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# Factors Associated with Perioperative Serum Calcium Levels in Percutaneous Kyphoplasty for Osteoporotic Vertebral Compression Fracture: A Prospective Clinical Study

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Background:** Long-term hypocalcemia can result in osteoporotic vertebral compression fracture (OVCF). Transient paralysis and tetraplegia due to hypocalcemia is a rare but severe complication after kyphoplasty. The aims of this prospective clinical study were to investigate the clinical factors associated with serum calcium levels in patients undergoing percutaneous kyphoplasty (PKP).


**Material/Method:** Sixty-eight patients with OVCF were clinically evaluated before and after PKP. Serum calcium was measured before surgery and 24 hours after surgery. Clinical information included the time between vertebral fracture and surgery, the number of involved vertebral bodies, the dose of bone cement required during surgery, and bone mineral density. Correlation coefficient and simple linear regression analysis were performed to identify the clinical factors associated with serum calcium levels.

**Results:** Peri-operative serum calcium levels were significantly and positively associated with the dose of bone cement required during PKP and the number of affected vertebral bodies. There was a significant and negative correlation between the time from vertebral fracture to surgery and bone mineral density, which were shown by linear regression analysis to have a predictive value of 5.8% and 47.3%, respectively.

**Conclusions:** For patients undergoing PKP, the amount of bone cement required and the number of affected vertebral bodies were associated with low serum calcium levels. Surgeons should be aware of the importance of measuring and monitoring serum calcium levels in this patient group.

**MeSH Keywords:** **Bone Cements • Cementoplasty • Hypocalcemia**

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## Background

Worldwide, with the increasing aging population, more elderly people suffer from painful osteoporotic vertebral compression fracture (OVCF). According to a study that included 27 countries in the European Union, the prevalence of OVCF was estimated to be 1.9% and was shown to be associated with increasing age and female gender [1]. The incidence of OVCF in women aged between 85–89 years was shown to be almost eight-time higher than that in women aged between 60–64 years [1]. The incidence of OVCF in women is reported to be between 2–3.5 times more than that in men [1–3].

Patients who have OVCF require urgent management due to the serious complications of this condition, which can include nerve damage and paralysis. Currently, there are two treatment approaches for the management of patients with OVCF, conservative treatment, and surgical treatment. Conservative treatment includes bed rest, physiotherapy, analgesia, and treatment with bisphosphonates to preserve bone density. In the elderly patient population, conservative management increases the risk of adverse outcomes due to the side effects of opioid analgesic medication, and prolonged inactivity, which also can seriously affect the quality of life [2]. Surgical treatment includes balloon kyphoplasty, vertebroplasty, and surgical stabilization. Kyphoplasty and vertebroplasty, are minimally invasive procedures that can be performed percutaneously and with good efficacy and are widely used. However, these procedures are associated with complications, including leakage of bone cement, deep venous thrombosis and pulmonary embolism, infections, and new fractures at adjacent vertebral levels [4–6]. Transient paralysis and tetraplegia due to hypocalcemia is a rare but severe complication following kyphoplasty.

Because there have been few published studies on the risk factors and effects of hypocalcemia in patients undergoing surgical management of OVCF, the aims of this prospective clinical study were to investigate the clinical factors associated with serum calcium levels in patients undergoing percutaneous kyphoplasty (PKP).

## Material and Methods

### Ethical approval and patient consent

This study was approved by the Medical Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong University prior to patient enrolment. The study participants provide written informed consent to participate in this research, and their rights and confidentiality were protected during the study and during data analysis.

### Patients studied

A single-center prospective study was conducted at the Shandong Provincial Hospital Affiliated to Shandong University between February 2016 and September 2017 and included consecutive patients who were diagnosed with osteoporotic vertebral compression fracture (OVCF) with planned elective percutaneous kyphoplasty (PKP). Patients were excluded from the study if they had severely compressed vertebral bodies (burst fractures), secondary osteoporosis due to inflammation, endocrine disorders, or corticosteroid treatment, neurological symptoms, primary bone tumors, and spinal metastases.

