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BACKGROUND AND PURPOSE: **Previous investigators have described an association between polymethylmethacrylate (PMMA) use in hip arthroplasty and cardiovascular derangement. Our purpose was to evaluate the effects of PMMA injection on patient vital signs during percutaneous vertebroplasty.**

METHODS: **We retrospectively reviewed patient charts at our institution to gather blood pressure, heart rate, and arterial oxygen saturation data for the following time points: before, during, 5 minutes after, and 10 minutes after PMMA injection during percutaneous vertebroplasty. These data were obtained for 142 injections (78 patients), and preinjection vital signs were compared with vital signs during and after PMMA injection. Multivariable regression modeling was used to ascertain the effects of cardiopulmonary comorbidities on vital signs.**

RESULTS: **Mean arterial blood pressure and heart rate during, 5 minutes after, and 10 minutes after PMMA injection were not significantly different from their respective preprocedure values ($P = .19–.92$). Values for oxygen saturation during PMMA injection and 5 minutes thereafter were not significantly different from preprocedure values ($P = .80$ and .89, respectively). Oxygen saturation was significantly lower at 10 minutes after injection than before injection ($P = .007$), although the mean difference was negligible (0.6%).**

CONCLUSION: **We find no generalized association between PMMA injection during percutaneous vertebroplasty and systemic cardiovascular derangement.**

Polymethylmethacrylate (PMMA) has been used for many years as a bone cement in orthopedic procedures such as hip arthroplasty. There have been multiple reports of an association between adverse cardiovascular events such as severe arterial hypotension, bradycardia, bronchospasm, and asystole and the use of PMMA during hip arthroplasty (1–7). A variety of causal mechanisms of these events have been postulated, such as direct PMMA toxicity, fat embolism, and release of vasoactive mediators (1, 5, 7–11).

Percutaneous vertebroplasty was first described in France in 1987 (12) and has been performed in the United States since 1993 (13). Percutaneous vertebroplasty is an image-guided procedure that involves the injection of bone cement into vertebral compression fractures that are either osteoporotic or neoplastic. The bone cement ostensibly provides stabilization, or internal casting, of the vertebral compression fracture. PMMA represents the most commonly used bone cement for percutaneous vertebroplasty in the United States (13).

There have been two case reports of an association between the injection of PMMA during percutaneous vertebroplasty and untoward cardiovascular or pulmonary effects: a report of the symptomatic pulmonary embolism of PMMA (14) and a report of transient arterial hypotension (15). To our knowledge, apart from these cases, no systematic study has been published that examines the possible relationship between adverse cardiovascular or pulmonary effects and PMMA injection during percutaneous vertebroplasty.

Therefore, for cases of percutaneous vertebroplasty, we retrospectively compared patient vital signs before PMMA injection with vital signs during and after PMMA injection. In addition, we analyzed the association between selected patient comorbidities and vital signs during and after PMMA injection.

Methods

We retrospectively reviewed charts of consecutive patients who underwent percutaneous vertebroplasty from October 1999 to May 2001 at our institution, a medium-size academic

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medical center. The study was given exempt status by our institutional review board. A total of 142 PMMA injections in 78 patients were identified, and the unit of analysis was the PMMA injection. Systolic and diastolic blood pressure, heart rate, and systemic arterial oxygen saturation were recorded from before, during, 5 minutes after, and 10 minutes after PMMA injection. Arterial oxygen saturation was measured with pulse oximetry. We did not correlate the administration of sedative and analgesic medications with vital signs. Conscious sedation was administered by experienced interventionalists and titrated for effect. For each patient, the presence of the following cardiovascular comorbidities were abstracted from the charts: chronic obstructive pulmonary disease (COPD), prior myocardial infarction, coronary artery disease, atrial fibrillation, use of a cardiac pacemaker, and systemic arterial hypertension.

