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SCIENTIFIC ARTICLE

Preliminary results: use of multi-hole injection nails for intramedullary nailing with simultaneous bone cement injection in long-bone metastasis

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Abstract

Objective For symptomatic metastasis of the long bones, intramedullary nailing has been the most accepted fixation method. Intramedullary nailing has effective control of pain, perioperative bleeding, and local tumor progression by augmentation with bone cement around the nail. Here, we report the preliminary results of a new surgical implant that allows for simultaneous injection of bone cement while inserting a percutaneous, flexible intramedullary nail.

Materials and methods We performed palliative surgeries for long-bone metastasis using a multi-hole injection nail (MIN) with multiple side holes in the distal one third. When the nail tip entered the metastatic cancer lesion, the bone cement injection was started, and continued until the nail was completely seated. Ten patients with advanced cancer underwent palliative surgery using the new implant with simultaneous bone cement injection for humeral ($n = 4$), femoral ($n = 4$), and tibial ($n = 2$) metastases.

Results The mean operative time was 42 min (range, 36–52 min). The mean length of the injection nail was 23.0 cm (range, 18.0–33.0 cm), and the mean volume of cement was 28.0 ml (range, 14.0–40.0 ml). Marked pain palliation ($p < 0.001$) and functional recovery ($p = 0.01$) were verified. The mean Musculoskeletal Tumor Society (MSTS) functional score improved significantly from 12.5 at 6 weeks preoperatively, to 24.9 postoperatively. No acute postoperative complications, including cement embolism, occurred.

Conclusion This minimally invasive surgical method with MIN could be useful for stabilization of long-bone metastases in patients with advanced cancer.

Keywords Cancer · Bone metastasis · Palliative · Minimally invasive · Intramedullary nail · Cementoplasty

Introduction

Patients with multiple bone metastases suffer from severe pain, affecting their quality of life. Various methods, such as analgesics, chemotherapy, radiation therapy, radiopharmaceutical agents, and surgery have been developed for palliative pain improvement [1, 2]. These patients generally require structurally augmenting surgery of the vertebrae, pelvis, femoral neck, or long bones of the limbs. Surgical techniques for bone metastases include curettage and internal fixation, open or closed interlocking intramedullary (IM) nailing, and prosthesis or allograft reconstruction [3]. Until now, IM nailing has been the most accepted fixation method for femoral and tibial metastases because of the ease of insertion, and load-sharing properties [4].

The need for stabilization of a bone metastasis remains controversial, particularly in patients with multiple organ failure and short life expectancy because of advanced cancer. Minimally invasive surgery has become available for high-risk patients, with the advantages of a small surgical incision, minimal blood loss, and short operative time. Palliative surgical techniques that do not involve tissue dissection include cementoplasty, ethanol injection, cryoablation, and radiofrequency ablation [5]. Among them, percutaneous polymethylmethacrylate (PMMA) cementoplasty produces

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favorable outcomes for patients with spinal tumors and tumors in flat bones, such as the pelvis, scapula, and sternum [6, 7]. However, the risk of a pathological fracture remains high when percutaneous cementoplasty is performed in a long bone without metal fixation [8, 9]. The hollow perforated screw is a new device for achieving fixation for femoral neck metastasis, while simultaneously injecting PMMA into the weak bone area through multiple side holes [10]. Percutaneous flexible Ender nail fixation and IM PMMA injection was introduced for diaphyseal metastases of the humerus, femur, and tibia [11]. In this method, the cement injection needles are placed into the IM area through new portals in the skin and bone [12].

The new implant described here is a flexible titanium nail that has hollow perforations and multiple side holes on the distal portion (MIN, multi-hole injection nail [Solco Biomedical, Seoul, Korea]). The implant can be used to inject bone cement through the nail during percutaneous fixation without making additional skin incisions and bone holes for cement needles. Here, we report the preliminary results of this new surgical instrument.

Materials and methods

Patient characteristics

From the prospectively collected database of our hospital, 10 consecutive patients who underwent MIN fixation with simultaneous bone cement injection for long-bone metastases between 2015 and 2017 were identified. Medical records were reviewed to collect information, including: patient and primary tumor characteristics, details of surgery, and surgical results. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The institutional review board of our institute approved this study (NCC2014–0215). Informed consent was waived by the institutional review board of our institute (NCC2014–0215).

