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RESEARCH ARTICLE

Effect of surgical factors on the augmentation of cement-injectable cannulated pedicle screw fixation by a novel calcium phosphate-based nanocomposite

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Abstract **Bone cement-augmented pedicle screw system demonstrates great efficacy in spinal disease treatments. However, the intrinsic drawbacks associated with clinically used polymethylmethacrylate (PMMA) cement demands for new bone cement formulations. On the basis of our previous studies, a novel injectable and biodegradable calcium phosphate-based nanocomposite (CPN) for the augmentation of pedicle screw fixation was systematically evaluated for its surgical feasibility and biomechanical performance by simulated and animal osteoporotic bone models, and the results were compared with those of clinical PMMA cement. ASTM-standard solid foam and open-cell foam models and decalcified sheep vertebra models were employed to evaluate the augmentation effects of CPN on bone tissue and on the cement-injected cannulated pedicle screws (CICPs) placed in osteoporotic bone. Surgical factors in CICPs application, such as injection force, tapping technique, screw diameter, and pedicle screw loosening scenarios, were studied in comparison with those in PMMA. When directly injected to the solid foam model, CPN revealed an identical augmentation effect to that of PMMA, as shown by the similar compressive strengths (0.73 ± 0.04 MPa for CPN group vs. 0.79 ± 0.02 MPa for PMMA group). The average injection force of CPN at approximately 40–50 N was higher than that of PMMA at approximately 20 N. Although both values are acceptable to surgeons, CPN revealed a more consistent injection force pattern than did PMMA. The dispersing and anti-pullout ability of CPN were not affected by the surgical factors of tapping technique and screw diameter. The axial pullout strength of CPN evaluated by the decalcified sheep vertebra model revealed a similar augmentation level as that of PMMA (1351.6 ± 324.2 N for CPN vs. 1459.7 ± 304.4 N for PMMA). The promising results of CPN clearly suggest its potential for replacing PMMA in CICPs augmentation application and the benefits of further study and development for clinical uses.**

Keywords bone cement; pedicle screw; degenerative spinal diseases; calcium phosphate; injectable

Introduction

Pedicle screw system has gained popularity during the past two decades for stabilizing the posterior spine in the treatments of degenerative disorders, unstable fractures, deformities, and spinal tumors. However, the inadequate stability of pedicle screws has been a persistent clinical challenge for ideal internal fixation, especially in patients with osteoporosis. Reduced bone density and bone mass in patients with osteoporosis result in the poor holding strength of pedicle screws [1], leading to the loosening and displacement of pedicle screws, fixation failure, and reduced mechanical force on the screw/bone interface [2–6]. Pedicle screw augmentation with polymethylmethacrylate (PMMA) bone cement has been developed to cope with this difficulty and is an effective way to improve the fixation strength of pedicle screws for patients with osteoporosis or osteopenia [7–9].

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Although PMMA cement has been used for many years and is effective in increasing the pullout strength of pedicle screws [10,11], it also has apparent drawbacks, including exothermic setting behavior [12], lack of biodegradability and osteoconductivity [13], monomer toxicity [14], and limited time frame for injection [15,16]. An injectable, self-setting, biodegradable calcium phosphate-based nanocomposite (CPN) for the augmentation of cannulated pedicle-screw fixation has been developed, in which CPN exhibits similar pullout strength as that in PMMA cement evaluated by ASTM-approved simulated osteoporotic bone and decalcified sheep vertebra models [17,18]. CPN exhibits similar fluidity and dispersing ability as that of PMMA, enabling its injection through cannulated pedicle screws [17,18]. It has superior biodegradability that PMMA lacks and exhibits high osseointegrative capability that forms strong bone/cement interface. *In vivo* evaluation by rat femur-defect model and rabbit model of femoral bone defect has also revealed the explicit biodegradation of CPN and active bone ingrowth to cement after 8 and 24 weeks of implantation. The results suggested that CPN has a moderate rate of bio-resorption that matches the progression of new bone ingrowth [17,19].

CPN has demonstrated promising material properties to cope with the drawbacks of PMMA. However, the effect of surgical factors on CPN augmentation has not been evaluated. Numerous crucial factors affect the fixation ability of a pedicle screw, including vertebra bone density, pedicle screw parameters, such as cannula design and screw diameter, and screw insertion techniques, such as tapping technique and salvage of loosened screw path [20,21]. The performance of CPN in improving the fixation ability of pedicle screws has yet to be evaluated by considering the factors above.

The present study aims to evaluate the augmentation effect of CPN- and PMMA-injected cannulated pedicle screws in an osteoporotic-simulated vertebra model, focusing on the specific surgical factors associated with pedicle screw placement. ASTM-standard solid foam and open-cell foam models and decalcified sheep vertebra models were used for this study. This study provides insights and important surgical references for the further clinical applications of CPN as augmentation material for cement-injected cannulated pedicle screws (CICPs).

Materials and methods

Preparation of CPN

α-Tricalcium phosphate (Suzhou Dingan Science and Technology Ltd., China) and analytical $CaHPO_4 \cdot 2H_2O$ (DCPD, Sigma Aldrich, St. Louis, MO, USA) powders were mixed at a mass of 90:10 and ball-milled in ethanol and $BaSO_4$ ([BS], Sigma Aldrich, St. Louis, MO, USA) [22]. After ball-milling, the mixed slurry in the tank was poured into a tray, dried in a 60 °C vacuum oven, ground into powder, sieved through a 60-mesh screen, and then stored in a vacuum drying cabinet for use.

The solid content of CPN was composed of CPC (60 wt.%) and pre-gelatinized starch (Jianjie Industrial Group, China), and the setting liquid was 0.25 mol/L Na_2HPO_4 (Sigma-Aldrich, St. Louis, MO, USA) solution. In the experiment, the solid and liquid phases were uniformly stirred at a liquid/solid (L/S) ratio in accordance with experimental requirements. By contrast, clinically used PMMA cement (Mendec Spine, Tecres SPA, Sommacampagna, Italy) was used, and 0.5 mL/g L/S ratio was selected in accordance with product instructions.

Osteoporotic bone models

Solid foam model

Commercially available synthetic composite bones (Sawbones®, #1522-23, Pacific Research Laboratory Inc., Vashon Island, WA, USA) were used as the osteoporotic-simulated test material for evaluating the augmentation effect of bone cement [23].

Open-cell foam model

A 0.09 g/cm^3 open-cell polyurethane foam was purchased from a reputable vendor (Sawbones®, model#1522-507, Pacific Research Laboratory Inc., Vashon Island, WA, USA), and a 95% open-celled structure was used as the osteoporotic bone model *in vitro* [23]. The selected sawbones model mimicked human vertebra with severe osteoporosis and has radiopaque properties for CT imaging. It provided a homogeneous and consistent material similar to human cancellous bone.

