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Methods: Retrospective chart review produced 88 patients who received PVA at a tertiary care outpatient pain clinic. Cement volume, type of PVA, gender, level (thoracic vs lumbar) were collected, as well as clinical outcomes of numeric pain score (NPS) reduction, opioid percent change (OPC), and complications. Both pre-procedure and post-procedure (between 2-4 weeks) data were collected.

Results: Sixty-four patients (72.7%) had statistically significant NPS reduction of ≥50% pain (p
Conclusion: Cement volume does not correlate with clinical outcomes of NPS reduction or OPC. Furthermore, our study reinforced PVA as a beneficial treatment for reducing pain and opioid consumption in patients with painful VCF.

Keywords

Kyphoplasty, Vertebroplasty, Back Pain/therapy, Pain Management, Treatment Outcome, Chronic Pain, Cementoplasty, Fractures Compression

The Clinical Relevance of Cement Volume in Percutaneous Vertebral Augmentation

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Introduction

Background: Vertebroplasty and kyphoplasty are two forms of percutaneous vertebral augmentation (PVA) used to treat symptomatic or painful vertebral compression fractures (VCF).[1,2] VCF are associated with an estimated average hospital stay of 10 days and increased mortality if untreated.[3,4] An estimated cost of $1.14 billion dollars was spent in VCF treatment alone in 2005.[5] Symptomatic VCF can be associated with pain, chronic opioid consumption, and reduced quality of life.[6,7]

Cement volume is a commonly discussed topic in PVA. Increased cement volume has been suggested to be biomechanically advantageous for improving individual vertebral body stiffness, height, and load-sharing among the vertebral bodies.[2,8-11] However large fill volumes could incidentally promote biomechanical instability due to asymmetric distributions.[12] Also adjacent vertebral fractures may be associated with increased cement volume possibly due to the increased stiffness of the repaired level.[13] Besides biomechanics, dose-dependent increases in cement volume have been correlated with increased extravasation into the epidural space, neural foramen, intervertebral disc space, and vasculature that could lead to pulmonary embolism.[11,14-15]

Rational/Significance: Sometimes to avoid adverse events, clinicians minimize cement volume. A few studies suggest that increased cement volume does not correlate with improved clinical outcomes.[16-18] However, another study suggests that clinical improvement does correlate with higher volumes, although the rate of complications was higher.[19] Additionally, it is important to mention that some clincians question the benefit of PVA. Two seminal randomized controlled trials (RCT) using vertebroplasty showed no benefit in comparison to conservative treatment.[20,21] However multiple studies of PVA and a recent kyphoplasty RCT did demonstrate improved outcomes of PVA when compared to conservative treatment.[1,22-23] As such, there is a need for further studies to determine if low cement volumes would produce the same clinical benefit as high volumes.

Objective: The primary aim of this study is to evaluate the relationship between cement volume and clinical outcomes, including pain reduction, opioid use, and complication rate. Secondarily, this study sought to provide further evidence of PVA as a beneficial treatment for painful VCF.

Methods

A retrospective chart review was performed of all the patients that underwent kyphoplasty or vertebroplasty by a single experienced pain management physician at a tertiary care center between January 2009 and December 2016. The Institutional Review Board (IRB) approved this study, and waived the requirement for written informed consent. This manuscript was written to adhere to applicable Equator guidelines. Inclusion criteria consisted of accurate documentation of numeric pain scores (NPS), exact dosage of narcotic pain medication being consumed, surgical complications listed, and cement volume utilized during procedure. All patients who met the inclusion criteria were included in the study.