All 10 patients (3 men and 7 women; mean age, 56.4 years; range, 46.0–72.0 years; mean body mass index (BMI), 22.1 kg/m^2; range, 17.0–28.1 kg/m^2; Mirels' score, 8–11; grade 8 = 1, grade 10 = 2, and grade 11 = 7 patients] underwent MIN fixation with simultaneous bone cement injection when their advanced cancer had progressed. The primary cancers were lung ($n = 5$), breast ($n = 4$), and endometrial cancer ($n = 1$). All patients had multiple metastases over bones and organs, with osteolytic lesions located in the diaphysis of the long bones. Of the 10 patients, 8 showed circumferential cortical erosion from the medullary space within a cortical shell; the other 2 patients had cookie-bite lesions and of them, the patient with the largest lesion had a 50% area affected in a transverse section of the cortical bone. All patients experienced limb pain because of impending fractures in the long bones, but none had a pathological fracture. The locations of MIN surgery were the humerus ($n = 4$), femur ($n = 4$), and tibia ($n = 2$). Preoperative or postoperative radiation therapy was performed in 90% of patients. The severity of regional pain was measured by a visual analog scale (VAS) ranging from 0 (no pain) to 10 (worst pain). Pain was measured on the day before surgery, and 1 and 4 weeks postoperatively. The functional outcomes for the upper and lower limbs were objectively assessed through the Musculoskeletal Tumor Society (MSTS) on the day before surgery, and 4 weeks postoperatively [13]. Only 2 of the 10 patients survived until the last follow-up (Table 1). For the 8 patients who died of disease after surgery, mean survival was 12.6 months (range, 5.0–29.0 months). No implant failure occurred during the remaining survival period.

Multihole injection nail

The MIN was developed as a hollow, flexible, titanium nail with multiple side holes in the distal third. The MIN is connected to an injector handle with a stylet. Bone cement can be injected deeply during percutaneous fixation without adding bone cortex holes (Fig. 1).

Surgical method

The patient was positioned in the lateral decubitus or supine position according to the nail insertion site. We selected the appropriate length MIN and confirmed the length under fluoroscopy. The length of the nail was chosen so that the tip could reach the healthy bone through the tumor. The MIN was tightened with the injector handle and shaped manually to match the curvature of the bone with a press bender. A 2.2-mm Steinmann pin fixation was placed at the entrance point and a small skin incision was made for cannulated drilling. After cannulated drilling of the cortex, the MIN was inserted into the bony entrance hole. The MIN was advanced into the medullary canal manually, and with hammering, until fully seated in the entrance bone. If the predicted path of the nail was inappropriate for advancement, the MIN was pulled out and re-bent. We checked the precise nail length and curvature under fluoroscopy before fully inserting the nail. The nail tip and side holes were repositioned at the osteolytic lesion, and the PMMA bone cement was prepared.

The low-viscosity, radiopaque PMMA was mixed and transferred to a 30- or 50-ml syringe, depending on the number of cement packs needed (20 g/pack). Then, PMMA was transferred into several 1-ml syringes. We aspirated fluid in the bone marrow space such as blood or tumor necrosis through the hollow nail with an empty syringe before injecting the bone cement. The bone cement was injected under

Table 1 Patient characteristics and surgical results

Number	Age/sex	Primary cancer	Operativesite	Mirels' score	Operative time (min)	Length the of nail (cm)	Amount of cement injection (ml)	C, R (preoperatively/ postoperatively)	VAS score (preoperatively/ postoperatively 1 week/4 weeks)	MSTS functional score (preoperatively/ postoperatively 4 weeks)	Survival after surgery (months)/final status
1	65/female	Lung	Femur left	11	43	24	37	C/C + R	9/4/0	13/26	29/DOD
2	46/female	Breast	Humerus left	11	36	18	19	C/R	7/3/3	10/25	6/DOD
3	55/female	Breast	Humerus left	8	38	21	14	C/C + R	6/3/2	18/27	24/DOD
4	54/female	Breast	Femur right	11	45	33	32	C/C + R	8/4/1	12/26	15/DOD
5	55/male	Lung	Humerus right	10	37	24	14	C + R/C	8/3/2	10/25	7/DOD
6	54/female	Breast	Humerus right	10	41	21	30	C/no	8/4/2	18/27	9/DOD
7	72/male	Lung	Femur left	11	48	24	40	C/R	9/4/4	5/10	6/DOD
8	60/female	Lung	Tibia right	11	38	24	34	C/C + R	9/5/3	18/25	5/DOD
9	60/male	Lung	Femur left	11	52	18	32	C + R/C	9/7/7	9/18	22/AWD (amputation at 6 months postoperatively)
10	43/female	Endometrial	Tibia left	11	35	21	18	C + R/no	8/3/3	7/14	6/AWD

