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Effect of prophylactic infusion of norepinephrine on the prevention of hypotension during vertebroplasty: a randomized clinical trial

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Abstract

Background Transient hypotension is a common occurrence during the implantation of bone cement. This placebo-controlled randomized clinical trial study investigated the effect of prophylactic infusion of norepinephrine on the incidence of hypotension in senior patients who underwent vertebroplasty.

Methods The trial recruited patients who were greater than or equal to 65 years of age, had an American Society of Anesthesiologist physical status classification of I to III, and underwent vertebroplasty from August 2020 to August 2021 at the Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine in China. The patients were randomly grouped according to whether they received either a norepinephrine infusion of 0.05 μg/kg/min or an equivalent volume of saline 10 min before implantation of bone cement. Intraoperative hemodynamics were monitored continuously by the MostCare system at the following 7 time points: 10 min before implantation of bone cement and immediately, 30 s, 1, 3, 5, and 10 min after implantation of bone cement. We also recorded the number of hypotensive episodes and the total number of vasopressors after implantation of bone cement. Multivariable logistic regression was used to assess the risk factors associated with hypotension after implantation of bone cement.

Results A total of 63 patients were randomized to the control group ($n=31$; median [IQR] age, 74 [69–79] years) and the norepinephrine group ($n=32$; median [IQR] age, 75 [71–79] years). The incidence of hypotension in the norepinephrine group was significantly lower than that in the control group after implantation of bone cement (12.5% vs. 45.2%; relative risk [RR], 3.61 [95% CI, 1.13–15.07]; $P=0.005$). Moreover, the median (IQR) number of hypotensive episodes (0 [0–0] vs. 0 [0–2]; $P=0.005$) and the total number of vasopressors (0 [0–0] vs. 0 [0–1]; $P=0.004$) in the norepinephrine group were significantly lower than those in the control group. Furthermore, compared with the baseline, the MAP significantly decreased at 1 min ($P=0.007$) and 3 min ($P<0.001$) after bone cement implantation in the control group. However, the MAP at 3 min in the norepinephrine group was significantly higher

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than that in the control group ($P < 0.001$). The incidence of complications was not different between the groups. In multivariable logistic regression, the FRAIL score (OR, 2.29; 95% CI, 1.21–4.31) was identified as a risk factor associated with hypotension.

Conclusion Prophylactic infusion of norepinephrine before bone cement implantation can stabilize hemodynamics and reduce the incidence of hypotension after implantation of bone cement.

Keywords Hypotension, Norepinephrine, Vertebroplasty, Hemodynamics, Bone cement implantation

Background

Vertebral compression fractures, which are common injuries in the aged population, are mostly associated with osteoporosis [1]. Vertebroplasty is reported to be a successful surgical procedure for improving the physical activity and quality of life for patients suffering from painful fractures [2–4]. These patients are mostly elderly [5] and have multiple underlying diseases [6]; hence, minimally invasive vertebral augmentation procedures have been widely used to treat vertebral compression fractures caused mainly by osteoporosis and, less commonly, osteolytic tumors [7].

Polymethylmethacrylate (PMMA) is the main material of choice for vertebroplasty with bone cement augmentation, which has been widely used in this procedure but has been associated with cardiovascular deterioration in patients receiving percutaneous vertebroplasty [3, 4]. PMMA has several disadvantages, such as toxicity, exothermic curing, and uncertain long-term biomechanical effects, and may leach into the circulation and cause cardiovascular complications, such as hypotension and fat embolism [8]. In addition, PMMA and bone wax leakage into epidural and paravertebral veins has been discovered postmortem in animals [9]. A transient hypotensive phenomenon may be observed while injecting PMMA into a vertebral body; however, there is presently no clear explanation of the mechanisms underlying PMMA-induced hypotension, which may involve potential toxic, vasodilating, or allergic effects of the cement, as well as possible bone marrow microemboli.

To date, there is no universal definition of hypotension, and how best to characterize hypotension remains unclear. Several recent studies have reported associations between low mean arterial pressure (MAP) and organ injury [10], with hypotension defined in terms of minutes or integrated pressures below various absolute thresholds [11]. The definition of physiologically relevant perioperative hypotension remains elusive, but a MAP less than 65 mmHg [12] or a ≥ 30% reduction in MAP from baseline during surgery is increasingly used as a pragmatic population harm threshold [13]. Furthermore, MAP below absolute thresholds of 65 mmHg or relative thresholds of 20% are progressively related to both myocardial and kidney injury [14].