Decalcified sheep vertebra model

Fresh lumbar vertebra, including lumbar 1–4 vertebral bodies, was obtained from the sheep weighing approximately 60 kg. A scalpel was used to separate the lumbar vertebra into individual lumbar spine samples along the intervertebral disc. All the appendages around the vertebral bodies were then removed with an oscillating saw, and similarly sized lumbar samples were selected for the next experiment.

Sheep vertebral bodies were fixed in 10% formalin for 1 day and immersed in 20% EDTA-Na_2 solution at room temperature for 15 days, with the solution replenished every day. Before and after decalcification, the bone

mineral density (BMD) of each vertebral body was measured using dual-energy radiograph absorptiometry (XR-800, NORLAND, USA) to confirm that the specimens were osteoporotic lumbar vertebra. In addition, sheep vertebral bodies were scanned via Micro-CT (Brightspeed CT/e, GE Healthcare, USA) to observe changes in the trabecular structure of the vertebral cancellous bone.

Pedicle screws

The CICPs (UPASS and Mispine, respectively, Weigao Orthopedic Materials Co., Shandong, China) used in this experiment were made of Ti_6Al_4V measuring 5.5, 6.5, and 7.0 mm in outer diameter, 45 mm in length, and a cannula 1.6 mm in diameter. The end of the screw contains precision threads, and each side of the screw has three holes which gradually increase in diameter from near to distant at 0.9, 1.2, and 1.5 mm, respectively.

Evaluation of augmentation effect in the solid foam model

To evaluate the augmentation effect of bone cement, the solid foam models were cut into the shape of a cylinder, 30 mm in diameter and 19.8 mm in height, and the size of the model was similar to that of the T6–T8 thoracic vertebral bodies [24,25]. The cylinder blocks were then divided from the lateral midline portion into two halves, and a 16 mm-diameter hemispherical cavity was cut in each half. Finally, the two hemispheric cavities were glued together, and a spherical cavity that was approximately 16% of the total volume was formed in the cylinder. The mechanical strength test model of the bone cement was then obtained (Fig. 1A).

CPN and PMMA cements were then injected into the spherical cavity until the defect was filled, which simulated the clinical PKP cement augmentation. To simulate clinical experimental conditions, we operated all the bone cement preparation of the experiment at 21 °C. X-ray radiographs of the augmented solid foam blocks were collected using a veterinary X-ray machine (radiation 60 kV and 3.2 mAs; SPL-HF-VET-4.0, SEDECAL, Spain) to observe cement dispersion (Fig. 1B). All the samples were then stored at 37 °C for 24 h before mechanical tests.

Screw augmentation with different L/S ratios of CPN

To explore the mechanical property of CPN at different L/S ratios, a screw 6.5 mm in diameter was inserted in the open-cell foam model and 1.5 mL of CPN with different L/S ratios of 0.40, 0.45, 0.50, 0.60 and 0.8 mL/g were injected, respectively.

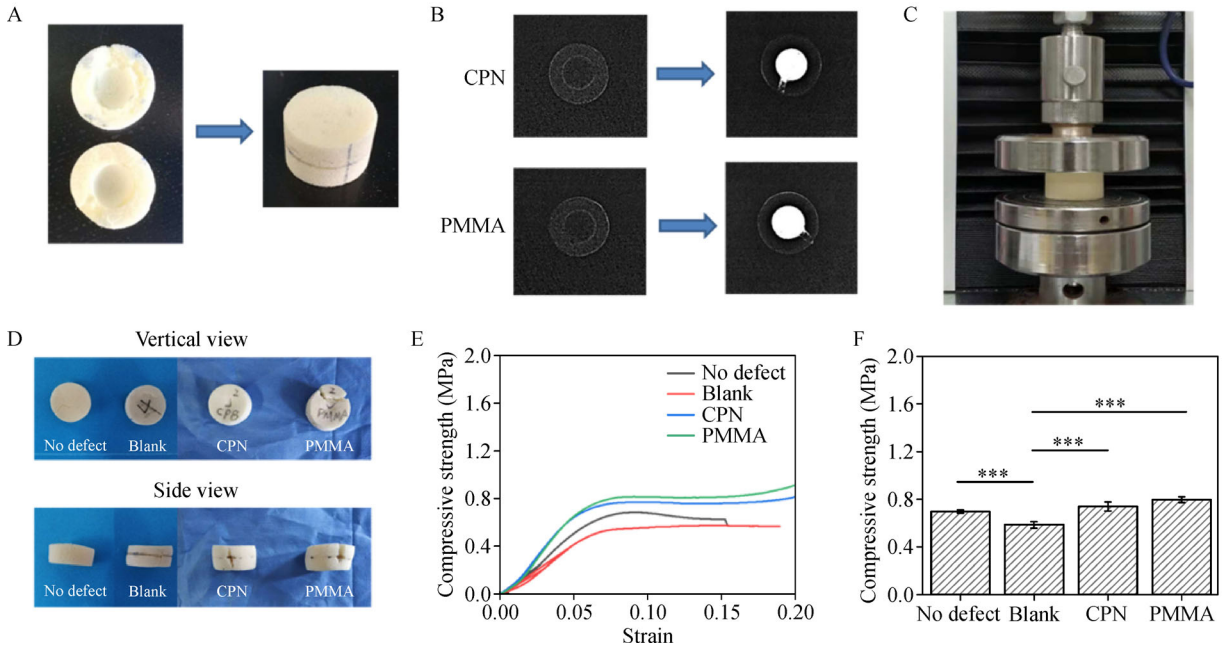

Fig. 1 Augmentation effects of bone cements evaluated by solid foam model. (A) Cylindrical solid foam model (D = 30 mm, H = 19.8 mm) with a spherical cavity (D = 16 mm); (B) X-ray radiographs of the solid foam blocks injected with different bone cement; (C) setup of uniaxial compression tests; (D) sawbones–cement complexes after uniaxial compression tests; (E) typical stress–strain curves; and (F) averaged compressive strength of the cement-augmented solid foam blocks. Data are represented as mean ± standard deviation (***$P < 0.001$).

Surgical factors for pedicle screw placement and bone cement augmentation

Bone cement augmentation volume

To compare the relationship between CPN and PMMA bone cement that augmented the pedicle screw fixation and the volume of bone cement, we used an open-cell foam model as the osteoporotic simulated test material. The foam model was cut into 4.5 × 4 × 9 cm^3 size and then a 6.5 mm-diameter screw was affixed into the open-cell foam blocks. Next, the cannulas were filled with 1.0, 1.5, 2.0, 3.0, or 4.0 mL of PMMA or CPN, and after approximately 6 min, the cement was pushed through the screw cannula into the open-cell foam models. Injection was performed on a mechanical testing machine (HY-1080, Heng Yi Precision Instrument Co., Shanghai, China) at a speed of 300 mm/min (Fig. 2A). The load-displacement curves were recorded, and the maximum peak value of load was determined as the injection force of cement.