C chemotherapy, *R* radiotherapy, *VAS* visual analogue scale, *MSTS* Musculoskeletal Tumor Society, *DOD* death of disease, *AWD* alive with disease

fluoroscopic guidance. If the injection became difficult, a handle stylet was used to push the PMMA. Leakage to the surrounding soft tissue must be carefully observed at the initial stage. After sufficient PMMA was injected into the osteolytic area, we further advanced the nail by hammering the handle until it was completely buried in the bone, and continued to inject the bone cement. As the viscosity of the cement gradually increases over time, the cement injection typically started 3–4 min after mixing, and was completed within 10 min to ensure appropriate viscosity. The injector handle was detached by rotating it counter-clockwise and removed within 12 min, before the cement hardened completely. During bone cement injection, temporary changes in vital signs need to be carefully monitored for blood pressure, pulse rate, and respiration, due to toxicity of PMMA fumes.

Statistical analysis

Changes in pain VAS and MSTS functional scores were validated by distribution-free methods for repeated measures. The Wilcoxon signed rank test and Friedman's test were used for variables measured two and three times respectively. A p value <0.05 was considered significant. Statistical analyses were performed using SPSS 18.0 software (IBM, Chicago, IL, USA).

Results

Surgical information

Spinal anesthesia was used in 6 patients for lower extremity surgery and the interscalene regional block was used in 4 patients for surgery on the humerus. The mean operative time from skin incision to closure was 41 min (range, 35–52 min). The mean volumes of cement used were 32.2 ml (range, 18.0–40.0 ml) and 19.2 ml (range, 14.0–30.0) for the lower and upper extremities respectively (Figs. 2, 3 and 4). Perioperative red blood cell transfusions were performed in 3 patients (2 patients preoperatively and 1 patient postoperatively; Table 1).

Surgical outcomes

Marked pain palliation was noted 1 week postoperatively ($p < 0.001$). The pain level had improved even more, 4 weeks after surgery ($p < 0.001$). The mean VAS pain score on the day before the operation was 8.1 (range, 6–9). The mean VAS pain scores 1 and 4 weeks after the operation were 4.0 (range, 3–7) and 2.7 (range, 0–7) respectively. The mean MSTS functional score improved significantly from 12.0 (40.0%) preoperatively to 22.3 (74.3%) postoperatively ($p = 0.01$). No thromboembolisms or cement embolisms were encountered. No MIN

