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Vertebral Body Lavage Reduces Hemodynamic Response to Vertebral Body Augmentation With PMMA

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Abstract

Study Design: Retrospective comparative study.

Objectives: To assess the effect of vertebral body lavage (VBL) on (1) systemic blood pressure, (2) heart rate, and (3) oxygen saturation following cement augmentation procedures for acute vertebral compression fractures (VCFs).

Methods: A total of 145 consecutive patients undergoing cement augmentation for acute VCF (mean age 74 $\pm$ 12 years, age range 42-96 years; 70% female; 475 levels treated) were allocated to the "lavage group" (n = 61 patients; VBL prior to cement application) and to the "control group" (n = 84 patients, no VBL). Mean arterial blood pressure (MAP), heart rate, and oxygen saturation were monitored immediately prior and 3 minutes after cement injection. Logistic regression analysis was performed with ΔMAP $\geq$10 mm Hg before and after cement injection as the dependent outcome variable and demographic, radiographic, and procedural factors as independent variables.

Results: MAP decreased by mean 3 $\pm$ 7.3 mm Hg before and after cement injection in the "lavage group" and 9 $\pm$ 10.5 mmHg in the control group (*P* < .001). There were no significant differences in terms of heart rate and oxygen saturation before and after cement application within each group, or between the 2 groups. Multivariate logistic regression analyses revealed VBL as an independent factor influencing MAP (adjusted odds ratio: 3.49 [confidence interval, 1.16-10.50], *P* = .03).

Conclusion: VBL prior to cement augmentation procedures reduces the hemodynamic response, most likely resulting from decreased amounts of bone marrow substance displaced into the circulation thereby decreasing the risk of pulmonary fat embolism syndrome.

Keywords
osteoporotic vertebral compression fracture, vertebroplasty, kyphoplasty, vertebral body lavage, fat embolism syndrome

Introduction

The prevalence of osteoporotic vertebral compression fractures (VCFs) has been reported to range between 7% and 46% worldwide.[1] Apart from the immense impact on the health care system,[2] VCFs are associated with a high degree of morbidity and mortality in the elderly population.[3,4] Although conservative treatment of VCF may lead to a satisfactory midterm patient outcome,[5] percutaneous cement augmentation procedures with polymethylmethacrylate (PMMA) cement present an effective treatment option allowing for immediate pain relief,[6] decreased progression of kyphotic deformity,[7] and lower incidence of adjacent vertebra fractures in the osteoporotic spine.[8] However, vertebral augmentation procedures with PMMA may be associated with a variety of potentially severe complications. The

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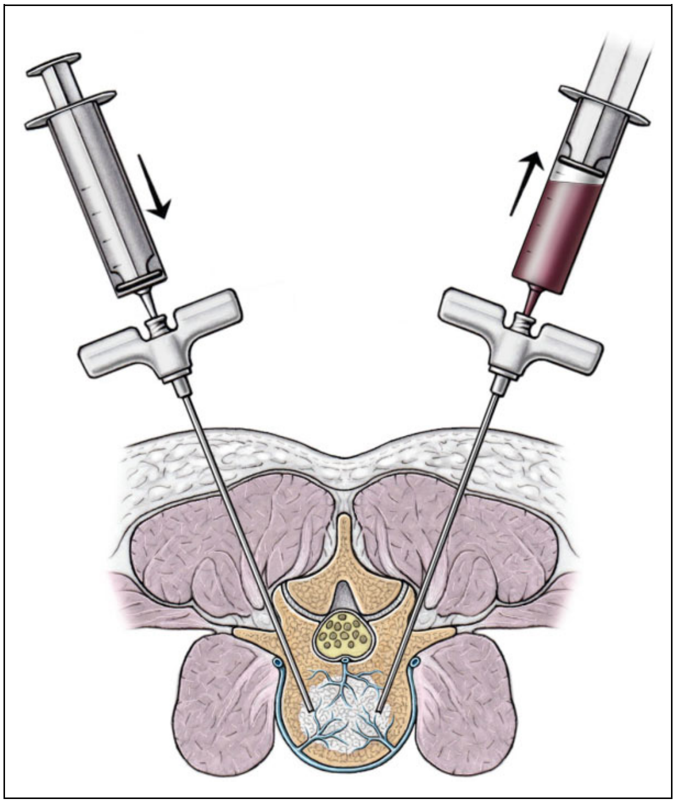