Tapping technique for screw placement

To study the effect of tapping technique on bone cement augmentation with pedicle screw fixation, screws were inserted using the same-size tapping, one-size-under tapping, or no-tapping techniques. Here 5.5 mm (or 6.5 mm) cannulated screw taps were used to tap screw channels before screws were inserted into the open-cell foam models. Finally, a 6.6 mm-diameter screw was inserted along the tapping direction, and 3.0 mL CPN or PMMA cement was injected through the screw cannula into the open-cell sawbones foam.

Screw diameter

Bone cement augmentation using different screw diameters was studied. In this experiment, cannulated screws of different diameters (5.5, 6.5, and 7.0 mm) were inserted into the open-cell foam models, and 3.0 mL CPN or PMMA cement was injected for screw augmentation.

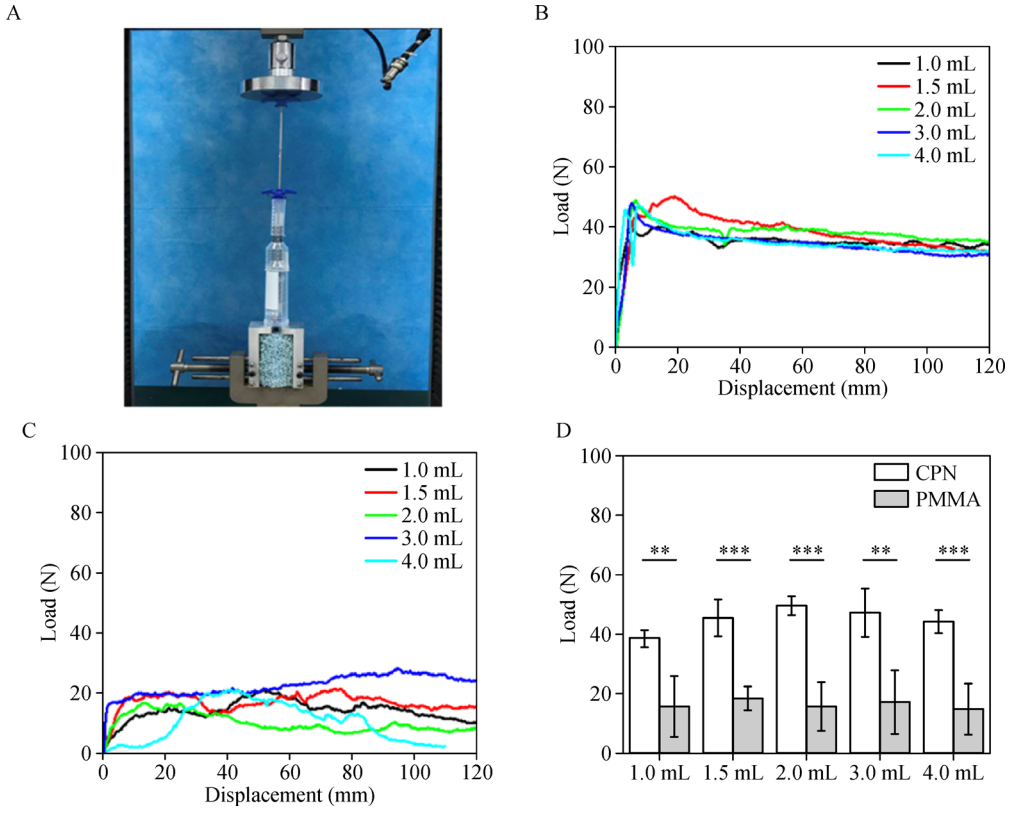

Fig. 2 Injection force measurement of bone cement. (A) Setup of injection force tests on a mechanical testing machine; (B and C) representative load–displacement curves of injection when different volumes of CPN and PMMA were injected, respectively; and (D) comparison of the injection force between CPN and PMMA in the open-cell foam models for different injected volumes. Data are represented as mean ± standard deviation (**$P < 0.01$, ***$P < 0.001$).

Pedicle screw loosening scenario

To produce a pedicle screw loosening model, we first placed a 7.0 mm-diameter screw in the open-cell foam models and then removed it by rotating out. A 6.6 mm-diameter cannulated screw was inserted into the loosening model, and 3.0 mL CPN or PMMA cement was injected for screw augmentation.

Screw augmentation with cement in decalcified sheep vertebra model

A 6.5 mm-diameter screw was vertically screwed into the decalcified sheep vertebral body at a depth of 3 cm. To prevent the leakage of cement, all the vertebral bodies were wrapped and sealed by denture base resins (Boer Chemical Co., Ltd., Shanghai, China). Then 0.5 mL CPN or PMMA cement was injected through the screw cannula into the vertebra.

Radiological evaluation of cement dispersion and interdigitation ability

After all the screws were augmented with different cements, X-ray and CT images were collected to compare the cement dispersion between CPN and PMMA. To compare the dispersion and interdigitation ability between PMMA and CPN, we performed 3-D reconstruction of CT scans on the open-cell foam models with cement-augmented CICPs (Fig. 4B). The maximum cross-sectional areas of the cements wrapped around the screw were measured (referring to the red frame of Fig. 4B) and defined as projection areas, which were separately viewed from the horizontal and vertical directions. Similarly, the dispersive volume of different bone cements was measured. Horizontal and vertical views of the CT scans of each single open-cell foam blocks were performed, and the projection area or volume was measured to further evaluate the dispersion properties of the bone cements.

Biomechanical evaluation

Uniaxial compression test

After the bone cement in solid foam blocks hardened, a standard uniaxial compression test was performed on the block samples. Both end surfaces of the blocks were machined to be parallel and placed under the compression mold of the mechanical testing machine (HY-1080, Shanghai, China) (Fig. 1C). The 5 mm/min loading rate was used to uniaxially compress the augmented solid blocks, and the stress–strain curves were generated. Compressive strength was determined from the first peak of the curve. Each type of sample was tested at least five times.

Screw pullout test

Each augmented sample was placed in L-shaped metal holders, and the screw was attached to the testing machine (HY-1080, Shanghai, China) by a rod threaded to the screw head (Fig. 3A). After the sample was fixed, the screw was axially pulled out at a constant speed of 5 mm/min, and force–displacement curves were recorded. The maximum pullout force before failure was defined as the axial pullout strength. The screw–cement complex after the pullout test was also photographed.