The reasons underlying the pathogenesis of PMMA-induced hypotension are poorly understood; thus, there are few studies regarding prophylactic agents or techniques for PMMA-induced hypotension. Norepinephrine is a strong α receptor agonist and has a weak effect on the β_1 receptor, a commonly used vasopressor in the critical care setting, especially for the management of septic shock. The maximal improvement in flow occurred with norepinephrine, which caused an increase in MAP and cardiac output (CO), making it the optimal vasopressor to use in patients with hypotension after free flap surgery [15]. However, it is unknown whether prophylactic infusion of norepinephrine can reduce the incidence of PMMA-induced hypotension.

We hypothesized that prophylactic infusion of norepinephrine would reverse the MAP decrease in senior patients undergoing vertebroplasty. The primary aim of the present study was to compare the incidence of PMMA-induced hypotension with or without norepinephrine. The secondary objectives were to determine the number of hypotensive episodes, the total number of vasopressors, and other complications after injecting PMMA.

Materials and methods

Study design

We performed a prospective, double-blind, placebo-controlled randomized clinical trial. Approval for the study was obtained from the Ethics Committee of the Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, Nanjing, China (no. 2020LWT012) and the study was registered before patient enrollment in the Chinese Clinical Trial Registry (http://www.chictr.org.cn) with registration no. ChiCTR2000036315 (date of first registration, 22/08/2020). Written informed consent was obtained from all participants.

The trial recruited patients who were greater than or equal to 65 years of age, had an American Society of Anesthesiologist (ASA) physical status classification of I to III (I indicates a healthy patient, II indicates a patient with mild systemic disease, and III indicates a patient with severe systemic disease), and underwent vertebroplasty from August 6, 2020, to August 5, 2021, in the Affiliated Hospital of Integrated Traditional Chinese and

Western Medicine, Nanjing University of Chinese Medicine. The trial exclusion criteria were as follows: patient refusal to participate in the study; body mass index (BMI) higher than 30 kg/m^2 or less than 18 kg/m^2; ASA physical status classification of IV or above; severe cardiovascular and cerebrovascular diseases; arrhythmia; and recent contact with other researchers.

Group allocation was conducted with a computer-generated random number table, and then numbered opaque sealed envelopes were prepared by our investigator. The envelope was opened just before general anesthesia was induced. A syringe containing 50 ml of solution was prepared and labeled as 'study drug'. Patients were randomly assigned to receive either norepinephrine infusion 0.05 μg/kg/min [15] or an equivalent volume of saline 10 min before implantation of bone cement. The infusion was ceased 10 min after bone cement implantation. The investigator and the patients were blinded to the group allocation, which was not revealed until the patients were discharged from the hospital.

Anesthetic and surgical procedure

All patients received general anesthesia for vertebroplasty. Routine intraoperative monitoring, including invasive blood pressure measurement, pulse oximetry, electrocardiography, and end-tidal carbon dioxide partial pressure, was established. Anesthesia was induced with 0.02 mg/kg midazolam, 1-1.5 mg/kg propofol, 3–5 μg/kg fentanyl, and 0.6 mg/kg rocuronium to facilitate tracheal intubation. Anesthesia was maintained with remifentanil, 0.05–0.15 μg/kg/min, and propofol, 1-1.5 mg/kg/h, and the remifentanil and propofol infusion rates were titrated to keep the heart rate (HR) and MAP within 20% of baseline, and depth of anesthesia maintained bispectral index (BIS) value between 45 and 60. If stroke volume variation (SVV) > 13%, the fluid challenge consisted of 250 ml of crystalloid solution (either 0.9% saline or Ringer's solution) that was infused and utilized to improve hemodynamic instability or intravenous boluses of 50 μg phenylephrine or 5 mg ephedrine according to the decision of the attending anesthetist. To prevent postoperative nausea and vomiting, 4 mg of ondansetron was intravenously administered at the end of the surgery.