Patient Population: Percutaneous vertebral augmentation (PVA) was used to treat compression fractures in patients with axial back pain and either an underlying oncologic malignancy or osteoporosis. PVA would likely not be performed on compression fractures with symptoms exceeding one year unless MRI showed acute/subacute findings. Patients with the following imaging findings were excluded: 80% or greater vertebral height loss, burst fracture, disc retropulsion greater than 30%, or significant clinical neurologic compromise secondary to compression

Approach: With the patient under general anesthesia in the operating room, local anesthetic was infiltrated from the skin to the pedicle of each target. Employing biplanar fluoroscopy throughout, she advanced the needles using a bipedicular approach in all cases. Once a tract was formed into the vertebral body, she injected cement material made of polymethylmethacrylate for vertebroplasty. In the case of kyphoplasty, inflatable balloons were used to create a cavity before injecting the cement. The injection was terminated if leakage was noted in the venous distribution, or beyond the vertebral endplates.

Outcome Measurements: Multiple outcome measures were collected in both the pre-procedure and post-procedure settings. For the purpose of this study, pre-procedure was defined as the last data set collected prior to the procedure (typically between two weeks to one day before procedure). Post-procedure was defined as the data collected at the first outpatient visit following the procedure (typically between two to four weeks after procedure).

The following data were collected: numeric pain scores rated on a scale from 0 (no pain) to a 10 (worst imaginable pain), opioid dosage in morphine milliequivalents, and any complications during the procedure, ranging from any form of extravasation, infection, wound complications, or mortality. In addition, data relating to gender, cement

volume, level (thoracic versus lumbar), and number of levels augmented were collected. Cement volumes recorded reflected the total amount used in a bipedicular approach. The purpose of the study was not to compare kyphoplasty versus vertebroplasty and the data were not analyzed separately unless specified in the results.

Opioid dosages were used to calculate opioid percent change (OPC). OPC was calculated by dividing the difference of pre-procedure and post-procedure opioid dose by the pre-procedure dose and multiplying by 100 to give a percent. In patients with multiple opioid medications, doses were converted to oral morphine milliequivalents prior to the calculation. This study did not account for non-opioid analgesic changes.

If a patient had multiple levels augmented in a procedure, outcomes of NPS and OPC were the same since they reflect the cumulative result of the entire procedure. Instead of analyzing the data by individual level, cement volume was averaged across all levels in our analysis to produce a single data point. This approach was selected to prevent overpowering and skewing of statistics by those with multilevel PVA.

Statistical Analysis: All t-tests performed were two-tailed with pairing based on the data being studied. T-tests were performed to compare if the mean change of NPS and OPC were significant. Additionally, t-tests were utilized to determine if NPS change or OPC were different across type of vertebral level. If data were categorical in comparison, such as gender vs ≥50% or <50% improvement, a chi-square test was performed.

Linear regression adjusting for pre-NPS was performed to determine the relationship of either OPC or NPS change with cement volume. Logistic regression was used to analyze cement volume's influence on NPS when reported categorically (≥50% and <50% improvement). A professional statistician assisted with all the statistical analysis.

Results

Demographics: Eighty-eight patients were included in the study with females accounting for 53% of the patients. When analyzing the different types of PVA, 78 patients received kyphoplasty and 10 patients received vertebroplasty. For the entire cohort of 88 patients, 47 had PVA at multiple vertebral levels during the same procedure, with the following breakdown: 30 at two levels, 15 at three levels, 2 at four levels. The location of PVA during each procedure was as follows: 32 lumbar only, 28 thoracic only, and 28 who received both thoracic and lumbar PVA in the same procedure. Cement volume used per vertebral level ranged from 1 to 8mL with 55 patients receiving an average of ≤3mL and 33 patients receiving >3mL.

Change in Numeric Pain Score (NPS): For the entire cohort of 88 patients, we noted a statistically significant reduction in the mean NPS by 4.45% (p<0.0001) from a pre-procedure value of 6.92 to a post-procedure value of 2.37. (Figure 1). This outcome persisted even when comparing patients with ≥50% NPS (n= 64) with those patients with <50% reduction (N=24, p<.001). In contrast, we found no statistically significant difference (p=0.26) for decrease in the NPS between lumbar (mean reduction of 4.16) versus thoracic (mean reduction of 5.06) levels of PVA. Similarly, gender had no influence with an equivalent percentage of females (72.34%) and males (73.17%) demonstrating ≥ 50% reduction in NPS (p=0.93).

