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Effects of bone cement filling in rabbit proximal femoral medullary cavity on distal femoral blood flow and metabolism

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Abstract

Objective: A rabbit model was used to evaluate the effects of bone-cemented hip arthroplasty on distal femoral blood flow and metabolism relative to that of the non-cemented contralateral leg.

Methods: The marrow cavity of the right hind femur was filled with bone cement. At each of the following time points, rabbits were randomly selected to receive an injection of one dose of ^{99m}Tc-methylene diphosphonate and then immediately scanned using a gamma camera: immediately postoperatively and at 4 and 8 weeks postoperatively. A BL-410 model biofunction experimental system was used to analyze the acquired images and determine the radioactive counts of each hind leg.

Results: The X-ray and photographic images of the right femoral bones confirmed successful filling of the marrow cavity with bone cement. The radioactive counts were significantly lower in the experimental than control legs at each time point. The ratio of the radioactive count of the experimental to control leg increased considerably at each time point, but each ratio was <1.

Conclusion: Blocking the proximal femoral medullary cavity with bone cement was associated with significant lowering of the blood circulation of the femur and marrow, decreasing the distal femoral blood flow and bone metabolic rate.

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Keywords
Arthroplasty, distal femur, blood flow, metabolism, cement, medullary cavity

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Introduction

Artificial hip arthroplasty has been extensively used to replace damaged hips and improve patients' quality of life. Both cemented and non-cemented methods have been used to affix the artificial hip to the native bone.[1,2] The former, cemented fixation, has been judged preferable and is used more frequently because early stability is better and it is especially suitable for older patients with osteoporosis.[3,4] Therefore, bone cement fixation is considered the first choice in hip arthroplasty.[5] However, some clinical complications may accompany the procedure. The presence of bone cement can lead to high pressure inside the proximal femoral medullary cavity, systemic bone cement implantation syndrome, and other complications.[6,7] Fixing the artificial joint prosthesis using bone cement can also lead to long-term occlusion of the bone marrow cavity and destruction of the blood vessels in that area.[6,8–11] Previous studies have shown that the bone cement itself can stimulate the loss of bone, thus decreasing bone density to a great extent.[12,13] The toxicity and thermal effects of the bone cement can result in degeneration and necrosis of the surrounding tissues, and the leachate from the cement is corrosive.[14]

In our clinical practice, we have observed that patients are more likely to have knee pain after undergoing hip replacement with bone cement fixation. Our long-term observation revealed that patients who have undergone cemented hip replacement have a higher rate of knee osteoarthritis. To the best of our knowledge, however, few reports have described the effects of bone cement on the blood flow and metabolism of the distal femur.

The present study used a rabbit model to evaluate the effects of cemented hip arthroplasty on the blood flow and metabolism of the distal femur relative to that of the non-cemented contralateral leg. The blood circulation and bone metabolism of the distal femur were evaluated by measuring the radioactivity of the hind legs after an intravenous injection of 50 to 150 MBq of ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) via the marginal ear veins.

Methods

The authors' Institutional Animal Care and Use Committee approved the use of rabbits in this study. The study complied with the National Institutes of Health Guide for Care and Use of Laboratory Animals (Publication No. 85-23).

Animals and surgery

Thirty New Zealand white rabbits (2.6–3.5 kg) were purchased from the Animal Center of Guangxi Medical University (Nanning, China).

All surgical procedures were conducted in accordance with a previous report.[15] Briefly, the rabbits were anesthetized with an intramuscular injection of ketamine (50 mg/kg) and xylazine (10 mg/kg). The hair at the bilateral surgery sites of the hind legs was shaved after cleansing of the area with 9% sodium sulfide. The rabbits were placed in the prone position on the surgical table. The operation field was disinfected using an iodophor and covered with a surgical drape.

A 4-cm curved incision was made at the third femoral trochanter to access the bone marrow cavity. After half of the femur had been reamed with an intramedullary reamer, the medullary cavity was repeatedly irrigated with physiological saline and then dried with gauze. Bone cement was prepared immediately before the experiment by mixing 40 g of polymethyl methacrylate (PMMA) powder with 20 mL of methyl methacrylate (MMA) monomer liquid (Tianjin Synthetic Material Industry Research Institute, Tianjin, China). The medullary cavity of the right femur was filled with the dough-like bone cement. The left femur was used as the control; no bone cement was used. The wounds were washed using sterile saline, and the tissues were sutured to close the incision. After the surgery, each rabbit received one 1-mL gentamicin injection and 400,000 units of penicillin sodium.