### Percutaneous kyphoplasty (PKP)

All patients underwent PKP in the operation room, which allowed availability of immediate open decompression surgery, if required. The patients were in the prone position, with two transverse bolsters under the chest and pelvis to maintain the spine in a position of extension. The surface position of the target vertebral body was marked under fluoroscopy. As a pain reducing measure, all newly fractured vertebrae underwent vertebral augmentation with the use of bone cement. All the PKP surgical procedures were performed under local anesthesia combined with sedation and used a bilateral approach. Heraeus OSTEOPAL®V spinal cement with precision cement delivery was used (Heraeus, Hanau, Germany). Anteroposterior and lateral images were performed using a mobile C-arm fluoroscopic X-ray system during surgery. All other procedures were standard surgical procedures.

### Clinical data

Preoperative and 24-hour postoperative clinical data collected for each patient included serum calcium measurements, the amount of bone cement used during surgery, the time between vertebral fracture and surgery, the number of vertebral bodies that required surgery, and bone mineral density. Any change in preoperative and postoperative serum calcium levels was noted.

### Statistical analysis

Data were analyzed using SPSS version 16.0 statistical software (IBM, Chicago, IL, USA). Pearson's correlation coefficient was used to analyze the correlation with changes in serum calcium and other variables. Any significant associations ( $p < 0.05$ ) were also analyzed using simple linear regression.