Statistical analysis

Data were analyzed using Origin (Version 8, OriginLab, Massachusetts, USA) and reported as mean ± standard deviation. Statistical analysis was conducted by one-way ANOVA. All pairwise comparisons were performed with Tukey's post hoc test.

Results

Augmentation effect of cements evaluated by solid foam model

Fig. 1B shows the X-ray radiographs of the cement-augmented solid foam blocks, in which the spherical cavity was fully filled with both types of bone cement, indicating that CPN and PMMA cements had similar fluidity and dispersing ability. Fig. 1E shows the typical stress–strain curves of the uniaxial compression tests on the cement-augmented solid foam blocks. The results showed that CPN- and PMMA-augmented blocks were much higher than those without cement augmentation. The averaged compressive strengths of the CPN group (0.73 ± 0.04 MPa) were similar to those of the PMMA group (0.79 ± 0.02 MPa), as shown in Fig. 1F, and both cement groups had significantly improved strength compared with the hollow solid foam model without cement filling (***$P < 0.001$). Fig. 1D shows the photos of the foam–cement complexes after compression tests, where CPN-foam was not disintegrated after compression, whereas PMMA-foam was crushed to pieces.

Injection force of bone cement

Fig. 2B shows the representative load–displacement curves of injection when different volumes of cement were injected. The injection force of CPN elevated rapidly at the beginning of injection but then remained constant, suggesting a consistent setting behavior of the cement. By contrast, the injection force of PMMA increased at the beginning but then irregularly changed (Fig. 2C), indicating a non-uniform setting behavior. The statistical results of the injection force of CPN and PMMA (Fig. 2D)

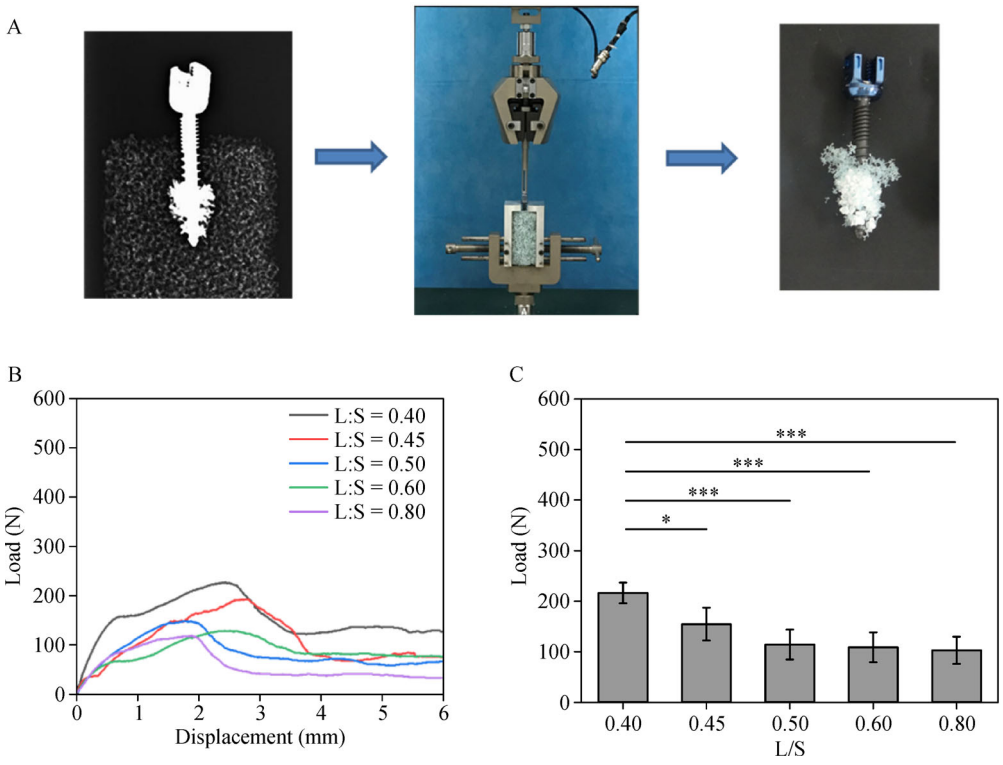

Fig. 3 Effect of L/S ratio of CPN on screw augmentation performance. (A) X-ray radiograph of cement-augmented screw in open-cell sawbones foam, setup of axial pullout test, and photo of the screw–cement complexes after axial pullout test; (B) typical load–displacement curves of pullout tests for the different L/S ratios of CPN; and (C) average axial pullout strength of CPN-augmented pedicle screws. Data are represented as mean ± standard deviation (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$).

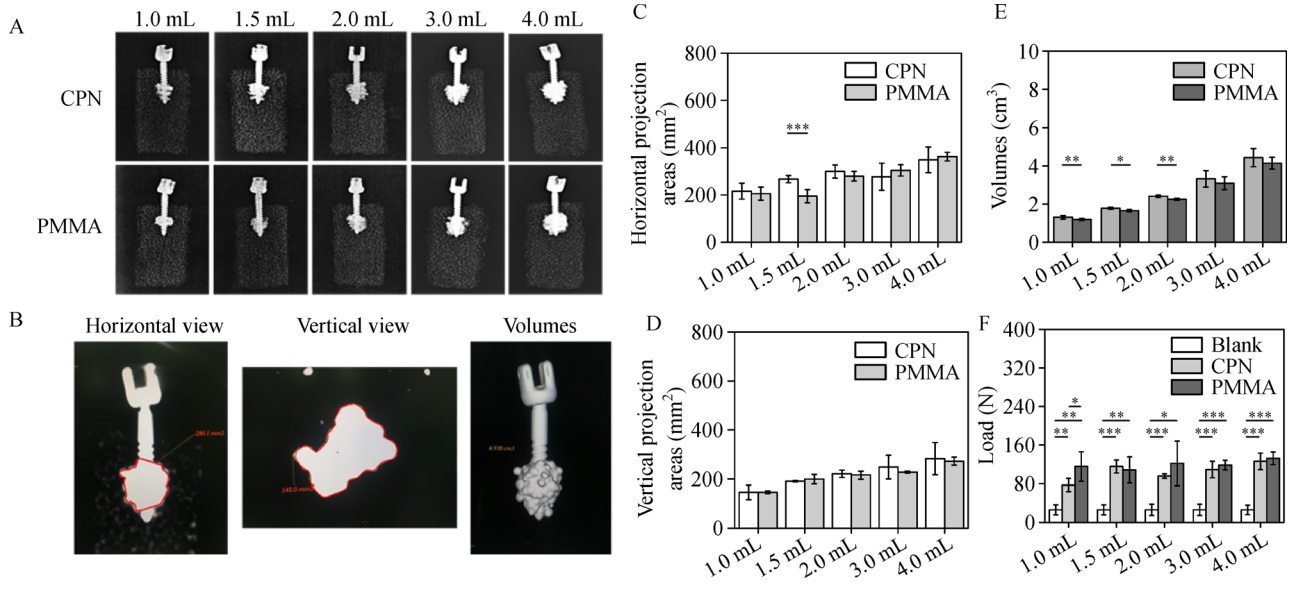

Fig. 4 Effect of different volumes of bone cement on the augmentation of pedicle screws. (A) X-ray radiographs of the different volumes of bone cement-augmented pedicle screws in the open-cell foam model; (B) 3-D reconstruction of CT scans viewed horizontally and vertically; (C and D) horizontal and vertical projection areas of bone cement, respectively; (E) dispersing volumes of CPN and PMMA; and (F) statistical results of the axial pullout strengths of cement-augmented pedicle screws. Data are represented as mean ± standard deviation (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$).

