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AJNR Am J Neuroradiol 2001, 22 (6) 1212-1216
http://www.ajnr.org/content/22/6/1212

AJNR Am J Neuroradiol 22:1212–1216, June/July 2001

An Ex Vivo Biomechanical Evaluation of a Hydroxyapatite Cement for Use with Kyphoplasty

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BACKGROUND AND PURPOSE: **Previous ex vivo biomechanical studies have shown that kyphoplasty with polymethylmethacrylate cement increases vertebral body (VB) strength and restores VB stiffness and height after compression fracture. The purpose of the current study was to determine if a hydroxyapatite cement used as a void filler during kyphoplasty provides mechanical stabilization similar to that of a polymethylmethacrylate cement.**

METHODS: **Simulated compression fractures were experimentally created in 33 osteoporotic VBs harvested from female cadaver spines. VBs were assigned to one of three groups: 1) kyphoplasty with a custom mixture of Simplex P; 2) kyphoplasty with BoneSource; and 3) no treatment. The kyphoplasty treatment consisted of inserting a balloon-like device into the VB via both pedicles, inflating the tamp, and filling the created void with Simplex P bone cement or BoneSource. VBs in the no-treatment group received no interventions. Pre- and posttreatment heights were measured, and the repaired VBs were recompressed to determine posttreatment strength and stiffness values.**

RESULTS: **Kyphoplasty with altered Simplex P restored strength, whereas kyphoplasty with BoneSource and the no-treatment protocol both resulted in significantly weaker VBs relative to initial strength. All treatments resulted in significantly less stiff VBs relative to their initial condition. All VBs lost significant height after initial compression, but a significant amount of lost height was restored by kyphoplasty with either cement.**

CONCLUSION: **Kyphoplasty with either cement significantly restored VB height. Kyphoplasty with altered Simplex P resulted in stronger repairs than did no treatment or kyphoplasty with BoneSource.**

Recently, a new procedure has been developed to restore vertebral body (VB) height lost to compression fractures in osteoporotic vertebrae (1, 2). The procedure, termed kyphoplasty, consists of placing an inflatable bone tamp (IBT) inside the compressed VB via a cannula and inflating it in an attempt to elevate the VB endplates and create a void in the trabecular architecture. The void is then typically filled with polymethylmethacrylate (PMMA) cement. Because the void can be filled under lower pressure than that needed for percutaneous vertebroplasty, bioresorbable cements that are currently difficult to introduce into VBs (3) may be usable with kyphoplasty. BoneSource (Stryker-Howmedica-Osteonics, Rutherford, NJ) is a hydroxyapatite cement currently approved by the Food and Drug Administration for use as a cranial defect filler and is proposed for use with kyphoplasty.

The purpose of the current study was to determine the acute biomechanical efficacy of using BoneSource as a void filler in conjunction with kyphoplasty. The current authors hypothesized that: 1) there would be no significant difference in the strength and stiffness between VBs treated by kyphoplasty with BoneSource and those treated by kyphoplasty with modified Simplex P; 2) VBs treated by kyphoplasty with BoneSource would be stronger and stiffer than they were in their prefracture state or if they were left unrepaired; and 3) kyphoplasty, regardless of filler used, would provide height restoration significantly greater than that of untreated, fractured VBs.

Methods

Thirty-three VBs (T11–L1) from 11 fresh spines were harvested from female cadavers (average age at death, 80.5 ± 10

Received September 29, 2000; accepted January 26, 2001.

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years; range, 64 to 92 years) obtained from the State Anatomy Board. Rice bags were placed along the spine to serve as surrogate soft tissue, and dual-energy X-ray absorptiometry (DEXA) (Lunar DPX-IQ, Lunar Corp., Madison, WI) indicated the spines were osteoporotic (mean t-score ± SD, −3.7 ± 1.1; range, −2.5 to −5.4), with a mean bone mineral density of 0.76 ± 0.14 g/cm^2 (range, 0.56 to 0.98 g/cm^2). The vertebrae were disarticulated, their disks were excised, and the posterior elements were removed to facilitate mechanical testing. The VBs were considered as homogeneous specimens within a given donor and were assigned to one of the three treatment groups by using a Latin square design, thus distributing VBs from each level equally between the three groups. The three groups were: 1) kyphoplasty with modified Simplex P (KS); 2) kyphoplasty with BoneSource (KB); and 3) no treatment (NT). The VBs were wrapped in saline-soaked gauze, sealed in plastic bags, and stored frozen at −20°C until the day before testing.