Figure 1. Schematic illustration of the setup of vertebral body lavage is shown. Two Jamishidi cannulas are placed into the vertebral body (bipedicular access) to flush the vertebral body with 30 mL of saline solution. For this purpose, one syringe filled with 10 mL saline solution is attached to one cannula (left), whereas a second empty syringe is attached to the contralateral cannula (right). Vacuum is applied on the empty syringe thereby rinsing the vertebral body with saline solution and removing bone marrow particles from the vertebral body. This procedure is repeated three times. Positive pressure on the syringe filled with saline solution has to be avoided to not mimic the effect of direct cement injection and to prevent displacement of bone marrow and fat into the circulation.

risk of cement leakage through the fracture gaps has been reported to range between 3% and 74% in different studies,[9] and subsequent neurological compromise from compression of neurological structures occurred in 0.3% to 5%.[9] Furthermore, endovascular cement leakage causing pulmonary cement embolism occurs in up to 25%. Finally, displacement of the bone marrow particles from the injected cement into the vascular system causes fat embolism in the downstream blood vessels, most frequently occluding arterioles and capillaries of the lung[9] resulting in fat embolism syndrome.[10] Three strategies have been developed to counteract cement leakage and endovascular bone marrow displacement, including limited cement volume injected per session,[10,11] high viscosity of the cement during the injection,[12,13] and removal of bone marrow from the vertebral body prior to cement injection.[14] The latter is achieved by a previously described technique of vertebral body lavage (Figure 1). Vertebral body lavage has been shown to decrease the injection forces thereby allowing the injection of more viscous PMMA in a cadaveric study.[15] Moreover, it improved the systemic cardiovascular response and to decreased the rate of pulmonary fat embolism in tissue biopsies in an in vivo sheep model.[15] Finally, a recent study revealed lower vascular and cortical (ie, through the fracture gaps) cement leakage rates in patients that previously underwent vertebral body lavage as compared with a control group.[16] However, there is a lack of clinical evidence regarding the influence of vertebral body lavage on the systemic hemodynamic response to cementation. We therefore asked whether vertebral body lavage in patients undergoing cement augmentation procedures for acute VCF leads to (1) decrease of systemic blood pressure, (2) increased heart rate, and (3) drop of oxygen saturation immediately after injection of PMMA cement compared with a nonlavage control group.

Materials and Methods

A retrospective comparative study was conducted including 145 consecutive patients undergoing cement augmentation procedures for acute VCF at our institution between January 2012 and August 2014. The mean age at surgery was 74 $\pm$ 12 years (range 42-96 years) and 70% of the patients were female. In total, 475 levels were augmented in all patients. Patient charts were reviewed for age, gender, level of fracture, number of fractured vertebrae, number of cemented vertebrae, cardiovascular, and pulmonary comorbidities, type of augmentation procedure, cement leakage (cortical defect, intradiscal, vascular) on postoperative anterior-posterior and lateral standing radiographs, and perioperative complications related to surgery. The indication for surgery was new onset of back pain (<6 weeks) with or without recalled trauma, and the radiographic diagnosis of an acute VCF. The age of VCF was assessed by magnetic resonance imaging (MRI) of the affected spinal levels (thoracic, lumbar, both). Presence of increased intraosseous signal intensity on short-τ-inversion recovery (STIR) sequences determined an acute fracture. All patients undergoing cement augmentation procedures for acute VCF within the predefined period were included in the study. Patients with severe cardiopulmonary comorbidities, systemic or local infection, known malignant disease, or compression of neurological structures with radicular or spinal cord compression syndrome were excluded from the study. The study was approved by the institutional review board.

Three different augmentation procedures were performed: vertebroplasty (VP), kyphoplasty (KP), and stentoplasty (SP). The procedures were performed by 4 senior spine surgeons. Two surgeons routinely performed vertebral body lavage, whereas the other 2 injected cement without prior lavage. Accordingly, all patients were assigned to the "lavage group" and the "control group." The "lavage group" consisted of 61 patients with a total of 203 vertebral levels treated, and the "control group" of 84 patients with a total of 273 vertebral levels treated (Table 1). The groups did not differ significantly in terms of age, gender, number of fractured vertebra, number of cemented levels, location of fracture (thoracic, thoracolumbar, lumbar), isolated VP, SP, or cardiovascular comorbidities. There were more KP procedures

Table 1. Patient Demographics.