Radioactive evaluation

Immediately after the surgery and at 4 and 8 weeks postoperatively, 10 rabbits were randomly selected and scanned. The scans were performed using a gamma camera (Elscint Apex 400; Elscint, Haifa, Israel) connected to a small online computer (Medical Data Systems A^2; Medical Data Systems, Ann Arbor, MI, USA) for the storage of imaging data and a low-energy all-purpose collimator. The obtained imaging data were recorded as a 256- $\times$ 256-byte matrix for computer analysis. The distal segments of the bilateral femurs were chosen as the region of interest (ROI) for each rabbit.

Briefly, the rabbits were anesthetized and placed in the prone position on a surgical table. Each rabbit received one intravenous injection of 50 to 150 MBq of ^{99m}Tc-MDP (Wuxi Institute of Nuclear Medicine, Wuxi, China) via a marginal ear vein. Both hind legs were immediately scanned (dynamic scan) for 60 seconds (one image per second) as previously described.[16,17] Four hours later, both hind legs were scanned again (static imaging) for 5 minutes. The ROI was drawn over the distal femur region. The obtained imaging data were processed using a BL-410 model biofunction experimental system (Taimeng Science and Technology Ltd., Chengdu, Sichuan, China) to determine the radioactivity for each region of the right and left hind legs. The radioactivity counts have been shown to reflect the bone metabolism and blood flow.[18]

Statistical analysis

Each experiment was performed in triplicate unless otherwise noted. All numerical data are reported as mean $\pm$ standard deviation. Either the *t*-test or Student–Newman–Keuls q test was used to determine whether a statistically significant difference was present between two groups of data. A *P*-value of <0.05 indicated a statistically significant difference between two groups of data.

Results

The proximal femoral cavity of the right hind leg was successfully occluded with bone cement as evidenced by X-ray and photographic images taken immediately after surgery (Figure 1). Further images were obtained from dynamic and static scans of the right (experimental) and left (control) hind legs immediately after the surgery and at 4 and 8 weeks postoperatively (Figure 2). These static and dynamic scan images clearly showed that the uptake of ^{99m}Tc-MDP in the ROI of the experimental hind legs was significantly less than that in

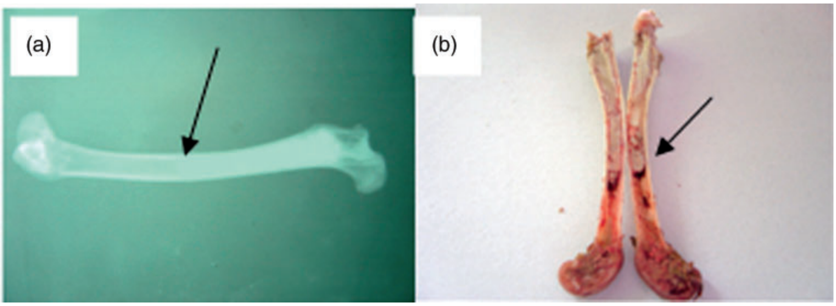

Figure 1. Representative images showing bone cement filling the medullary cavity of the right femur. (a) X-ray image. (b) Photograph. Black arrows indicate the bone cement.

