shape memory alloys of vertebral body*

The Ni-Ti shape-memory alloy (Ni-Ti SMA) has the ability to “remember” its original cold-forged shape and can return to its pre-deformed shape by heating. The vertebral reduction implant in collapsed status at lower temperature can be installed into a fractured vertebral body through the pedicle. By heating to the characteristic transformation temperature of the Ni-Ti SMA and returning the implant to its stretched status, fractured vertebral body reduction can be achieved without using PMMA. Therefore, a prototype implant was designed and tested in this study.

The Ni-Ti shape-memory alloys of the vertebral reduction implant were designed and crafted in the Shanghai Institute of Traumatology and Orthopaedics, (China Patent and Trademark Office, Patent Number: 201020629287.1). The implant was made of Ni-Ti shape memory alloys material in a lantern shape with six evenly placed leaflets around the core stem and with
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both ends closed. One end of the implant stem was connected to the implant delivery system. After the implant was deployed, the leaflets were expanded under a physician’s control by rotary force using a mechanical actuation system. The total length of the implant was 29.5 mm. The diameter of the stem at both ends was 5.5 mm. The designed martensite temperature of the Ni-Ti shape-memory alloy was 4°C, at which the implant was in its collapsed elliptical cylinder shape. Each leaflet was 24.5 mm, 2.5 mm, and 0.5 mm in length, width and thickness, respectively. At the austenite temperature of 35°C, the Ni-Ti implant returned to its expanded lantern-shape status with a maximum diameter of 5.5 mm (Figures 1 and 2).

Table 1. Bone mineral density (BMD) (g/cm^2) (Mean ± Standard Deviation)

<table>
<thead>
<tr>
<th>Groups</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.33±0.02</td>
</tr>
<tr>
<td>PKP</td>
<td>0.32±0.02</td>
</tr>
<tr>
<td>Ni-Ti implant</td>
<td>0.33±0.04</td>
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</table>

The development of fracture model

Compression fractures were developed in 24 specimens from the PKP and Ni-Ti groups but not in the 6 control group specimens. After the specimen was mounted to the biomechanical device (Instron 5569, Norwood, MA), vertical uniaxial compressive force was applied until approximately 25% loss of middle vertebral body height in the middle vertebra was achieved. The height loss was later verified in plain X-ray or CT reconstruction films.

Compression fracture treatment

After the specimens were thawed, three different treatment procedures were performed by one author (C.P.), who has 20 years experience in spine surgery, assisted by other authors (Z.Y.H and C.B. and Z.T.).
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Control group: No repairing procedures were applied to the 6 specimens in the control group. Vertebral height was measured and peak load was tested.

Percutaneous kyphoplasty (PKP) group: The unipedicular kyphoplasty was performed according to a previously described technique under biplanar fluoroscopic control [3]. A deflated balloon tamp was inserted into the fractured vertebral body by cannulating one of the pedicles. The cannula was positioned at a relatively large convergent angle so that the tamp could be placed as close to the center of the vertebral body as possible. Balloon inflation was carefully controlled until it reached the subchondral plate, the lateral borders, or the anterior cortex. Upon removal of the tamp, polymethylmethacrylate cement was injected to an average volume of 3.0 ml (range 2.8-3.2 ml) per vertebra. Injection stopped when cement leakage occurred. The specimen was covered with gauze and preserved in saline at 4°C for 24 hours before vertebral height was measured and peak load was tested.

Percutaneous Ni-Ti shape memory alloys implant group: The Ni-Ti implant was soaked in an ice-water mixture to preserve its original collapsed form before the procedure. An implant of appropriate size, which was determined by measurement of the vertebra after X-ray before the procedure, was inserted into the fractured vertebral body using procedures similar to those described in the above kyphoplasty group. When the implant reached its desired position in the vertebra, where the collapsed endplate was located under fluoroscopic imaging, the specimen was transferred to 37°C saline in an incubator to allow the transformation of the implant to its extended formation. The reduction of the vertebra with the expanded lantern-shape implant was confirmed with plain X-ray radiography. If vertebral endplate reduction was not satisfactory due to inadequate implant expansion, the actuator rod of the implant could be rotated allowing further expansion and higher supporting force to vertebral endplates. Vertebral height was measured and peak load was tested.