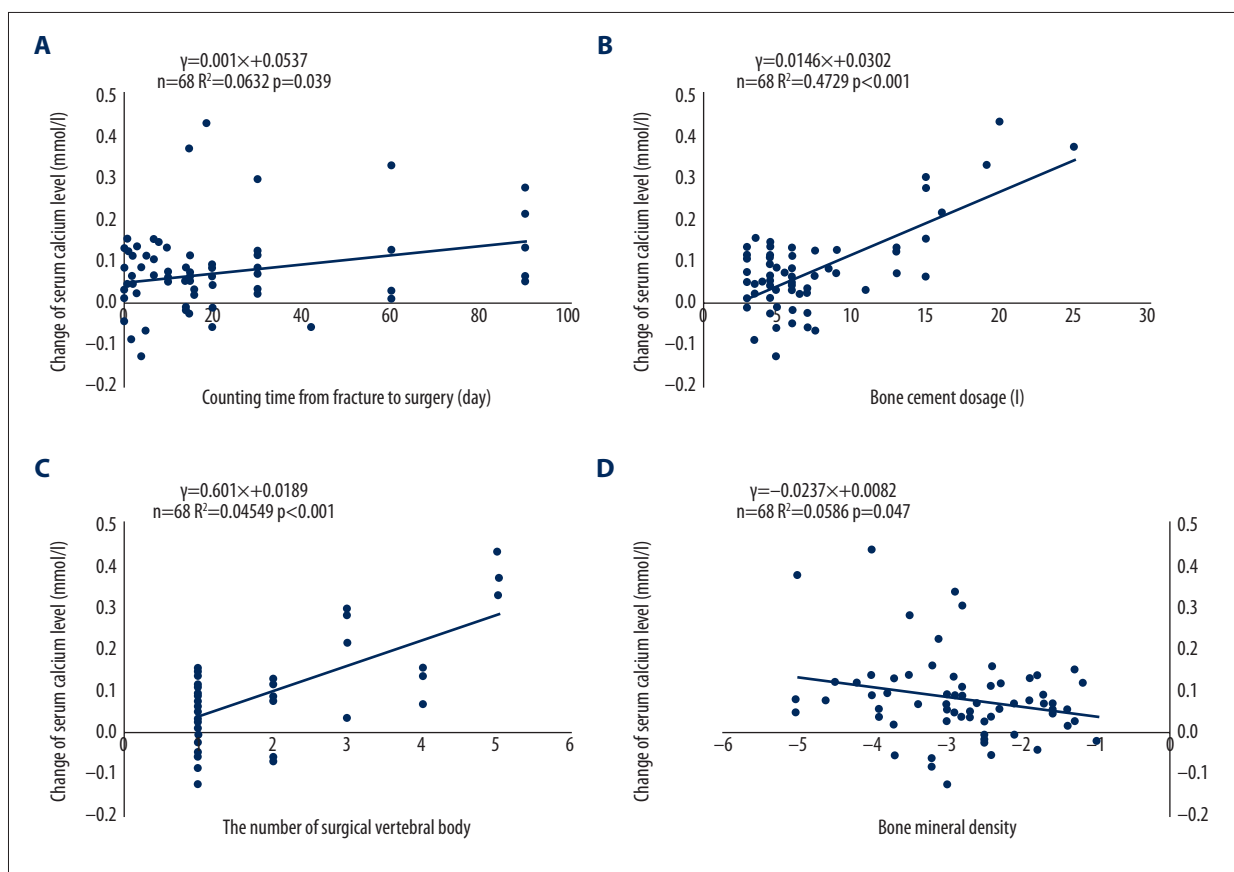
## Results

Between February 2016 and September 2017, 82 patients were initially included in the study cohort, 73 met the study

**Table 1.** Correlations between clinical factors and change in serum calcium level (n=68).

	Clinical variable				
	BCD	TFS	Age	NSVBs	BMD
r-value	0.688	0.251	-0.073	0.674	-0.242
p-value	<0.001	0.039	0.557	<0.001	0.047

BCD – bone cement dosage; TFS – time from fracture to surgery; NSVBs – the number of surgical vertebral body; BMD – bone mineral density.



**Figure 1.** Scatter plots and linear regression values for all significant correlations with change in serum calcium levels. (A) A significant correlation is shown between the change in serum calcium level and the time between vertebral fracture and surgery. (B) A significant correlation is shown between the change in serum calcium level and degree of bone cement. (C) A significant correlation is shown between the change in serum calcium level and the number of the surgical vertebral body. (D) A significant correlation is shown between the change in serum calcium level and bone mineral density. n – sample size; R<sup>2</sup> – the coefficient of determination; Y – linear regression equation; p – p-value for the regression coefficient.

inclusion criteria, but 5 refused to participate in. Finally, 68 patients were included in the study, all of whom had a diagnosis of osteoporotic vertebral compression fracture (OVCF) and underwent elective percutaneous kyphoplasty (PKP).

Out of the 68 cases, there were 11 men (16.2%) and 57 women (83.8%). The average age was 69 years (range, 50–90 years). All patients were diagnosed with vertebral compression fracture

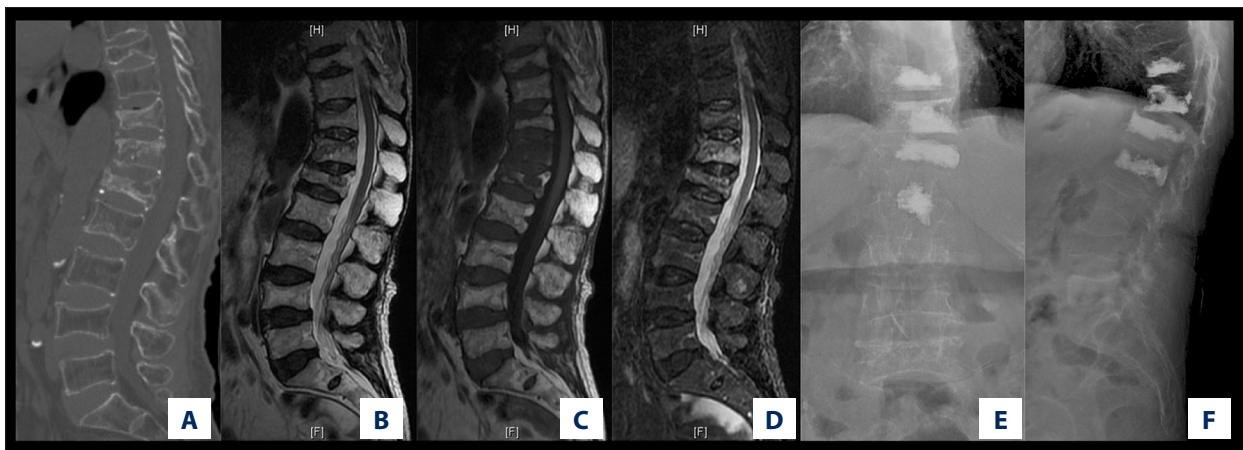
by magnetic resonance imaging (MRI), which showed hypointense signals on T1-weighted imaging, and a hyperintense signal on T2-weighted imaging.