All specimens were thawed at room temperature (~20°C) 24 hours before testing. An impression of the endplates of each vertebra was made with a common epoxy resin (Fastray, Bosworth, Skokie, IL). VB heights were measured at the anterior, posterior, and lateral aspects with digital calipers accurate to 0.01 mm (Mitutoyo MTI Corp, Aurora, IL). Each VB was seated between its respective impressions, and placed between platens on an Instron materials testing machine (Instron, Canton, MA). A compressive preload of 89 N was applied for 2 minutes. Immediately thereafter, compression was applied in stroke control with the actuator acting along the vertical axis through the center of the VB (4) at a rate of 5 mm/min (5) until the average height of the VB was decreased by 25% of its average initial VB height. Force and deformation data were recorded at 10 Hz, and the initial strength and stiffness of the VB were measured. Strength was defined as the load value after which load decreases with increasing compression; ie, inflection point on the force versus displacement curve. Stiffness was defined as the slope of the force versus deformation curve between 500 N and half the initial VB strength (1). The VBs were returned to their plastic bags and floated in a bath maintained at 37°C for at least 1 hour before treatment.

For VBs in the KS and KB groups, the smaller of the VBs was treated first. A drill channel was created for placement of the IBT by passing a 3.2-mm diameter bit (Kyphon Inc., Santa Clara, CA) through each pedicle and ending medial and inferior in the VB. A size 15/3 IBT (Kyphon Inc.) was centered in each drill channel between the anterior and posterior walls of the VB. The IBTs were then inflated with radiopaque contrast medium in 0.5-mL increments using an inflation device (Basix25, Merit Medical Corp., Salt Lake City, UT) to maintain similar volumes on each side and effect an en masse reduction. The maximum pressure was noted at each increment of contrast volume (using the gauge on the inflation device). The smaller of the two VBs per spine was inflated to one of the following endpoints: 1) fracture reduction, 2) cortical contact, 3) maximum inflation volume (4.0 mL/IBT), or 4) maximum inflation pressure (220 psi) without pressure decay. The larger of the two VBs per spine was inflated to the same volume as that of the smaller. Thus, the same volume of cement would be injected into both VBs. This protocol was used to eliminate cement volume as a variable.

The IBTs were then deflated and removed, and the void was filled with an assigned cement. In the KB group, each VB was injected with a mixture of a 10-g vial of BoneSource powder (hydroxyapatite-forming cement) and a 5-g vial of methylcellulose solution. This liquid consisted of a 2% solution of methylhydroxypropylcellulose (Benecel type MP-824, Aqualon, Hercules Inc, Hopewell, VA) in 0.25 M sodium phosphate. The methylcellulose solution was used with BoneSource to facilitate the cement's injection through the cannulae and infiltration into the VB bony structure. The cement components were stored and mixed at ambient temperature (~20°C). BoneSource is naturally radiopaque, so no additional opacification was required.

The BoneSource cement was transferred from the mixing bowl to 5-mL syringes, which were used to fill cement introducers (Kyphon Inc.) that were placed into the cannulae. The cement was then injected by pushing a stylet through the introducer, thereby expelling the cement. The final volume of cement injected into each VB was 1.5 mL more than the final balloon cavity volume, as determined by the combined volume of contrast medium used to inflate each IBT.

VBs in the KS group were injected with an altered formula of Simplex P, ie, a 20-mL vial of monomer liquid was added to 40 g of powder that contained 28 g of PMMA and 12 g of $BaSO_4$. The combination was then mixed by hand, and it yielded a cement with a 30% $BaSO_4$ content by weight and a monomer-to-PMMA ratio of 0.71 mL/g. This mixture was consistent with those used clinically (6), but was a departure from the commercially available Simplex P, which, when mixed as directed by the manufacturer, results in cement containing 10% $BaSO_4$ by weight and a monomer-to-PMMA ratio of 0.56 mL/g. The components of the modified Simplex-P cement were chilled to 4°C for a minimum of 24 hours before mixing to prolong working time. VBs in the NT group were exposed to the same environmental conditions as were those in the two kyphoplasty groups; however, no repairs were attempted.