Mechanical tests and measurement of vertebral height and ultimate load

After the treatment of the vertebral body, each unit was mounted on an electromechanical testing system (Instron 5569, Norwood, MA). A 20-time-cycling vertical preload of 100 N was applied to avoid creep and fatigue damage to the bone. Subsequently, vertical uniaxial compressive force was applied to each vertebral unit at a speed of 2 mm/min, under the environmental conditions of 26°C temperature and 75% humidity. The load-deflection curve was recorded with a data acquisition rate of 100 Hz, from which the ultimate load value was calculated.

The vertical height of all middle vertebrae in each unit was measured before and after the procedure using lateral radiographs of the spine. Particular attention was directed to the

Figure 3. X-ray films of the vertebral body compression fracture (A) and vertebrae endplate reduction after implantation (B).
middle height. The techniques used for measuring the vertebral body height were described in Li’s [18] and Zheng’s [8] studies. Briefly, a horizontal line was first drawn between the midpoints of anterior and posterior edge of the middle vertebral body. A vertical line was drawn across the midpoint of the horizontal line to connect the most concave points in the cranial and caudal endplates. The length of this second line indicated the vertebral height of middle vertebral body. The measurements were performed by two orthopedic surgeons (S. CH. and L. J.) who had 20 and 10 years of experience in spinal imaging, respectively. An average value between the two measurements was used in this study.

**Statistical analysis**

Experimental data were analyzed by one-way analysis of variance (one-way ANOVA) or paired t-test. A p-value < 0.05 was considered statistically significant.

**Results**

Due to the fact that different bone mineral density can significantly affect vertebral endplate reduction and its biomechanical stability, vertebral body specimens were collected from donors with similar age in order to reduce experimental errors. Bone mineral density (BMD) of Control Group, PKP Group and Ni-Ti Implant Group were measured by dual-energy x-ray before surgical procedures. No statistically significant difference in BMD was found among the three groups (P > 0.05, Table 1). This suggests that specimens before procedures were comparable.

Before the repairing procedures, the average height of the fractured vertebra bodies was 2.00±0.18 cm for the Ni-Ti implant group, and 2.01±0.21 cm for PKP group. No significant difference was identified between the two experimental groups (P ≥ 0.05). After repairing procedures, the average height of vertebral bodies was 2.31±0.17 cm and 2.27±0.18 cm for the Ni-Ti implant and PKP groups, respectively, in which the vertebral body height of Ni-Ti implant group was significantly greater than that of PKP group (P < 0.05) (Figure 3 and Table 2). These results suggest that implantation of Ni-Ti memory shape alloys could restore vertebrate body height better than PKP.

In the vertical uniaxial compression test, no significant difference was observed in ultimate load between Ni-Ti implant and PKP groups (P > 0.05). However, ultimate load in both experimental groups were significant higher than that of control group (P < 0.05) (Table 3).

**Discussion**

The current study showed that a novel and minimally invasive technique using Ni-Ti shape-memory alloy implants was capable of effectively restoring vertebral morphology and biomechanical strength after human adult vertebral compression fracture without using PMMA. The Ni-Ti shape-memory alloy implants achieved similar therapeutic efficacy to the conventional kyphoplasty using the bone cement PMMA.

This vertebral body reduction implant made of Ni-Ti shape memory alloy can serve as a substitute for a dilated balloon. It can provide effective endplate reduction, as well as ensure immediate biomechanical spinal stability after implantation. It could also reduce the side effects induced by PMMA injection.