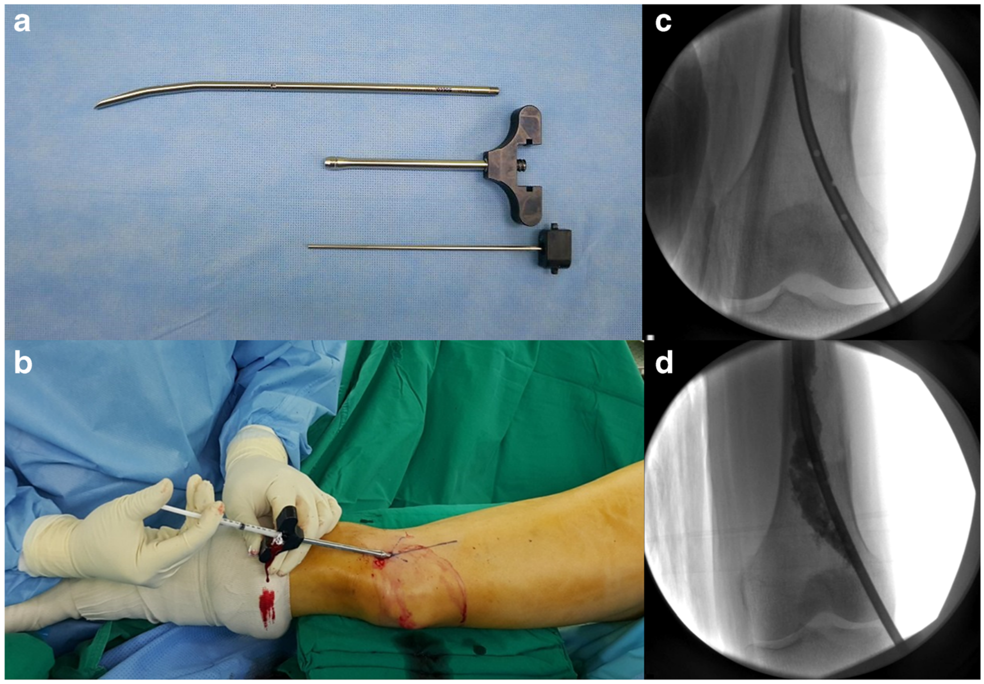

Fig. 1 **a** Multihole injection nail composed of a hollow, perforated, titanium, flexible nail with multiple side holes on the distal portion, an injection handle, and a stylet. **b** Intraoperative photograph and **c**, **d** fluoroscopy shows injection of the bone cement while inserting the nail

Fig. 2 A 55-year-old man had multiple surgical treatments because of bone metastases from lung cancer. **a** The preoperative plain radiograph shows an osteolytic lesion of the humerus. **b** The postoperative plain radiograph shows sufficient filling of bone cement around a multi-hole injection nail without extraosseous leakage

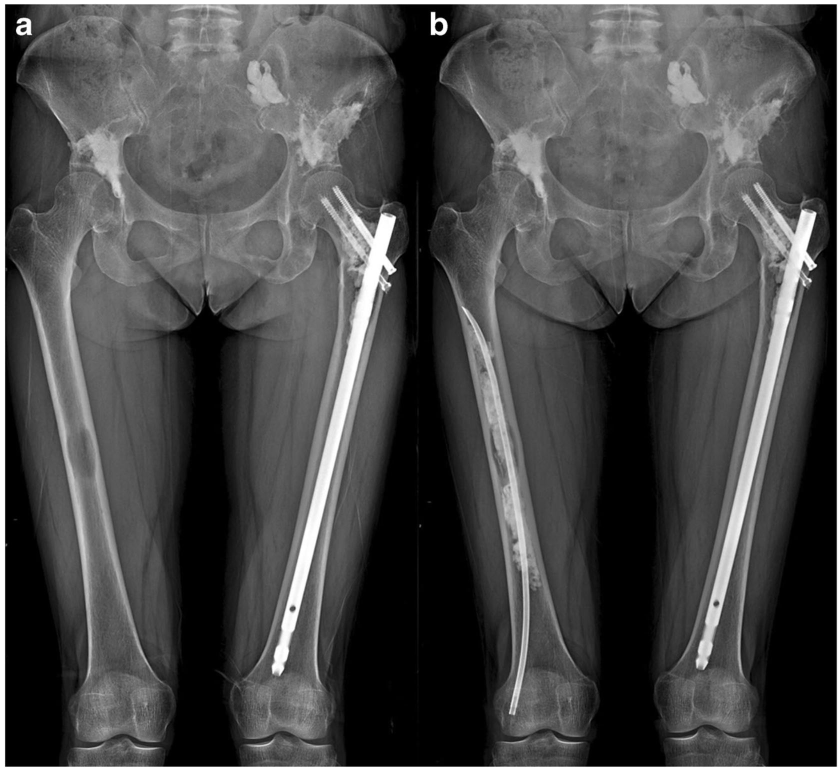

Fig. 3 A 54-year-old woman had multiple surgical treatments because of bone metastases from breast cancer. **a** The right femur shows an osteolytic lesion. **b** Earlier surgical intervention before massive bony destruction is performed

breakage, and no further IM osteolysis of operative bone was observed (Table 1).

Discussion

Using the MIN with augmentation by injected bone cement provides immediate mechanical stabilization, resulting in early pain relief and acceptable functional recovery. Surgery required regional anesthesia in all patients, and was performed with a short operative time. Among the palliative stabilization methods using the IM nail, MIN surgery is the least invasive; thus, the recovery period is short, and the possibility of wound problems is low. Therefore, it is less disturbing to scheduled chemotherapy or radiation therapy.