revealed that the maximum injection force of CPN was 49.8 ± 3.0 N, higher than that of PMMA at 15.8 ± 8.3 N (***$P < 0.001$). The average injection force of PMMA was approximately 20 N, which was lower than that of CPN regardless of the amount of injected bone cement. The peak force of CPN group was below 50 N, which is the average force that surgeon's hands can apply [26]. Thus, even though the injection force of CPN was higher than that of PMMA, CPN could be a good augmentation material for CICPs because the consistency of the injection force is a key factor for surgery.

Effect of L/S ratio of CPN on screw augmentation performance

CICPs augmentation using different L/S ratios of CPN was evaluated by the open-cell foam model and axial pullout tests (Fig. 3A). The typical load–displacement curves of pullout tests for the different L/S ratios of CPN are shown in Fig. 3B, where the axial pullout strength of cement-augmented pedicle screws was increased as the L/S of CPN decreased. The average axial pullout strength of CPN was 218.5 ± 20.3 N at 0.4 mL/g L/S ratio, which was higher than that at 0.45 mL/g (*$P < 0.05$) and significantly higher than that at 0.50, 0.60, and 0.80 mL/g (***$P < 0.001$, Fig. 3C). The rightmost photos of Fig. 3A show the screw–cement complexes after axial pullout tests from open-cell foam blocks. Both CPN and PMMA could be completely pulled out from the open-cell foam, indicating the screw–cement interface was more robust than the cement–foam interface.

Effect of surgical factors on the CICPs augmentation performance

Bone cement volume

The different volumes of bone cement used to augment pedicle screws were radiologically examined before the pullout test (Fig. 4A). The projection areas of horizontal and vertical views were counted on the basis of the methods shown in Fig. 4C and 4D. The results revealed no remarkable difference in the projected area of CPN and PMMA in all directions, regardless of the injected bone cement volume. However, for the dispersing or interdigitation volume, CPN exhibited higher dispersing volumes than PMMA when 1.0 (**$P < 0.01$), 1.5 (*$P < 0.05$), and 2.0 mL (**$P < 0.01$) of cement were injected (Fig. 4E). Fig. 4F shows the average pullout strengths of the cement-augmented pedicle screws that were evaluated in the open-cell foam models. The pullout strength of PMMA (114.9 ± 31.0 N) was higher than that of CPN (76.2 ± 13.6 N) when 1.0 mL cement was injected. However, for other injection volumes, the pullout strength of CPN was statistically similar to that of PMMA. Both CPN and PMMA showed significantly higher pullout strengths than those of the screws without cement augmentation (**$P < 0.01$).

Tapping technique for screw placement

The X-ray radiographs of the augmentation of CICPs in the open-cell foam model are shown in Fig. 5A. Screws were inserted into the open-cell foam model using the same-size tapping (6.5 mm in diameter), one-size-under tapping (5.5 mm in diameter), or no-tapping technique (as control). The projection areas of cements at horizontal and vertical views (Fig. 5B and 5C, respectively) and the dispersing volumes of cements (Fig. 5D) showed no statistical significance between the groups. Fig. 5E shows the pullout strengths of the CPN and PMMA groups under different tapping conditions, which were similar without statistical significance but remarkably higher than those of the screws without cement augmentation. The results suggested that the tapping technique of screw placement slightly affect the dispersing and augmentation performances of both CPN and PMMA in osteoporotic bones.

Screw diameter

CICPs with different diameters were augmented with bone cements and evaluated for biomechanical properties (Fig. 6). The projection areas and dispersing volumes of CPN and PMMA cement were similar regardless of the diameters (5.5, 6.5, or 7.0 mm) of the screws used (Fig. 6B and 6C). Fig. 6E shows that the pullout strengths of CPN-augmented screws were slightly lower than those of PMMA-augmented ones without statistical significance. The pullout strengths of both cement-augmented screws were considerably higher than those of the screws without augmentation. The results suggested that the screw diameter selection has no influence on the cement-augmented screw performance.

Pedicle screw loosening scenario

The X-ray radiographs of the augmentation of CICPs in the open-cell foam model are shown in Fig. 7A, where screws were inserted into a loosening model and a no-loosening model (as control). The projection areas of cements from horizontal and vertical views are shown in Fig. 7B and 7C, respectively, and dispersing volumes of CPN and PMMA are shown in Fig. 7D. The results revealed that the dispersion ability of CPN and PMMA were similar in the scenario of pedicle screw loosening. The pullout strengths of CPN and PMMA under pedicle screw loosening scenario were similar (Fig. 7E), which were considerably higher than the case without cement augmentation. The