	All Patients	Lavage Group	Control Group	*P*
No. of patients, n	145	61	84	—
Age, years, mean ± SD (range)	74 ± 12 (42-96)	75 ± 12 (42-96)	74 ± 12 (48-96)	.703
Gender, % female	70	80	67	.080
No. of patients with >1 fractured vertebra	20	11	9	.145
No. of cemented vertebra, mean ± SD (range)	3 ± 1.5 (1-6)	3 ± 1.3 (1-6)	3 ± 1.6 (1-6)	.324
Thoracic	17	9	8	.213
Thoracolumbar	95	40	55	.403
Lumbar	33	12	21	.291
Isolated vertebroplasty	104	39	65	.057
Kyphoplasty[a]	17	14	3	<.001
Stentoplasty[a]	24	8	16	.236

[a] At least 1 vertebra treated with kyphoplasty or stentoplasty.

performed in the "lavage group" whereas the number of VP and SP of at least 1 vertebra did not differ significantly between the 2 groups (Table 1).

All procedures were performed under general anesthesia and systemic blood pressure was monitored invasively with an arterial line. Mean arterial pressure (MAP) was documented directly prior to cement injection and 3 minutes after the injection was completed. The anesthesia protocols were evaluated by an anesthetist for blood pressure, vascular or cardiac complications, the need of catecholamines following cement injection, and postoperative treatment on the intensive care unit.

The surgical technique has been described in detail previously.[16] Briefly, all procedures were performed under general anesthesia with the patient positioned prone on a radiolucent operating table. Bipedicular Jamishidi needles (T-Lok Bone Marrow Biopsy Needle, Argon Medical Devices, Frisco, TX, USA; 8 gauge, 16 inches) were inserted under biplanar fluoroscopic guidance. For VCF treated with kyphoplasty or stentoplasty, commercially available systems were used (SYNFLATE–Vertebral Balloon System; VBS–Vertebral Body Stenting System, respectively; Depuy Synthes, Bettlach, Switzerland). Prophylactic cement augmentation (VP) of the intact supra- and subjacent vertebra was performed in all patients. All vertebrae in the "lavage group" underwent vertebral body lavage prior to cement injection according to a previously described protocol (Figure 1).[15,16] Cement preparation was performed according to the manufacturer's recommendations (Vertecem V+, Depuy Synthes, Bettlach, Switzerland). Cement was injected under lateral and posterior-anterior fluoroscopic guidance to recognize cortical defect (ie, through the fracture gaps), intradiscal, or endovascular cement leakage. Any type of cement leakage detected on fluoroscopic images initiated immediate termination of cement injection. In all other cases, cement injection was stopped when sufficient filling of the vertebral body was achieved (endplate to endplate) as assessed by the treating surgeon.

We performed a priori power analysis for the primary research question regarding decrease of blood pressure after cement application with a 2-tailed level of significance of 5%, beta error of 20%, known arterial blood pressure of 116.4 ± 18.9 mm Hg before and 112.5 ± 20.2 mm Hg after cement injection,[17] and a minimum detectable difference of 10 mm Hg resulting in a minimum sample size of 58 patients per group.

Data with normal distribution was illustrated as means, standard deviations, ranges and confidence intervals. Comparisons between the groups were calculated using the Mann-Whitney *U* test, and comparisons within one group using the Wilcoxon signed rank test for continuous data. The Fisher's exact test was applied for binominal data. Multivariate, binary logistic regression analyses were performed for the primary research question with the dependent output variable defined as a minimum MAP drop of Δ10 mm Hg after cement injection, and the independent variables vertebral body lavage, age, gender, number of cemented vertebra, cardiac comorbidities (ie, any type of coronary heart disease, arrhythmogenic heart disease, cardiomyopathy, congestive heart failure), level of cement augmentation (thoracic, thoracolumbar, lumbar), number of fractured vertebra, type of augmentation performed (VP, KP, VS), cement leakage (endovascular and cortical leakage detected on postoperative radiographs), and increase of heart rate ≥10/min using IBM SPSS V21.0.0 (Armonk, NY, USA).

Results

In the lavage group, 11 patients (18%) had a drop of MAP (ΔMAP) ≥10 mm Hg before and after cement injection. Mean MAP decreased from 78 ± 13.3 mm Hg (range, 57-126 mm Hg; [confidence interval, CI, 75-82] before cement injection to mean 75 ± 13.5 mm Hg (range, 53-127 mm Hg; [CI, 71-78]; $P < .002$) after cement injection (Table 2). In the control group, 36 patients (43%) had ΔMAP ≥10 mm Hg before and after cement injection. Mean MAP decreased from 82 ± 11.9 mm Hg (range, 60-120 mm Hg [CI, 79-85]) to 73 ± 13.9 mm Hg (range, 47-120 mm Hg; [CI, 70-76]; $P < .001$). The mean difference of MAP before and after cement injection (ΔMAP) was 3 ± 7.3 mm Hg (range, 0-30 mm Hg; [CI, 0.5-6.7]) in the lavage group, and 9 ± 10.5 mm Hg (range, −3 to 35 mm Hg; [CI, 7-11]; $P < .001$) in the control group, respectively (Table 2).