After injection or no treatment, all VBs were rewrapped in saline-soaked gauze, placed in sealed plastic bags to prevent dehydration, and floated in a bath maintained at 37°C for 24 hours to allow complete polymerization or curing of the cements before retesting. After 24 hours, but just before testing, height and width measurements were obtained for each VB, and new endplates were cast. Each VB was then recompressed according to the initial crush protocol. Posttreatment stiffness was measured as before. Strength after repair was defined as the maximum load, which occurred within the first 6 mm of compression. On average, 6 mm equaled 25% compression (3). The deformation at maximum load was also recorded. Percent height lost for each VB was calculated as:

$$\frac{(\text{average initial height} - \text{average postcompression height})}{\text{average initial height}}.$$

Percent height restored was calculated as:

$$\frac{(\text{average posttreatment height} - \text{average postcompression height})}{(\text{average initial height} - \text{average postcompression height})}.$$

The data were analyzed for an effect of treatment (KS, KB, and NT) and condition (initial versus posttreatment) on VB height, stiffness, strength, and deformation at maximum load by using a repeated measures analysis of variance. Differences were evaluated for significance by using a Tukey's post-hoc test. Significance was set at $P \leq .05$, unless otherwise specified.

Results

There were no significant differences in initial parameters of interest (ie, strength, stiffness, deformation at maximum load) for VBs in the three groups, thus suggesting a homogeneous distribution of specimens among the groups (Table).

Initial strength was restored to VBs in the KS group, but VBs in the KB and NT groups were significantly weaker after treatment than they were initially. There was no significant difference in posttreatment strengths between the KB and NT groups.

Summary of mechanical and height restoration data

Group	Strength[a] (N)		Stiffness[b] (N/mm)		Height[c] (mm)			Height Change (%)	
	Initial	Treated	Initial	Treated	Initial	Postcompression	Posttreatment	Lost	Restored
KS (n = 11)	2730	2528	1929	677[d]	25.2	22.2[e]	24.6[f]	12	74
KB (n = 11)	2721	2125[d]	1682	406[d]	24.5	22.0[e]	23.9[f]	10	81
NT (n = 11)	2923	2060[d]	2232	609[d]	24.6	22.1[e]	22.3	9	29

[a] SEM, 149.
[b] SEM, 185.
[c] SEM, 0.3.
[d] Treated strength was significantly different ($P < .05$) than initial strength.
[e] Postcompression height was significantly different ($P < .05$) than initial height.
[f] Posttreatment height was significantly different ($P < .05$) than postcompression height.

Posttreatment stiffness was significantly less than initial stiffness for VBs in all treatment groups. The posttreatment stiffness values between the three groups were not significantly different.

The deformation at which posttreatment maximum load (approximately 5.6 mm) occurred was not significantly different between groups. It was, however, significantly greater (approximately 3.4 mm) than the average deformation at which initial failure occurred (approximately 2.2 mm).

Average VB height after the first compression test was significantly less (approximately 3 mm) than initial VB height for all groups. After treatment (both KS and KB), VB height increased significantly from postcompression heights, but was not significantly different than initial height. For the NT group, height remained significantly less than initial height.

IBT inflation was suspended because of cortical contact in 20 specimens and because maximum pressure was reached in the remaining two specimens. Of the 20 specimens with cortical contact, 19 had endplate fractures and one had a lateral wall fracture.

In two VBs, injection of cement was suspended before the desired volume was obtained (one, 0.7 mL less of BoneSource; one, 0.2 mL less of modified Simplex P) because of the onset of extravasation. Nevertheless, paired *t* test analysis indicated no significant difference in average volumes of injected cement in the KS (4.71 mL) and KB (4.66 mL) groups.

Discussion

The kyphoplasty procedure creates a void inside a VB that may be filled with some augmentation material under lower pressure than would be required for standard vertebroplasty. This fact opens the possibility for bioresorbable augmentation materials such as hydroxyapatite cement to be used as void filler. Thus, the objectives of the current study were to investigate the effect of using a hydroxyapatite cement to fill voids and to compare the cement's performance with that of a PMMA cement and no treatment.

Height restoration, strength, stiffness, and deformation at maximum load were measured in VBs left untreated and those treated with kyphoplasty by use of modified Simplex P or BoneSource to fill the resulting void. The results of the current study indicated that kyphoplasty restored 2–3 mm of lost VB height. The height restoration was statistically significant and supports our original hypothesis and previously reported results (1). Morbidity associated with osteoporosis and vertebral compression fractures and subsequent kyphosis (7–10) are the impetuses for developing a means of restoring VB height. Furthermore, the presence of one vertebral compression fracture is related to a fivefold higher chance of experiencing a second vertebral compression fracture in the subsequent 5 years (11). If

multiple VBs were to succumb to compression fractures and lose height, it could be postulated that the resulting progressive kyphosis would adversely affect normal spine function, pulmonary capacity, and activities of daily living (10). In such cases, restoration of VB height over several levels may have the most pronounced and desirable effect. This hypothesis, however, has not been tested. In addition, the clinical significance of restoring approximately 3 mm of height to a single VB remains unknown.