There were 57 patients (83.8%) who had a decrease in postoperative serum calcium levels, which was significantly and positively correlated with the amount of bone cement required during surgery, and the number of affected vertebral. There

**Table 2.** Associations between the changes in the perioperative serum calcium levels and clinical factors, determined by multiple linear regression analysis.

Parameters	UC		SC	t	Sig.	95% CI for Beta		Adjusted R <sup>2</sup>
	Beta	Std. error	Beta			Lower bound	Upper bound	
<b>Model 1</b>								<b>0.461</b>
BCD	0.016	0.002	0.736	6.984	<0.001	0.011	0.020	
TFS	<0.001	<0.001	-0.128	-1.221	0.227	-0.001	<0.001	
BMD	-0.005	0.009	-0.049	-0.514	0.609	-0.024	0.014	
<b>Model 2</b>								<b>0.441</b>
NSVB	0.064	0.010	0.720	6.687	<0.001	0.045	0.083	
TFS	<0.001	<0.001	-0.122	-1.140	0.259	-0.001	<0.001	
BMD	-0.005	0.010	-0.046	-0.472	0.638	-0.024	0.015	

UC – unstandardized coefficient; SC – standardized coefficient; Std – standard; Sig. – significance; CI – confidence interval; BCD – bone cement dosage; TFS – time from fracture to surgery; BMD – bone mineral density; NSVB – the number of surgical vertebral bodies.



**Figure 2.** Computed tomography (CT) and magnetic resonance imaging (MRI) of the spine. (A) Computed tomography (CT) images show compression fractures of T10, T11, T12, L1, L2, and L4. (B–D) Sagittal magnetic resonance imaging (MRI) shows low signal intensity on the T1-weighted image, high intensity on T2-weighted images, and especially high intensity on short tau inversion recovery (STIR) sequences, suggesting acute vertebral compression fracture (VCF) in T11, T12, L1, and L2. (E) Anteroposterior and (F) lateral radiographs confirm appropriate positioning of cement within the vertebral body.

was a significant and negative correlation between the time between vertebral fracture and surgery, and bone mineral density (Table 1), which were shown by linear regression analysis to have a predictive value of 5.8% and 47.3%, respectively (Figure 1). Simple linear regression analysis showed that the amount of bone cement used during surgery and the number of vertebral bodies involved were significant predictors of a change in serum calcium.

Significant relationships ( $p < 0.05$ ) underwent multivariate regression analysis. The amount of bone cement required during surgery and the number of affected vertebral bodies that required surgery were evaluated by two statistical models. Multivariate

regression analysis showed that the amount of bone cement used during surgery and the number of fractured vertebral bodies were a constant significant predictor of a change in postoperative serum calcium level for all patients. Following multivariate regression analysis, the time between vertebral fracture and surgery, and bone mineral density were no longer predictors of a change of serum calcium level (Table 2).