Table 2. Primary Outcome Parameters.[a]

Parameter	Lavage Group		Control Group	
	Before Cement Injection	After Cement Injection	Before Cement Injection	After Cement Injection
Mean arterial blood pressure (mm Hg)	78 ± 13.3 (57-126) [75-82]	75 ± 13.5 (53-127) [71-78][b]	82 ± 11.9 (60-120) [79-85]	73 ± 13.9 (47-120) [70-76][b]
Mean heart rate (beats/min)	73 ± 14.4 (45-110) [70-76]	73 ± 13.8 (45-105) [71-76]	72 ± 10.7 (50-100) [69-75]	71 ± 10.0 (50-95) [68-73]
Oxygen saturation (%)	99 ± 1.3 (95-100) [99.1-99.7]	99 ± 1.6 (95-100) [99.1-99.7]	99 ± 1.7 (90-100) [98.7-99.4]	99 ± 1.3 (95-100) [99.0-99.5]
Difference of mean arterial blood pressure, ΔMAP (mm Hg)	3 ± 7.3 (0-30) [0.5-6.7]		9 ± 10.5 (−3 to 35) [7-11][c]	

[a] Values are presented as means ± standard deviations with range in parentheses and confidence intervals in brackets.
[b] $P < .05$ compared with before cement injection within each group.
[c] $P < .001$ compared with lavage group.

Table 3. Logistic Regression Analysis.[a]

Parameter	*P*	Adjusted Odds Ratio (95% CI)
Age	.839	0.99 (0.95-1.04)
Gender	.406	0.65 (0.23-1.79)
No. of cemented vertebra >1	.850	0.97 (0.72-1.31)
Thoracic	.224	0.36 (0.07-1.86)
Thoracolumbar	.287	0.58 (0.21-1.59)
Lumbar	.345	0.42 (0.14-1.45)
Vertebroplasty	.999	0.0 (—)
Kyphoplasty	.999	0.0 (—)
VBS–Vertebral Body Stenting System	.999	0.0 (—)
Vertebral body lavage	.026	3.49 (1.16-10.50)
Vascular/osseous cement leakage	.537	1.45 (0.45-4.73)
No. of fractured vertebra >1	.999	1.33 (0.34-5.11)
Heart rate	.999	39.55 (—)
Cardiac comorbidities	.908	0.94 (0.34-2.61)

[a] Binary, logistic regression analysis was performed with mean arterial pressure (MAP) drop >10 mm Hg as the dependent variable.

There were no significant differences in terms of heart rate before and after cement injection in both groups. In the lavage group, mean heart rate was 73 ± 14.4/min (range, 45-110/min; [CI, 70-76]) before cement application, and 73 ± 13.8/min (range, 45-105/min; [CI, 71-76]; $P = .722$) after cement injection. In the control group, mean heart rate was 72 ± 10.7/min (range, 50-100/min; [CI, 69-75]), and 71 ± 10.0/min (range, 50-95/min; [CI, 68-73]; $P = .075$), respectively (Table 2).

Oxygen saturation did not change significantly before and after cement injection in both groups. In the lavage group, oxygen saturation was 99% ± 1.3% (range, 95%-100%; [CI, 99.1-99.7]) and 99% ± 1.6% (range, 95%-100%; [CI, 99.1-99.7]; $P = .789$). In the control group, oxygen saturation was mean 99% ± 1.7% (range, 90%-100%; [CI, 98.7-99.4]) prior to cement application, and mean 99% ± 1.3% (range, 95%-100%; [CI, 99.0-99.5]; $P = .085$), respectively (Table 2).

Multivariate, binary logistic regression with a minimum MAP decrease of 10 mm Hg (ΔMAP ≥10 mm Hg) after cement application as the dependent variable revealed vertebral body lavage as the only independent factor with an impact on systemic blood pressure (Table 3). If no vertebral body lavage was performed prior to cement application, relative risk for a decrease of MAP (ΔMAP ≥10 mm Hg) was increased by 3.49 (adjusted odds ratio, [CI, 1.16-10.50]; $P = .026$). None of the other factors evaluated in the analysis reached statistical significance.