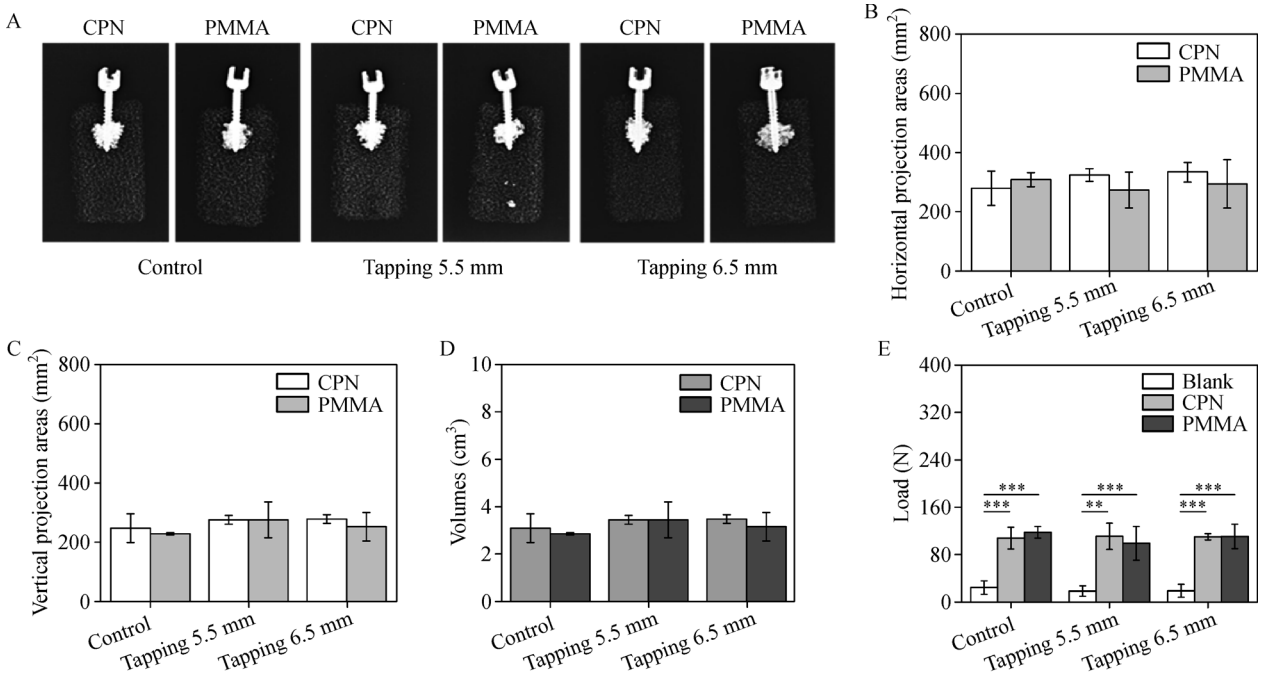

Fig. 5 Tapping technique for screw placement. (A) X-ray radiographs of the augmentation of CICPs in the open-cell foam model, where screws were inserted using the same-size tapping (6.5 mm in diameter), one-size-under tapping (5.5 mm in diameter), or no-tapping technique (as control); (B and C) horizontal and vertical projection areas of bone cements, respectively; (D) dispersing volumes of CPN and PMMA; and (E) statistical results of the axial pullout strengths of cement-augmented pedicle screws. Data are represented as mean ± standard deviation (**$P < 0.01$, ***$P < 0.001$).

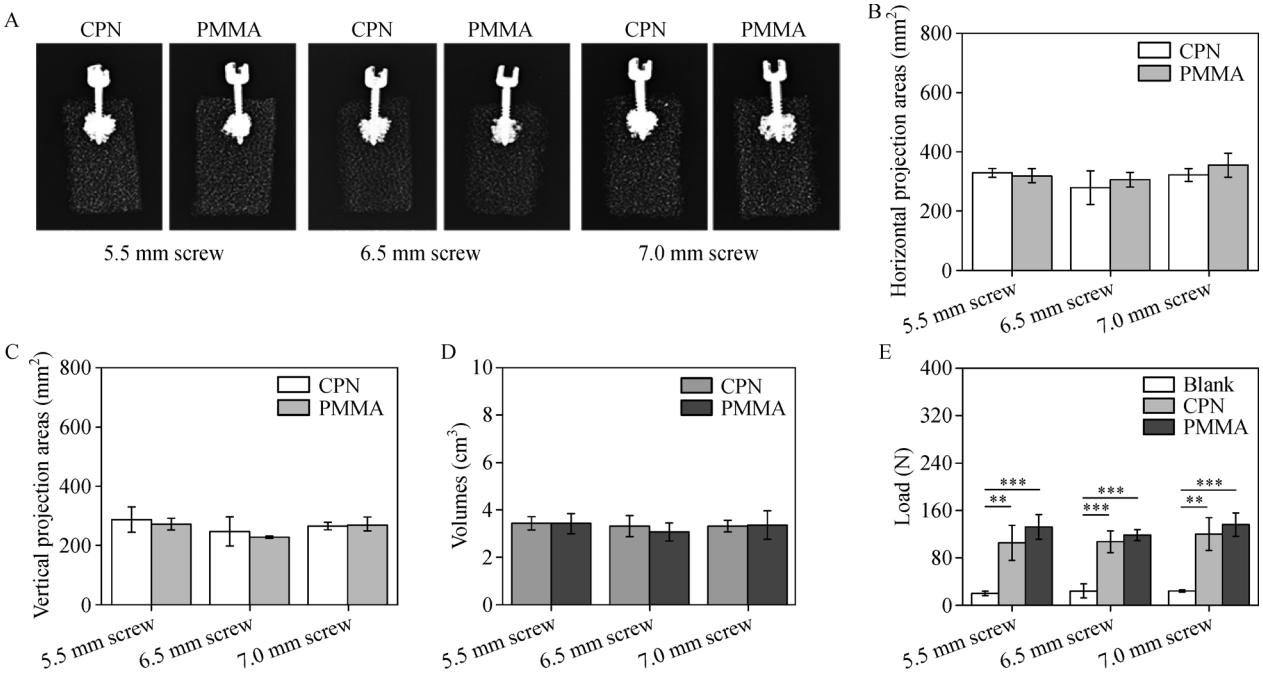

Fig. 6 CICPs with different diameters were augmented with bone cements. (A) X-ray radiographs of CICPs with different diameters were augmented with bone cements; (B and C) horizontal and vertical projection areas of bone cement, respectively; (D) dispersing volumes of CPN and PMMA; and (E) statistical results of the axial pullout strengths of cement-augmented pedicle screws. Data are represented as mean ± standard deviation (**$P < 0.01$, ***$P < 0.001$).