Mean arterial blood pressure (MAP) was calculated by adding one-third of the pulse pressure to the diastolic pressure. MAP and heart rate during, 5 minutes after, and 10 minutes after PMMA injection were compared with preinjection values for each patient by using the paired Student *t* test. Percentage systemic arterial oxygen saturation during, 5 minutes after, and 10 minutes after PMMA injection were compared with preinjection values for each patient by using the Wilcoxon signed rank test because of the nonnormal, negatively skewed distributions of oxygen saturation. Statistical analysis was performed with S-Plus statistical software (Insightful Corporation, Seattle, WA). A *P* value less than .05 was considered to indicate a statistically significant difference.

Multiple linear regression using the ordinary least squares method was used to test for associations between patient comorbidities and vital signs during, 5 minutes after, and 10 minutes after PMMA injection, holding preinjection vital sign values and other comorbidities constant. Age, preinjection MAP, preinjection heart rate, and preinjection arterial oxygen saturation were entered as continuous predictor variables in each model. Patient sex, presence of COPD, history of either coronary artery disease or myocardial infarction, and systemic hypertension were entered as binary predictor variables in each model. Atrial fibrillation and the presence of a cardiac pacemaker were not included as predictor variables because they were rare in our patient sample. Spearman correlation (ρ^2) was used to evaluate the potential predictive punch, or impact, of each predictor variable, which blinded us to the linearity of relationships between outcome and predictor variables before model construction. In each model, nonlinearity was allowed for in the relationships between the outcome variables and the predictor variables with the greatest potential predictive punch. Accordingly, each model tested nine parameters.

Our technical approach to vertebroplasty has been previously described (13), but since that previous publication we have made minor changes with respect to needle placement and use of venography. We used a transpedicular approach with an 11-gauge Cook bone biopsy needle (Cook, Bloomington, IN) to place the needle tip in the ventral aspect of the midline of the vertebral body. Vertebral venography was performed in approximately half the cases before PMMA injection, at the discretion of the operator. Approximately 6–8 g of powdered Codman Cranioplastic PMMA (DePuy CMW, Blackpool, England) was mixed with 1.2 g of tobramycin (Eli Lilly, Indianapolis, IN) and 6 g of barium (Parallax Medical, Scotts Valley, CA). To this mixture, we added approximately 6–8 mL of liquid Codman Cranioplastic methylmethacrylate monomer until a moderately viscous solution was achieved. The material was then transferred to a 10-mL syringe and transferred into 1-mL syringes for injection. The PMMA was injected slowly, on the order of 0.25–1 mL/min, by using continuous lateral fluoroscopy in an angiography suite. If resistance was encountered, the needle was withdrawn 5–8 mm before we resumed injection. If extravertebral extravasation to disk space or paravertebral veins was noted, injection was temporarily halted to allow partial polymerization before resuming. Injection was terminated when the cement mixture traversed to the dorsal one fourth of the vertebral body or if extravasation into the endplate or the venous system continued despite needle repositioning and further cement polymerization. Needle placement and cement injection via the contralateral vertebral pedicle was rarely used. On average, we injected 3–4 mL of cement per level.

Results

The mean age of the patients and 25th, 50th, and 75th percentiles were 72, 67, 75, and 80 years, respectively. Of the 142 injections, 104 (73%) were performed in women and 38 (27%) were performed in men. Fifty-two injections (37%) were performed in patients with systemic hypertension, 36 (25%) in patients with COPD, 30 (21%) in patients with history of coronary artery disease, 15 (11%) in patients with prior myocardial infarction, eight (6%) in patients with a cardiac pacemaker, and six (4%) in patients with atrial fibrillation. More than 90% of vertebroplasties were performed for osteoporotic vertebral compression fractures, with the remainder performed for compression fractures secondary to multiple myeloma or metastatic disease. All procedures were performed with the patient under conscious sedation.