Each VB was compressed to 25% (approximately 6 mm) of its initial height to create vertebral compression fractures with height loss consistent with clinical criteria. The average permanent height loss (approximately 3.3 mm), measured immediately after the initial VB compression, was approximately 13% of the initial height. This fact suggests some elastic height recovery resulting in an unassisted height restoration of about half of the initial VB compression chosen for this test. Similar results were reported in a previous study (1), and an autorecovery phenomenon has also been noted to occur in vivo (12). Thus, even though the VBs were initially compressed by 25% of their initial height, the permanent height loss of the VBs treated in the current study was below the radiographic criterion of 15% (13), but on par with the less stringent criterion of 10% used by others (12).

The result that VBs injected with modified Simplex P exhibited stiffness values greater (although not significantly so) than VBs injected with BoneSource was consistent with the original hypothesis. The finding that both kyphoplasty treatment groups exhibited posttreatment stiffness values not significantly different than that of the NT group was unexpected. In a previous study, posttreatment stiffness equaled initial stiffness (1). In the current study, posttreatment stiffness was significantly less than initial stiffness (in some cases, 25% to 33% of intact values). One reason for the disparity in results between the two studies may be the different volumes of inflation and subsequent cement injection: an average of 4.7 mL of cement currently and an average of 9.4 mL previously (1). Therefore, the VBs in the previous study were inflated and subsequently injected by amounts almost twice those for VBs in the current study. The difference in findings between the two studies may also be attributed in part to the material properties of the cement. In the previous study (1), Simplex P was used as supplied from the manufacturer, whereas in the current study, the cement was altered by increasing the monomer-to-polymer ratio and adding more opacifier—procedures reported to decrease the cement's material properties (14, 15). However, the current study results are consistent with those from a related study, in which direct injection of 4 mL of the modified Simplex P into T8-T10 did not restore VB stiffness (16). In the current study, the finding that posttreatment stiffness values for the KB group were less (although not significantly so) than the stiffness of VBs left untreated was consistent with the results of a companion study in which 4- and 6-mL injections of BoneSource directly into the thoracic and lumbar VBs, respectively, did not restore VB stiffness (16). Stiffness restoration appears to be loosely associated with the volume of cement directly injected (percutaneous vertebroplasty) (17), but these measurements are not well associated with pain relief (18).

Strength was restored in the KS group but not in the KB group or the NT group. This result is contrary to what would be expected on the basis of previous reports (1) in which kyphoplasty with standard Simplex P increased VB strength. Disparity in results between the two studies is likely due in part to the different volumes injected and to differences in material properties of the cements. This disparity may be associated with how posttreatment strength was defined. In the previous study, posttreatment strength was defined as maximum load, without regard for the compressive deformation needed to attain that maximum. In the current study, posttreatment strength was defined as the maximum load up to a compressive deformation of 6 mm, which is on average 25% of initial VB height. Thus, strength in the current study was defined in what the authors believe is a more physiological range.

In keeping with clinical practice, extravasation of cement was an endpoint of injection in the current study; because injection of cement was suspended immediately upon onset of extravasation, no practical amount of extravasation was allowed to occur. Clinically, cement injection is stopped immediately when extravasation becomes radiographically apparent. In addition to local extravasation, pulmonary embolism of the cement is also a potential complication (19), and a confirmed case was recently reported (20).

In the current study, we sought to keep the volume of injected cement constant between specimens from a given spine. In this manner, the mechanical stability provided by the two cements could be compared without volume as a factor. In two VBs, one from the KS group and one from the KB group, cement injection was suspended because of the onset of extravasation. The average difference in volume injected between VBs from the same spine was 0.05 mL; thus, differences between the KS and KB groups in terms of mechanical properties associated with cement volume were considered to be negligible.

A methylcellulose solution was used to mix BoneSource to eliminate the difficulties of injecting apatite cements noted during pilot studies (in which BoneSource was mixed with sterile water) for the current investigation and as reported by others (3). Although the methylcellulose/BoneSource mixture was more viscous than the modified Simplex P, both cements were easily injected through the introducer. Injection pressure was not measured for

either cement. The effects of various methylcellulose solutions on BoneSource cement properties have been evaluated (21) and the biocompatibility of this specific grade of methylcellulose solution has been established (22). Hydroxyapatite materials have the potential advantage of being osteoconductive, not exothermic, and because there is no monomer, there are none of its potential deleterious effects (23, 24).

Conclusion

In conclusion, in the quantities injected, neither cement altered for use with kyphoplasty (the KS and KB groups) restored VB stiffness to their initial levels, and only KS restored initial VB strength. Kyphoplasty with either cement restored VB height.

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