Linear regression using pre-NPS as the covariate showed that cement volume did not have a significant effect on the change in NPS (p=0.173) as demonstrated in Figure 2. When analyzed as a categorical variable, there was no statistical difference in NPS reduction between patients who received cement volumes of ≤3ml (mean reduction of 4.16) versus those who received >3ml (mean reduction of 4.94, p =0.25).

Opioid Reduction: Seventy-two patients who were on opioids pre-procedure were included in this analysis. We noted a mean OPC reduction of 48%. A statistically significant difference (p<0.0001) was noted between patients with opioid reduction (n=63) when compared to patients (n=9) with no improvement in opioid consumption. (Figure 3). There was no difference (p=0.71) in opioid reduction between lumbar (n= 25, mean reduction= 44%) versus thoracic (n= 22, mean reduction= 49%) levels of PVA.

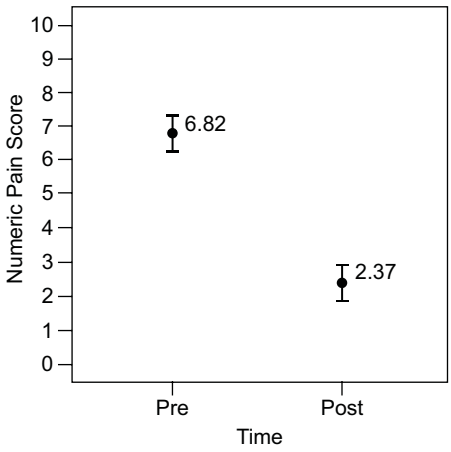

Figure 1. Average pain improvement. The mean Numeric Pain Score (NPS) pre-procedure (6.82) and post-procedure (2.37) with 95% confidence intervals displayed for a total of 88 patients. A mean reduction of 4.45 was present which was statistically significant (p<.0001).

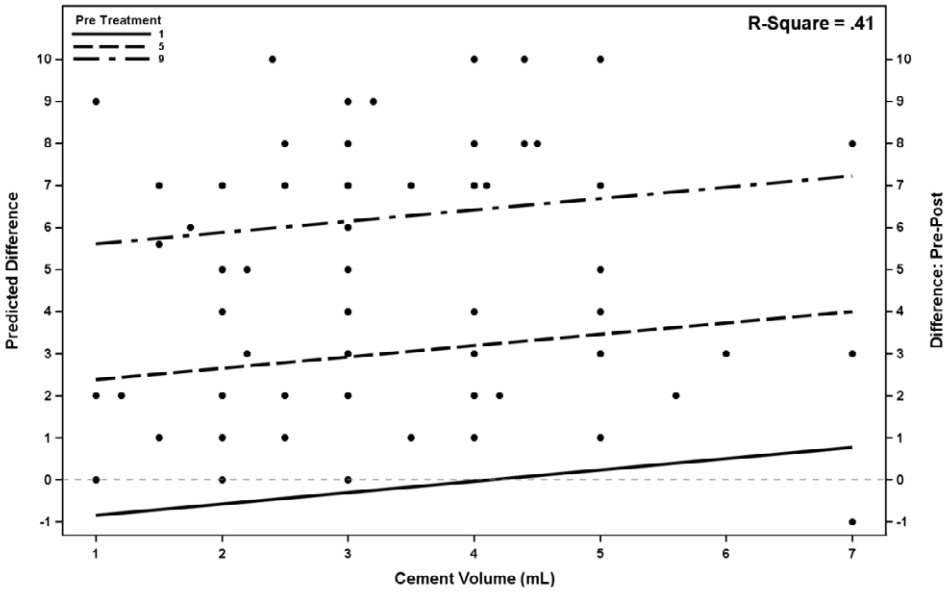

Figure 2. Difference in pain by cement volume and pre-treatment score. Scatter plot with linear regression analysis using pre NPS as the covariate shows the effect of cement volume on NPS change. Three regression lines are drawn with various pre-treatment NPS scores (1,5,9) that failed to show statistical significance (p=0.173; R2 =0.41). Although the vertical axes are the same for the difference scores, conceptually the left axis refers to the regression lines and the right vertical refers to the points plotted in the interior. *Abbreviations: NPS=Numeric Pain Score*