Mean MAPs were 99.2, 98.0, 100.3, and 100.5 mm Hg before, during, 5 minutes after, and 10 minutes after PMMA injection, respectively. No significant differences were noted between preinjection MAP and MAP during, 5 minutes after, and 10 minutes after PMMA injection ($P = .19$, .23, and .24, respectively). Mean heart rate was 80.5, 80.5, 80.4, and 80.0 beats per minute before, during, 5 minutes after, and 10 minutes after PMMA injection, respectively. No significant differences were noted between preinjection heart rate and heart rate during, 5 minutes after, and 10 minutes after PMMA injection ($P = .71$, .92, and .65, respectively). Mean arterial oxygen saturation was 98.0%, 98.0%, 98.0%, and 97.4% before, during, 5 minutes after, and 10 minutes after PMMA injection, respectively. No significant differences were noted between preinjection arterial oxygen saturation and oxygen saturation during and 5 minutes after PMMA injection ($P = .80$ and .89, respectively). The lowest four values of oxygen saturation in the comparison between before PMMA injection and 10 minutes after injection (78–92%) were seen at 10 minutes after injection. The difference between preinjection arterial oxygen saturation and oxygen saturation 10 minutes after PMMA injection was significant by use of a rank test ($P = .007$), although the difference in mean oxygen saturation, 0.6%, was negligible.

Power was greater than 98% to detect changes of at least 5 mm Hg in MAP, 5 heart beats per minute, and 5% oxygen saturation, assuming normal distributions of vital signs. Although the distributions of blood pressure and heart rate approximated the normal distribution in our patients, the distribution of oxygen saturation was negatively skewed.

Preinjection MAP was a significant, positively correlated predictor of MAP during, 5 minutes after, and 10 minutes after PMMA injection, holding all other

predictor variables constant ($P < .001$ for each). That is, as preinjection MAP increased, MAP during and after PMMA injection tended to increase as well. Patient age was a significant, positively correlated predictor of MAP during injection and 5 minutes after injection ($P = .012$, .016, respectively; $P = .252$ for the relationship between patient age and MAP 10 minutes after injection). Systemic hypertension had some explanatory value for MAP ($P = .057$, .022, and .075 for MAP during, 5 minutes after, and 10 minutes after injection, respectively). Patients with a history of hypertension tended to have higher MAP during and after PMMA injection, holding all other predictor variables constant.

Preinjection heart rate was a significant, positively correlated predictor of heart rate during, 5 minutes after, and 10 minutes after PMMA injection ($P < .001$ for each). No significant association was noted between any cardiovascular comorbidity and heart rate during and after PMMA injection, holding all other predictor variables constant.

Preinjection arterial oxygen saturation was a significant, positively correlated predictor of oxygen saturation during, 5 minutes after, and 10 minutes after PMMA injection ($P < .001$ for each). Preinjection MAP was a significant, positively correlated predictor of oxygen saturation during, 5 minutes after, and 10 minutes after PMMA injection ($P = .009$, $P < .001$, and $P = .009$, respectively). A patient history of hypertension had some explanatory value for arterial oxygen saturation ($P = .020$, .240, and .004 for oxygen saturation during, 5 minutes after, and 10 minutes after injection, respectively). Those with a history of hypertension tended to have lower oxygen saturation during and after PMMA injection.

Discussion

PMMA is a potentially toxic agent. Adverse cardiovascular events have been associated with the use of PMMA during hip arthroplasty (1–11), but the cardiovascular safety of PMMA use in percutaneous vertebroplasty, to our knowledge, has not previously been systematically studied. As PVP becomes more widely implemented, the safety of PMMA use in percutaneous vertebroplasty must be further evaluated.