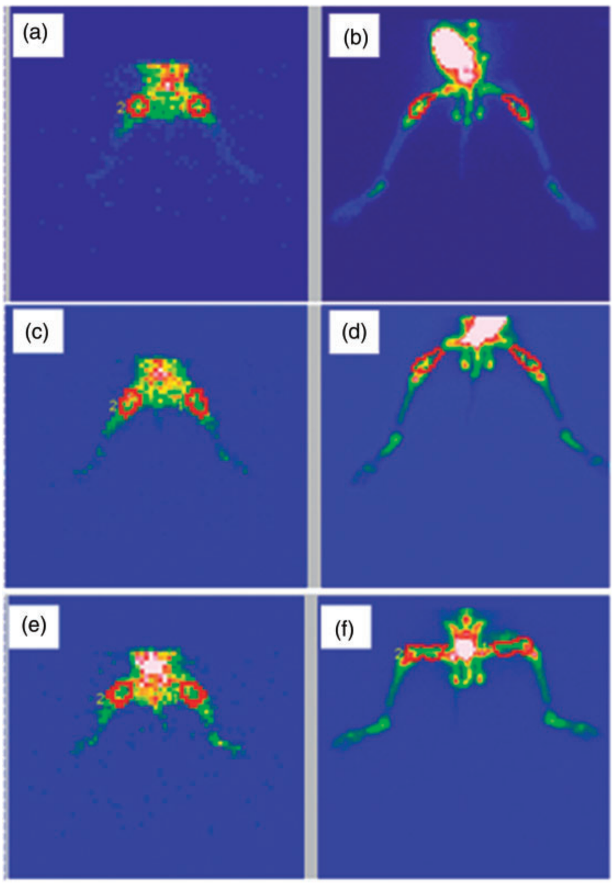

Figure 2. Representative scan images of rabbits. (a, c, e) Dynamic scans. (b, d, f) Static scans. (a, b) Immediately postoperatively. (c, d) Four weeks postoperatively. (e, f) Eight weeks postoperatively.

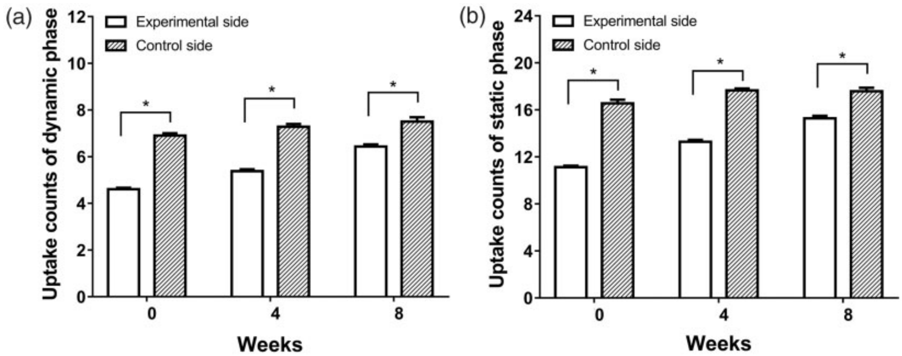

Figure 3. Radioactive counts of right (experimental) hind legs and left (control) hind legs at different time points after surgery. (a) Dynamic scans. (b) Static scans. *$P < 0.05$.

the control hind legs ($P < 0.05$). Meanwhile, the ^{99m}Tc-MDP was distributed less evenly in the ROI of the experimental hind legs.

The radioactive counts of the ROI in the experimental and control legs on both the dynamic and static scans were recorded at each time point. The dynamic scan images showed that the mean radioactive counts of the ROI in the experimental hind legs immediately after surgery and at 4 and 8 weeks postoperatively were 4.60 ± 0.07, 5.38 ± 0.08, and 6.43 ± 0.10, respectively (Figure 3(a)). According to the static scan images, the radioactive counts of the ROI in the experimental legs at these time points were 11.12 ± 0.13, 13.29 ± 0.15, and 15.28 ± 0.22, respectively (Figure 3(b)). In the control hind legs, the dynamic scans taken immediately after surgery and at 4 and 8 weeks postoperatively showed radioactive counts of 6.90 ± 0.10, 7.28 ± 0.12, and 7.50 ± 0.19, respectively (Figure 3(a)), while the static scan images indicated radioactivity counts of 16.55 ± 0.32, 17.65 ± 0.16, and 17.58 ± 0.30, respectively (Figure 3(b)). The ratios of the experimental leg-to-control leg radioactivity were determined from both the dynamic and static scans (Figure 4). In both the dynamic and static scans, the ratio of radioactive counts consistently and significantly increased at each postoperative time point ($P < 0.05$), but all ratios were <1. These results implied that both the blood flow and bone metabolic rate in the ROI of the experimental hind legs were lower than those in the control hind legs because the radioactivity counts were strongly and positively associated with the bone metabolism and blood flow rates.[18]

Discussion

Hip arthroplasty is well recognized as the gold standard for treatment of advanced hip disease. Cemented hip arthroplasty has been extensively applied since the development of third-generation bone cement in the last century.[1,2] However, the development and application of biomedicine not only brings convenience to patients' lives but also introduces some potential problems.[19,20] For example, bone cement placed in the femoral medullary cavity can lead to various complications.[6,7] In the present study, we used rabbits as models of cemented hip arthroplasty and successfully filled the right proximal femoral medullary cavity with bone cement made of PMMA powder and MMA monomers (Figure 1).