It is important to relieve pain and prevent pathological fractures when treating patients with metastatic bone cancer. Closed IM nailing is the most useful method for metastatic cancer of the long bone in the limbs [14]. However, because closed IM nailing in the long bone does not remove tumor tissue, patients are at risk for progressive bone destruction owing to IM spreading of the tumor during medullary reaming or when inserting the nail. Medullary reaming is often needed to fix rigidity because of sclerotic changes occurring in response to previous treatment of osteolytic bone such as radiation therapy and administration of bisphosphonate [15]. To overcome the disadvantages of closed IM nailing alone, a method of adding percutaneous cement augmentation has been introduced. Bone cement augmentation not only improved immediate postoperative stability, but also restricted the IM spread of tumors due to the PMMA, and reduced the frequency of reoperations due to osteolysis progression [16]. Concomitant bone cement injection and internal fixation of a metastatic bony lesion is a proven effective technique [10–12, 16]. However, the risk of a pathological fracture remains high when percutaneous cementoplasty is performed in a long bone without metal fixation [8, 9]. Moreover, in patients with advanced cancer, an important consideration is reducing the invasiveness of surgery, because of their high risk during the perioperative period. Therefore, it is critical to select a fixation method that is less invasive than closed IM nailing, but more stable than percutaneous cementoplasty, such as a low-profile flexible nail. The MIN is a type of flexible nail and a unique, minimally invasive surgical tool that does not require additional skin incisions or bony holes for cement needles, unlike the previously introduced flexible nail (Ender nail) fixation with a percutaneous cementing technique [11, 12].

Mechanical and oncological factors determine an optimal approach for long-bone metastases. Mechanical factors include the location of bone metastasis, patterns of bone destruction, and the presence of cortical breakage. Generally, the humerus is a more suitable area for applying MIN fixation with simultaneous cementing because it is nonweight-bearing. For the long bones in the lower extremity, the MIN with bone cement augmentation should be considered more carefully because the femur and the tibia need to be stable enough to