This study involves a large, consecutive series of detailed hemodynamic parameters during and after PVP. We found no clinically relevant generalized systemic cardiovascular effects related to PMMA injection during PVP. MAP and heart rate were unchanged by the injection of PMMA. Arterial oxygen saturation during and 5 minutes after PMMA injection was not affected. Oxygen saturation was statistically significantly lower at 10 minutes after PMMA injection compared with before PMMA injection by the use of a nonparametric rank test, in part because the lowest four values of oxygen saturation were seen at 10 minutes after injection. However, the difference in mean oxygen saturation at the two time points was miniscule (0.6%) and is not considered by us to be clinically relevant. We did not control for the depressive cardiorespiratory effects of the routinely administered sedatives and narcotics, and these effects could explain the lower summed ranks of the oxygen saturation values at 10 minutes after injection if the pharmacologic effects peaked after PMMA injection in the outlier patients.

Thus, although conscious sedation and general anesthesia pose cardiovascular risks and alteration of vital signs by themselves, and PMMA embolism to the lungs during percutaneous vertebroplasty has been reported (14), we conclude that the routine use of PMMA in percutaneous vertebroplasty poses minimal risk of adverse cardiovascular effects in the hands of experienced operators. We found no association between PMMA use in percutaneous vertebroplasty and arterial hypotension, as has been reported in one patient (15). We cannot exclude the possibility of uncommon or idiosyncratic adverse cardiovascular effects from the use of PMMA in percutaneous vertebroplasty, and we do not know the respective roles of conscious sedation, PMMA injection, and patients' comorbidities in producing the rare oxygen saturation value of less than 90% seen in a very few of our patients.

Patients who have abnormal vital signs during percutaneous vertebroplasty are best predicted by their vital signs before PMMA injection. However, from multivariable analysis, patients with a history of systemic hypertension may tend to have lower arterial oxygen saturation during and after PMMA injection.

Many authors have described an association between the use of PMMA in human hip arthroplasty and cardiovascular derangement such as hypotension, bradycardia, asystole, and bronchospasm (1–7). The etiology of these effects is uncertain, but mechanisms such as fat embolism associated with increased intramedullary pressure, air embolism, a neurogenic reflex, the release of vasoactive mediators such as histamine, direct depressive effects on the myocardium, peripheral vasodilatation, and activation of the coagulation cascade within the lungs have been proposed (1, 5, 7–11). Notably, hemodynamic derangement during total hip arthroplasty has been found during placement of the intramedullary femoral rod, usually performed under high pressure with large volumes of PMMA. Conversely, low pressure, manual packing of PMMA for the acetabular components has not been found to be associated with substantial hemodynamic derangements (1).

PMMA injection during percutaneous vertebroplasty differs from PMMA instillation during total hip arthroplasty in several ways. Less than 10 mL of PMMA is typically used per level treated during percutaneous vertebroplasty (13, 16–19), which is substantially less than the approximately 50 mL used in hip arthroplasty (D. R. Diduch, personal communication, 2001). It may be possible to expect a greater likelihood of adverse effects as the amount of PMMA instilled in the body increases. Also, because percutaneous vertebroplasty does not expose the intravertebral cavity to substantial amounts of air, air embolism may be less likely in percutaneous vertebroplasty.

It remains possible that mild pulmonary circulation changes, such as an increase in pulmonary arterial pressure or an increase in the arterial partial pressure of carbon dioxide (20), occur with PMMA injection; however, we did not perform the invasive monitoring that would be necessary to detect such changes. This study was susceptible to review bias in data collection, although we estimate this bias to be small because there was minimal requirement for interpretation of data by the data collectors. A prospective study could be more rigorous in this regard and could also allow for the effects of conscious sedation on cardiovascular parameters to be controlled. In our retrospective analysis, we did not control for the depressive cardiorespiratory effects of sedatives and narcotics, which may not be constant over the course of the procedure for at least some patients. The analysis of the association of less common cardiovascular comorbidities and cardiovascular derangement during PMMA injection was limited by the number of patients with these conditions in our sample.

Conclusion

We do not find any generalized, clinically significant association between the use of PMMA in percutaneous vertebroplasty and cardiovascular or pulmonary derangement in the hands of experienced operators.

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