When the femoral medullary cavity is filled with bone cement, the cement is

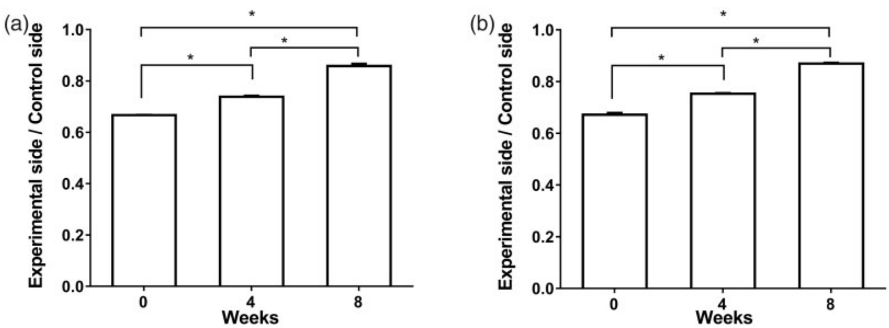

Figure 4. Ratio of radioactive counts of right (experimental) hind legs and left (control) hind legs at different time points after surgery. (a) Dynamic scans. (b) Static scans. $*P < 0.05$.

expected to reduce the volume of the bone marrow cavity. It may also cause mechanical, thermal, and chemical damage to the upper and middle femoral endosteum and intramedullary vessels, resulting in hemodynamic changes in the bone and intramedullary cavity.[8–10] Previously published studies have been limited to the proximal femur and associated effects around the prosthesis; few researchers have considered the effects of bone cement on the blood flow and metabolism of the distal femur.[14] In the present study, we compared the radioactivity counts of the experimental and contralateral control (sham-operated) hind legs after intravenous injection of 50 to 150 MBq of ^{99m}Tc-MDP via a marginal ear vein (Figures 2 and 3). The radioactivity count is considered to reflect the blood circulation and bone metabolism of the distal femur.

Blood flow is generally defined as the volume of blood flow per unit time and per unit cross-sectional area of bone tissue. Radionuclide bone imaging has been used to determine bone blood flow because it accurately reflects dynamic changes, the measurements are repeatable, the operative time is short, and minimal trauma occurs.[21] Nutton et al.[22] demonstrated that radioactivity counts taken within 60 seconds after intravenous injection of ^{99m}Tc-MDP were able to indicate bone blood flow. The distribution of radionuclide determined from the bone scan also reflects the blood supply and metabolism of the bone as well as the metabolic activity level.[23,24] Radionuclide bone imaging has been used to study the proximal femur, prosthesis, and bone cement used for cemented hip arthroplasty.[25,26] In the present study, we evaluated the effects of bone cement on the distal femoral blood flow and metabolism of experimental legs in which the proximal femoral medullary cavity was filled with bone cement relative to that of the control legs using both dynamic and static radionuclide bone scans.

Both the dynamic and static scans showed that the radioactive counts were significantly lower in the right hind legs than control legs at each tested time point (i.e., immediately postoperatively and 4 and 8 weeks postoperatively) (Figure 3). These results indicate that the bone cement was closely associated with a decrease in the local blood supply and metabolic activity of the distal femur. It appears likely that the bone cement in the femoral cavity led to a lowering of the blood supply to the distal femoral medullary cavity. This could have been due to injury of the intramedullary and metaphyseal blood vessels and nutrient arteries[8–10,27–29] and elevated intraosseous pressure in the distal femur.[9–11]

Further analysis of the radioactivity data at the various time points showed that the blood supply and metabolic activity in the experimental distal femur gradually improved over time. This may be attributed to revascularization within the right hind distal femur.[30] However, full recovery was not achieved within the 8-week postoperative period (Figure 4). An elevation of the intraosseous pressure and destruction of the microenvironment in the distal femur would seriously impede the regeneration of blood vessels and lead to osteonecrosis,[31,32] and bone metabolism is highly dependent on the corresponding blood supply.[30] The results from the dynamic and static scans clearly suggested a decrease in the blood flow of the experimental distal femur, which further indicated slower bone metabolism.

Conclusion

Blocking the proximal femoral medullary cavity with bone cement had significant effects on the blood circulation of the femur and marrow and decreased the blood flow and bone metabolic rate of the distal femur. Future studies are warranted to further confirm these findings in a clinical study and investigate the mechanisms of how bone cement occlusion in the proximal femoral medullary cavity exactly affects the distal femur.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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