We then analyzed if there was an effect of cement volume on opioid dosage reduction. Linear regression with two independent variables (adjusted for pre-NPS covariate and relationship of opioid decrease with cement volume) showed no relationship of opioid decrease with cement volume (p=.299) (Figure 4).

Complications/Adverse Reactions: A total of nine complications (four intradiscal extravasations, three pulmonary vessel cement uptakes, and two other uncomplicated extravasations) were reported for a total complication rate of 10.2%. However, it should be noted that all complications were asymptomatic with the exception of one patient treated for symptomatic dyspnea after pulmonary vessel cement uptake. The other complications were noted incidentally on follow up imaging or during fluoroscopy. None of the patients were noted to experience more than one complication. A complete breakdown of complications by cement volume (≤ 3ml vs >3ml) and type of procedure (kyphoplasty vs vertebroplasty) can be found in Table 1.

Discussion

Our retrospective study of 88 patients who received PVA demonstrated multiple findings. Patients experienced statistically significant NPS improvement, with 72.7% of them achieving ≥50% pain reduction at the first follow up appointment. Importantly, previous opioid consumers were able to decrease their opioid consumption by 48%, which was statistically significant. Our results are in congruity with the findings of other similar studies.[22,24] Our analysis also showed that neither gender nor vertebral level (thoracic vs. lumbar) had any influence on our measured outcomes.

Our study also demonstrated that cement volume did not have any statistically significant effect on NPS or opioid reduction, which is similar to findings from previous studies.[16,17] Although not statistically significant, the R^2 in both regression graphs (Figures 2 & 4) showed a positive correlation between cement volume and both NPS and opioid reduction. It is likely that a study with a larger sample size could potentially demonstrate a beneficial effect of cement volume.

We noted a cement leakage rate of 10.2% which is much lower than the findings reported by Zhan et al.[14] In their meta-analysis, Zhan et al noted a much higher cement leakage rate of 54.7% (vertebroplasty) and 18.4% (kyphoplasty) respectively. For our study we considered cement ≤3mL to be a relatively low volume and anything greater to be high volume. It was interesting that pulmonary vessel cement uptake occurred exclusively in high volume while intradiscal extravasation occurred exclusively in low volume. Both complications did occur predominantly in patients with kyphoplasty, which was unexpected. Intraoperative venous uptake of cement can go undetected, which can lead to injecting higher volumes of cement. In contrast, intradiscal extravasations are more easily detected intraoperatively, which leads to termination of the procedure at a lower volume of cement.

This study as several limitations. We did not analyze or account for a floor value of cement but arbitrarily determined a cut-off point of 3ml. It is likely that a lower volume of cement may have provided a therapeutic benefit as well. Molloy et al showed that 2cc of polymethylmethacrylate improved strength and stiffness in thoracic compression fractures by 69% and 80% respectively.[9] Thus based on this study, achieving 100% restoration is likely not needed to receive full clinical benefit. Nonetheless, in our study we did not use volumes lower than 1ml due to impracticality. The study does not include follow up beyond four weeks. We also included patients with a mix of benign and malignant diagnoses, which could have an effect on the measured outcomes. Finally, due to the small number of patients, we were not able to perform separate analysis for patients that underwent vertebroplasty and kyphoplasty.