Most of the vertebral compression fractures caused by osteoporosis are in a biconcave shape of varying degrees. Central endplate fractures are the most difficult parts to reduce with conventional instruments, and the remaining central endplates in a depressed shape are

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**Table 2.** The average vertebral height of vertebral bodies before and after procedure (cm) (Mean ± Standard Deviation)

<table>
<thead>
<tr>
<th>Group</th>
<th>Before procedures</th>
<th>After procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.98±0.26</td>
<td>N/A*</td>
</tr>
<tr>
<td>PKP</td>
<td>2.01±0.21</td>
<td>2.27±0.18</td>
</tr>
<tr>
<td>Ni-Ti implant</td>
<td>2.00±0.18</td>
<td>2.31±0.17</td>
</tr>
</tbody>
</table>

Note: *N/A: Not applicable.

**Table 3.** The ultimate load of vertebrae body under vertical uniaxial compression test (N) (Mean ± Standard Deviation)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Ultimate load</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2017.17±163.71</td>
</tr>
<tr>
<td>PKP</td>
<td>2880.75±126.17</td>
</tr>
<tr>
<td>Ni-Ti implant</td>
<td>2888.00±144.69</td>
</tr>
</tbody>
</table>
the main cause of intervertebral disc hernias, nonunion, long-term loss of vertebral height or continuous thoracic back pain due to instrument breakage [15, 16]. Therefore, in this study, the experimental vertebral specimens were made of 25% central endplate fracture units. The treatment efficacy was comparable between a percutaneous kyphoplasty group (PKP group) and an implant group using percutaneous Ni-Ti shape memory alloys for vertebral body reduction. This study took the middle position vertebral body of the experimental spinal unit at the vertebral mid-point surface as the measuring point for vertebral height. The vertebral heights of the PKP group and the Ni-Ti implant group improved from 2.01±0.21 cm and 2.00±0.18 cm, respectively, before the procedure to 2.27±0.18 cm and 2.31±0.17 cm after procedure. Statistical analysis showed that both methods achieved significant vertebral endplate reduction, in which the latter appeared to be more efficient. This is to some extent because supplementary distracting force was imposed by further rotation of the distraction rod during the surgical procedures. Close attention should be paid during the surgical procedure to avoid over-raised endplate or fractures due to excessive reduction force using the Ni-Ti implant, although they were not observed in this study.

Compared to the control group, the Ni-Ti implant and PKP groups had significantly higher ultimate load of the vertebral body in the vertical uniaxial compression test. The results demonstrated that Ni-Ti shape memory alloys of vertebral body reduction implants are able to achieve effective endplate reduction and provide biomechanical stability of the spine. In addition, Ni-Ti shape-memory alloy implants did not have the complications induced by PMMA cement injection in percutaneous kyphoplasty.

When a reduction implant is implanted into the vertebral body, the space within the implant can be filled with bone grafts with osteoinduction and osteoconduction to facilitate osteogenesis and to prevent the collapse of both endplate and leaflets of the Ni-Ti shape memory alloys. Further in vivo studies are required to investigate this possibility.

Ni-Ti shape memory alloys have been used as orthopedic and other medical devices for more than thirty years. However, it needs to be specially pointed out that the outcome of the vertebral body reduction implants heavily depends on positioning. There is no known means available to readjust the position of the implant once it is expanded. Therefore, it is important to choose an appropriate device that matches reduction height, as well as to improve the surgical skills of the clinician.

In summary, this study designed a novel Ni-Ti shape memory alloy and took advantage of human adult vertebral body compression fracture models to test its efficacy. The experimental results showed that the Ni-Ti shape memory alloy could achieve similar therapeutic effects in comparison with conventional percutaneous kyphoplasty. Importantly, Ni-Ti shape memory alloys avoid many of side-effects of conventional techniques. This study proved the efficacy of Ni-Ti shape memory alloy in the treatment of vertebral body compression fractures and will significantly contribute to improved design of therapeutics to treat fractures.

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Disclosure of conflict of interest

None.

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