Discussion

Complications associated with percutaneous PMMA application are known to be either local, such as cement extravasation or cement leakage into the spinal canal, or systemic, involving cardiopulmonary events such as pulmonary embolism.[6] The latter occur after elution of fat, bone marrow, or PMMA into the epidural or vertebral venous system.[15] In the current study, the effect of vertebral body lavage prior to PMMA augmentation on subsequent cardiovascular changes was investigated.

The cardiovascular reaction to PMMA injection was characterized by a significant decrease of MAP in the control group 3 minutes after PMMA application. Vertebral body lavage could diminish this effect significantly, in terms of absolute MAP decrease as well as in total numbers of patients affected.

According to previous research reports,[15] the protective effect might be explained by reduction of the bone marrow substance in the vertebral body prior to PMMA application. In the animal study oil-red O stained lung sections showed a significant reduction of fat droplets after lavage.[15] Even if we could not reproduce this effect directly, due to the inability to perform lung biopsies in our patients, it is likely that the pathophysiological mechanisms in the sheep model are similar to the effects observed in this study. In contrast to other studies reporting a decrease of oxygen partial pressure after kyphoplasty,[17,18] these findings were not reproduced in the current study. In accordance to these studies, however, the current study also did not reveal significant changes in heart rate.[17]

While several factors intuitively influence cardiovascular reactions, such as the number of vertebral bodies augmented, type of procedure (VP/KP/SP) or percentage filling,[9,11] multivariate analysis demonstrated vertebral body lavage to be the only factor influencing hemodynamic response. Furthermore, radiologically verified intravenous cement leakage, which may be an alternate cause for pulmonary embolism, was not detected as an independent factor for drop of systemic blood pressure. This may be explained by the fact that the surgeon stops PMMA injection as soon as first signs of venous leakage are present under fluroscopy. Thus, our results support the hypotheses that an increase in intravertebral pressure alone, resulting in a displacement of fat and bone marrow substance into the systemic circulation may be the source for cardiopulmonary complications.[15] Therefore, "pressure reducing" injection methods such as stepwise injection or the use of high-viscosity cement may reduce cardiopulmonary complications.[13,14]

This study has several limitations. First, we cannot provide proof that the lower incidence of MAP drop after cement injection with prior vertebral body lavage is due to a decreased rate of pulmonary fat embolism. In this retrospective study, no intraoperative echocardiogram was performed to objectify increased amounts of fat in the circulation, and lung biopsies—as previously done in an in vivo sheep model—were not conducted.[15] However, there were no significant differences in terms of radiologically visible vascular cement leakage between the two groups and vascular cement leakage was not identified as a risk factor for MAP drop as an alternative mechanism. Second, the authors did not assess whether different surgical techniques (VP, KP, SP) directly affected the observed effects. Previous studies report lower rates of cardiopulmonary complications when performing KP instead of VP alone likely due to decreased forces required during the cement injection process.[17,19] However, division of this patient series in subgroups would have jeopardized statistical power. Furthermore, all patients underwent prophylactic cement augmentation of the supra- and subjacent intact vertebra using the VP technique. Thus, there were no isolated KP or SP procedures allowing for procedure specific stratification. Finally, although this cannot completely rule out this limitation as a potential source of bias, none of the applied augmentation procedures were found statistically as independent factors affecting the hemodynamic response. Third, although there were patients with significant drop in MAP in both groups, none of these patients in this consecutive series died or had other clinically relevant complications. The protective effect of vertebral body lavage might be of particular importance in patients with a lower threshold for significant acute respiratory or heart failure.

The surgical setup using a bipedicular access to the vertebral body, applying a vacuum with a syringe on one side thereby rinsing the vertebral body with saline from the other side, proved to be feasible (Figure 1).[15,16] No cardiovascular side effects associated with vertebral body lavage were registered (eg, reducing systemic blood volume by intraosseous aspiration), therefore this technique appears to be safe in a clinical setting. In addition to the beneficial effect on MAP as observed in the current study, a previous study using the same technique found improved filling pattern, with significantly higher percentage of "coast-to-coast" filling and a significant reduction of radiologically visible venous leakage.[16]

In conclusion, vertebral body lavage before PMMA application results in a reduced hemodynamic response, most likely due to a decrease of the embolic load. It is a simple and cost-effective technique to increase the safety of percutaneous PMMA augmentation techniques, like vertebro- and kyphoplasty, which may ultimately prevent potentially life-threatening complications in patients with impaired cardiopulmonary function.

Declaration of Conflicting Interests

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