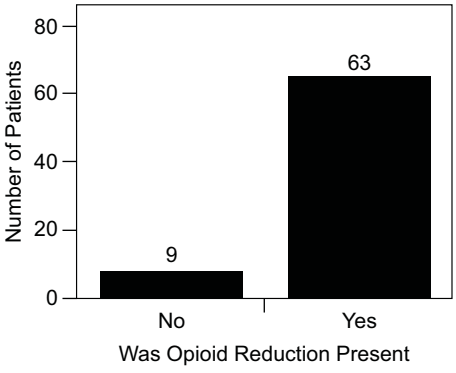

Figure 3. Reduction in opioids after treatment. Graphical display of patients who demonstrated any opioid reduction versus those with no improvement in opioid consumption in a categorical fashion. Seventy-two patients who were on opioids pre-procedure were included in this analysis. We noted a mean opioid percent change of 48%. Following treatment with percutaneous vertebral augmentation, a statistically significant number of patients experienced opioid reduction (n=63) when compared to patients (n=9) with no reduction in opioid consumption (p<0.0001).

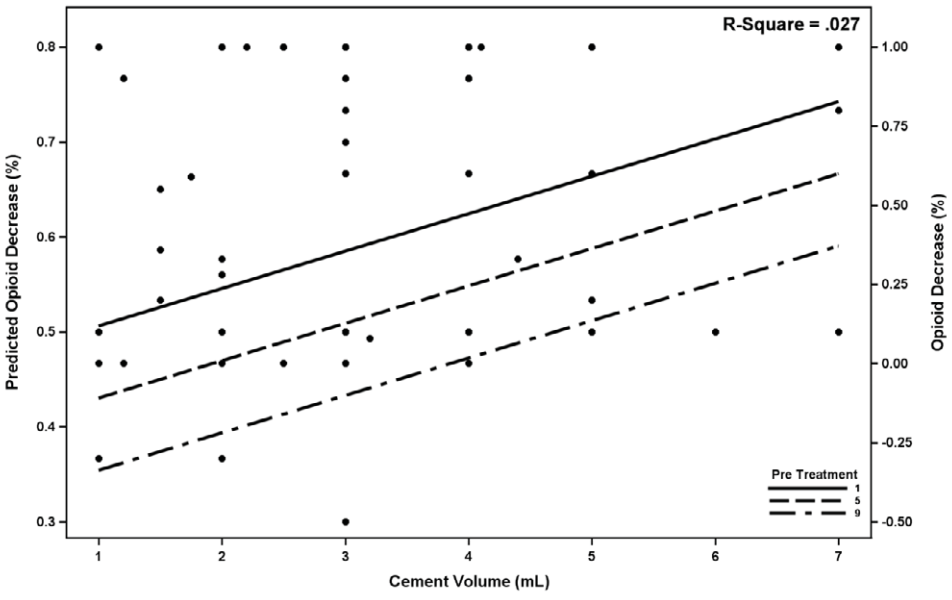

Figure 4. Opioid decrease by cement volume and pre-treatment score. Scatter plot displaying linear regression analysis with two independent variables (adjusted for pre-NPS covariate and relationship of opioid decrease with cement volume). Three regression lines are drawn with various pre-treatment NPS scores (1,5,9) that failed to show significance (p=.299 and R2 = 0.027). The left axis refers to the pre-treatment lines and the right axis refers to the plotted points. Positive opioid decrease implies a reduction, while negative infers opioid increase. *Abbreviations: NPS=Numeric Pain Score.*

In summary, the results of our study demonstrated a beneficial effect of vertebroplasty and kyphoplasty with a reduction in NPS and opioid consumption. Further studies with a larger number of patients are needed to validate our findings. ■

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Table 1.
The total number of complications by type of complication. Each type of complication is then further separated based on type of procedure and cement volume injected.

Type Of Complication	Total #	Complication %	Kyphoplasty #	Vertebroplasty #	Cement ≤3mL	Cement >3ml
Intradiscal Extravasation	4	4.5%	3	1	4	0
Pulmonary Embolism	3	3.4%	3	0	0	3
Uncomplicated Venous Extravasation	2	2.3%	1	1	1	1

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