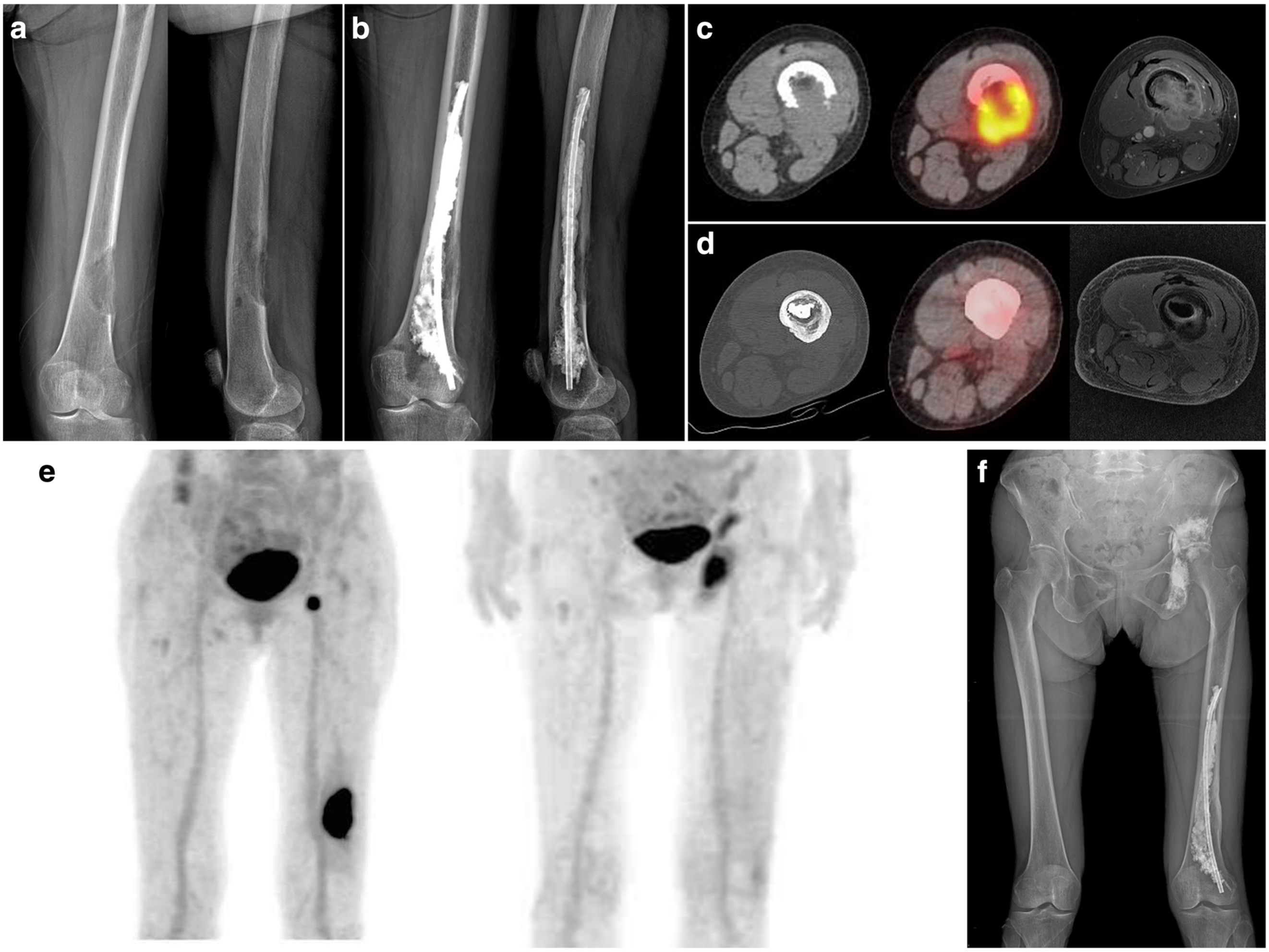

Fig. 4 **a** A 66-year-old female patient with advanced lung cancer had an impending fracture of the distal femur. **b** A postoperative radiograph shows bone cement injected through the multi-hole injection nail. **c** Preoperative computed tomography (CT), positron emission tomography-computed tomography (PET-CT), and magnetic resonance imaging (MRI) show cortical breakage and extraosseous extension of metastatic cancer. **d** The postoperative CT, PET-CT, and MRI show well-regenerated cortex around the bone cement. **e** Comparing the regional PET-CT images before and after surgery, the tumor of the left pelvis progresses, but the lesion of the left femur disappears. **f** The minimally invasive surgical method for metastatic bone cancer provides a better quality of life for patients with advanced cancer

bear weight. Oncological factors are primary cancer type, response to treatment, and patient characteristics, such as BMI, bone density, activity level, and remaining life expectancy. In our series, a patient underwent amputation above the knee at 6 months postoperatively. The location of bone metastasis was the distal metaphysis of the femur and the primary tumor was lung cancer that did not respond to chemotherapy. Despite the absence of a pathological fracture after MIN with cement augmentation, reoperation was needed because of the refractory cancer pain around the knee.

The most worrisome complications during bone cement injection are fat embolism, cement embolism [17–19], or extraosseous cement leakage [20, 21]. In our study, no fat or bone cement embolisms were encountered. Additionally, no extraosseous cement leakage was detected, even in the cortical cookie bite lesions of two patients with lung cancer.

Our study had some limitations. The number of the patients was relatively low. There is a possibility that the complications did not occur because of the small number patients in the study population; however, it is still necessary to pay attention to the complications. In addition, the patients had multiple factors associated with pain and limb function of the affected extremity. For example, radiation therapy and/or chemotherapy factors could be the confounding factor for more precise evaluation. Last, there were no control groups in this study. Theoretically, MIN with bone cement augmentation has the advantages of requiring less surgical time and reduced invasiveness than other similar palliative IM nailing with bone cement injection. However, this study did not provide a direct comparison between the results. The influence of combined therapy and comparison with standard surgical technique should be performed in the future.

In conclusion, the newly devised MIN may provide another option for palliative surgical management of long-bone metastases in patients with advanced cancer. Many other injectable materials besides PMMA bone cement, including tumor suppressive agents or bone healing materials, may be used with the MIN, but this needs to be verified through further studies.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

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