Also, in this study, two patients had complications following surgery. A patient who had an intravertebral injection of 25 mL of bone cement intraoperatively with no initial apparent leakage of bone cement (Figure 2), developed symptoms of numbness in the peripheries six hours after surgery. Urgent neurology

consultation was required to exclude neurological conditions. Urgent blood biochemistry showed that serum calcium was 1.96 mM/L, which was consistent with hypocalcemia. The patient's symptoms improved after intravenous treatment with 10 mL of calcium gluconate (10%). The other patient, who had an intravertebral injection of 22.5 mL of bone cement intraoperatively, developed weakness of the limbs four hours after surgery, but also recovered following treatment with intravenous calcium gluconate.

## Discussion

Patients with osteoporotic vertebral compression fracture (OVCF) who undergo kyphoplasty have been shown to respond with rapid and significant pain relief, which is why kyphoplasty is currently the treatment of choice [7,8]. However, serious postoperative complications can occur, and include spinal cord compression, nerve root compression, deep vein thrombosis, and pulmonary embolism. Previous studies have shown that kyphoplasty can be associated with an increased risk of adjacent level fractures and with cardiac associated postoperative mortality [9-10]. Olsen et al. [11] have previously described the condition known as cement implantation syndrome, which is characterized by hypotension, hypoxemia, and cardiac arrhythmia or cardiac arrest. Kaplan et al. [12] previously reported the occurrence of an allergic response to bone cement in total knee arthroplasty. However, there have been few studies that have investigated the effect of kyphoplasty and bone cement on perioperative serum calcium levels.

Therefore, the aims of this prospective clinical study were to investigate the clinical factors associated with serum calcium levels in patients undergoing percutaneous kyphoplasty (PKP). The findings showed that the amount of bone cement required and the number of affected vertebral bodies were associated with low serum postoperative serum calcium levels. Usually, during the PKP procedure, the number of affected vertebral bodies is associated with the amount of bone cement required, and it is expected that there is a positive correlation between the number of fractured vertebral bodies and the amount of bone cement used. The findings from this study indicated that the amount of bone cement used was associated with lower postoperative levels of serum calcium. This preliminary finding requires verification with further studies.

PKP was performed using local anesthesia, and there was no need for the patient to fast before surgery, so the effect of fasting on serum calcium was excluded. Also, no patients in this study suffered from hypoxia, hypotension, loss of consciousness,

or any manifestations of allergy occurring around the time of use of vertebral bone cement, and bone cement implantation syndrome and bone cement allergy could be excluded.

For patients with multiple vertebral fractures, the total amount of bone cement used should be controlled during surgery, with close attention to serum calcium levels. Postoperative prevention of hypocalcemia may include treatment with intravenous calcium gluconate, and a staged approach to vertebral surgery is a feasible option for cases with multiple vertebral fractures. For patients with weakness or numbness after PKP surgery, it is important to investigate these symptoms immediately with serum biochemistry to identify hypocalcemia.

The mechanism of the reduction of serum calcium in patients treated by PKP remains unclear, but several possible causes exist. Hypocalcemia may occur as a form of toxicity response to bone cement, the bone cement may absorb calcium, or PKP causes additional vertebral fractures in adjacent vertebrae that results in bone healing and increased bone uptake of calcium. Further studies are needed to determine the specific mechanisms involved.

The findings from this study have highlighted that some changes can be made to improve patient management during PKP surgery for patients with OVCF. Serum calcium levels should be measured at multiple time points following surgery to evaluate trends in postoperative serum calcium levels. Also, further studies are needed to determine if other causes of vertebral compression fracture, including spinal metastases and secondary osteoporosis, due to endocrine disorders and corticosteroids, are also associated with hypocalcemia after PKP surgery.

## Conclusions

Hypocalcemia is an important postoperative complication of percutaneous kyphoplasty (PKP) in patients with osteoporotic vertebral compression fracture (OVCF). The findings from this study showed that reduced serum calcium levels were associated with the amount of bone cement used during surgery, which was associated with the number of fractured vertebrae. These findings have clinical implications for the surgical management of patients with OVCF and indicate that the total amount of bone cement used during surgery should be controlled.

## Conflict of interests

None.

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