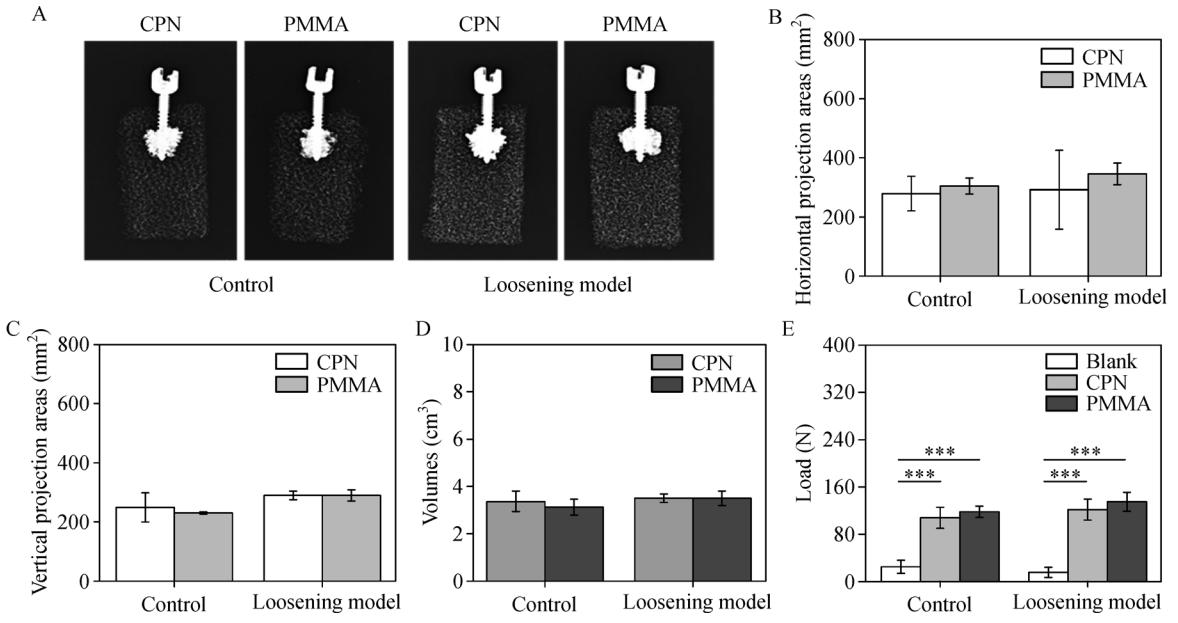

Fig. 7 Pedicle screw loosening scenario. (A) X-ray radiographs of the augmentation of CICPs in the open-cell foam model, where screws were inserted into a loosening model and a no-loosening model (as control); (B and C) horizontal and vertical projection areas of bone cement, respectively; (D) dispersing volumes of CPN and PMMA; and (E) statistical results of the axial pullout strengths of cement-augmented pedicle screws. Data are represented as mean ± standard deviation (***$P < 0.001$).

results demonstrated that, even in the pedicle screw loosening scenario, the augmentation of CICPs with CPN can remarkably improve biomechanical fixation in a similar way as that in PMMA cement.

Augmentation effect of cement evaluated by decalcified sheep vertebra model

All the decalcified sheep vertebras were wrapped with denture-based resins before the tests to prevent cement leakage, as shown in the leftmost photos in Fig. 8D. The representative micro-CT images of vertebral bodies in decalcification at different time periods are shown in Fig. 8A, indicating evident osteoporotic effect in the trabecular structure. The comparison of BMD before and after decalcification further confirmed that osteoporosis was simulated in decalcified sheep vertebra models. After decalcifying for 15 days, the BMD of sheep vertebra decreased from 0.56 ± 0.07 g/cm^2 to 0.36 ± 0.07 g/cm^2, an approximately 64% decrease (***$P < 0.001$, Fig. 8B). The pullout strengths of cements for the augmentation of CICPs were tested by a fixture system, as shown in Fig. 8C, and the photograph of the screw–cement complex was also recorded after the pullout test (Fig. 8D). Fig. 8E shows the average pullout strengths of cement-augmented pedicle screws in decalcified sheep vertebra. The axial pullout strength of CPN was 1351.6 ± 324.2 N, which was slightly lower than that of PMMA at 1459.7 ± 304.4 N, but notably higher than that of the screws without cement augmentation at 701.1 ± 181.9 N. The results suggested that PMMA and CPN exhibited a similar reinforcing effect of CICPs in osteoporotic bones.

Discussion

Clinical practice reveals that pedicle screw fixation procedures are unstable in osteoporotic vertebra, resulting in fixation failure such as screw loosening and even screw pullout. Current solutions to this instability problem include improved design of screws, surface coating of screws, improved nailing techniques, and cement augmentation. Cement augmentation is an effective way to increase the stability of CICPs, but the intrinsic property of PMMA, such as exothermic polymerization and non-degradability, also exposes apparent drawbacks affecting the efficacy of pedicle screw fixation. The possible replacement of PMMA cement with CPN, which is a novel biodegradable and osseointegrative cement with high injectability and strength, has been proposed. The cost of preparing CPN in the laboratory is less than one-third of the cost of purchasing PMMA cement. *In vivo* studies suggest that CPN biodegradation can match new bone ingrowth progression and maintain the mechanical stability of CICP fixation. However, CPN, including other calcium phosphate-based cements, have not been systematically studied for its surgical performance or its effects on surgery-related factors.

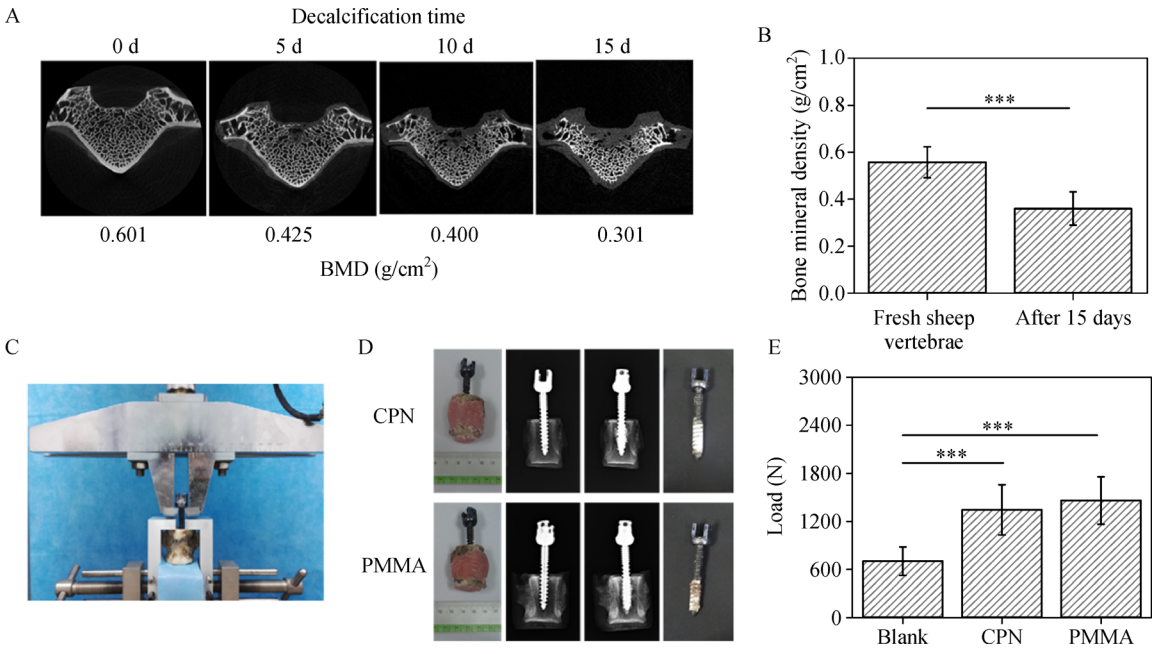

Fig. 8 Augmentation effect of cements evaluated by decalcified sheep vertebra model. (A) Representative micro-CT images of vertebral bodies in decalcification at different time periods; (B) comparison of bone mineral density before and after decalcification; (C) setup of axial pullout tests for the augmented CICPs; (D) the photographs of the screw–cement complex before and after the axial pullout tests; and (E) average pullout strengths of cement-augmented pedicle screws in decalcified sheep vertebra. Data are represented as mean ± standard deviation (***$P < 0.001$).

The present study first compared the injection forces of CPN and clinically used PMMA cement, revealing a higher average injection force of CPN than that of PMMA but with a more consistent and repeatable injection force pattern of CPN. This difference is mainly due to the different setting/hardening mechanisms of CPN and PMMA. CPN relies on the hydration reaction of calcium phosphates to set and has a comparatively long setting process transferring from highly viscous state to solid state. By contrast, PMMA cement sets via rapid monomer polymerization, in which monomer liquid initiates a cross-link to become a viscous slurry and transforms to a solid polymer with polymerization progression. The cross-linking of monomers occurs rapidly, and phase transformation from liquid to dough-like slurry to solid completes within a short time window, resulting in a drastically changed mechanical characteristic of PMMA and a less consistent evolution of injecting force. Thus, PMMA can be easily injected out in the early stage of setting, but the injection force changes drastically with less repeatability between trials. By contrast, CPN has a mild and comparatively slow two-stage phase transformation process, resulting in stable and consistent changes in injection force during the setting process.

The differentiated dispersing or interdigitation ability between CPN and PMMA cements has also been revealed by this study. The measured volumes of dispersed cement in the foam models were all greater than the volumes of injected cement, suggesting that both cements could flow along the grid and gap in the open-cell foam blocks that mimic the interdigitation process of cement in vertebra cancellous bone. In addition, the projection areas of CPN and PMMA injected in the osteoporotic bone models almost had no statistical significance at different view directions, indicating that CPN has a dispersing ability similar to that of clinically used PMMA cement. Although PMMA and CPN have different setting mechanisms and setting times, the dispersing and interdigitation ability in cancellous bone remain unaffected.

The compressive strengths of the augmented solid foam model (Fig. 1F) showed that the augmentation effect of CPN is similar to that of PMMA, even though CPN has less compressive strength than PMMA. The solid foam–cement complex photos after compression tests showed that CPN exhibits high cohesion with the foam, in which disintegration of the complex was not observed. The pullout strength results indicated that CPN exhibits similar reinforcing effect as that in PMMA on CICPs fixation from all the investigated factors associated with the surgical placement of pedicle screws. The animal vertebral model used here has some limitations. First, the size of the sheep vertebral body was smaller than the human lumbar vertebrae; thus, it could not completely simulate the structure of human vertebral bodies and pedicles. Second, the sheep vertebra was decalcified to simulate osteoporosis, which is certainly different from natural osteoporosis.

The evaluation by decalcified sheep vertebra model revealed that the anti-pullout ability of CPN is as good as that of PMMA. From the photograph of the screw–cement complex after the pullout test (rightmost of Fig. 8D), the surface of the screw pulled out from CPN specimens was smooth and had almost no bone tissue attached to the screw. By contrast, bone tissue residue was found on the surface of the screw augmented with PMMA after pullout. These results were attributed to the higher discrepancy in mechanical property between PMMA and osteoporotic bone compared with that between CPN and bone. PMMA, which is much stronger and tougher than osteoporotic bone, is prone to destroy the cement–bone interface during pullout, whereas the mechanical property of CPN is comparatively closer to the osteoporotic bone, and thus the screw–cement interface is more likely to fail during pullout. Therefore, CPN-augmented cannulated screw fixation provides an alternative fixation strategy against pulling out and exhibits similar fluidity, dispersion ability, and augmentation effect but less destruction to bone compared with PMMA.

Among the anatomical considerations of pedicle screw design, the size of the outer diameter influences pullout strength. A steady increase in the pullout strength as the diameter of screw increased by approximately 1 mm has been observed [27]. However, the results from this study revealed no evident effect of screw diameter on the biomechanical performance of both CPN and PMMA, suggesting that the screw diameter is not a sensitive surgical factor when CPN is used for augmenting CICPs.

During surgery, pre-tapping a pilot hole is sometimes necessary to accurately install screws in long bones and is also implemented in spinal surgery. Tapping the pilot hole prior to screw insertion weakens the pullout force of pedicle screws [28,29]. Our results suggested no evident effect of tapping technique (i.e., the same-size tapping (6.5 mm), one-size-under tapping (5.5 mm), or no-tapping) on the biomechanical properties of both CPN and PMMA. This information is important for surgeons who use CPN-augmented CICPs to select tapping technique because the loss of the pullout force of pedicle screws is not likely to occur.

Salvage surgery for failed spine fusion with a loosened pedicle screw is difficult. In general, the strategy includes replacement with large and long pedicle screws, extension of fused segments, and augmentation with cement [30]. In the present study, the investigation on the pedicle screw loosening model suggested that the augmentation of CICPs with CPN results in similar biomechanical improvement similar to the case with PMMA. This result suggested an alternative treatment option for salvage operations that the usage of CPN instead of PMMA could both avoid the extension of a fused segment and achieve successful bony union.

Conclusions

Previously developed CPN for the augmentation of cannulated pedicle-screw fixation were systematically compared with clinically used PMMA for biomechanical injection, dispersing properties, and surgical feasibility for CICPs application. The results of compressive strengths in the solid foam model showed that the augmentation effect of CPN that was directly injected to the foam is similar to that of PMMA. For the augmentation of CICPs fixation in the open-cell foam model, the anti-pullout strength of CPN increased as the L/S ratio of cement decreased. CPN revealed high dispersing ability and stable injection force pattern and reached the highest biomechanical strength when 1.5 mL CPN was injected. This strength was also similar to that of PMMA for CICPs augmentation. In addition, the dispersing and biomechanical properties of CPN were not affected by the surgical factors, such as tapping technique and screw diameter. The evaluation outcomes from the pedicle screw loosening model and decalcified sheep vertebra model further demonstrated that CPN had sufficient biomechanical performance in comparison with PMMA. These results suggested that CPN has promising potential as a replacement of PMMA in CICPs augmentation and is therefore worth further study and development for clinical uses.

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Compliance with ethics guidelines

Haolin Sun, Chun Liu, Shunlun Chen, Yanjie Bai, Huilin Yang, Chunde Li, and Lei Yang declare that they have no conflicts of interest in this study. All institutional and national guidelines for the care and use of laboratory animal were followed. The animal study protocol was approved by the Ethics Committee of Soochow University under case number ECSU-201700031.

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