The patient was placed on the fluoroscopy table in prone position, the surgical incision is made 15 min after hemodynamic stabilization. Vertebroplasty was performed using a conventional technique. Briefly, under the fluoroscopy of "C" type arm X-ray machine, the needle entry points of both sides were determined and marked, and aseptic preparation was completed, two hollow needles (Shandong Guanlong Medical Supplies Co., Ltd., Jinan, China) were inserted through the skin and muscle into the target vertebral body. Subsequently, PMMA (Heraeus Medical Co., Ltd., Shanghai, China) was injected into the fractured vertebra through the needles. The total volume of bone cement injected into the vertebral body was approximately 6 mL. Throughout the procedure, continuous imaging was used to ensure proper cement placement and vertebral height restoration. This cement hardened quickly, stabilizing the vertebra. Once the cement was in place and the surgeon was satisfied with the results, the needles were removed. After completing surgery, the tracheal tube was removed when adequate muscle strength was detected.

Data collection

We collected the following data: age; gender; height; BMI; ASA physical status; screening for frailty (the FRAIL scale is a 5-question assessment of fatigue, resistance, aerobic capacity, illnesses, and loss of weight) [16]; preoperative pain visual analog scale (VAS) score; smoking status; drinking status; surgical segment; comorbidities, including hypertension, diabetes, coronary artery disease, chronic obstructive pulmonary disease, anemia, and allergic disease; preoperative medications; duration of surgery and anesthesia; and intraoperative fluid administration, bleeding and urinary output.

Intraoperative hemodynamics were monitored continuously by the MostCare system (Vytech Health, Padua, Italy), which is the available pulse contour monitor uncalibrated pulse contour method that has been validated in various clinical settings [17, 18]. The data collected included MAP, HR, CO, stroke volume (SV), systemic vascular resistance (SVR), and SVV at the following 7 time points: 10 min before implantation of bone cement (baseline) and immediately, 30 s, 1, 3, 5, and 10 min after bone cement implantation.

We also collected the following postoperative data 30 min after extubation in the postanesthesia care unit (PACU): arrhythmia, nausea and vomiting, postoperative pain VAS score, and arterial blood gas: pH, PO_2, PCO_2, base excess, and lactic acid.

Outcome variables

The primary outcome of the study was the difference in the incidence of hypotension after implantation of bone cement between patients with vertebroplasty who received norepinephrine and those who received saline. Hypotension was defined as an MAP less than 65 mmHg [12] or a ≥ 30% reduction in MAP from baseline for which an intervention was needed, which included intravenous fluid infusion and/or the use of vasopressors [13].

We also evaluated the number of hypotensive episodes, the total number of vasopressors used, tachycardia (HR > 100 beats per minute), and bradycardia (HR < 60 beats per minute) after implantation of bone cement. The incidence of other variables, including arrhythmia,

nausea and vomiting, postoperative pain VAS score, and arterial blood gas, were also compared.

Statistical analysis

The estimated sample size was calculated from the results of a preliminary study, wherein the incidence of hypotension was 45% after implantation of bone cement in senior patients with vertebroplasty. The expected effect size was calculated to detect an 80% reduction in the incidence of hypotension after prophylactic infusion of norepinephrine, with a 2-sided $\alpha=0.05$ and 80% power; 56 patients were needed. Considering the possibility of loss to follow-up or consent withdrawals, 70 patients were included in this trial.

Statistical analysis was performed with MedCalc, version 15.2. The normal distribution of the parameters was tested using the Kolmogorov–Smirnov test. Continuous variables were reported as the mean (standard deviation, SD) and compared using the independent sample *t* test if distributed normally. Nonnormal distribution parameters are presented as the median (interquartile range, IQR) and were analyzed using the Mann–Whitney *U* test. Categorical variables were reported as frequencies and percentages (%) and compared using χ^2 or Fisher's exact test, as appropriate. Two-way repeated-measures analysis of variance was used for hemodynamic variables at corresponding time points. A logistic regression model was used to evaluate the potential risk factors associated with hypotension after implantation of bone cement. A p value <0.05 was considered statistically significant.

Results

We recruited participants from August 2020 to August 2021. The CONSORT recruitment diagram of the study is shown in Fig. 1. A total of 70 aged (greater than or equal to 65 years) patients were assessed for eligibility, and seven patients were excluded based on the exclusion criteria. Subsequently, 63 patients were randomized

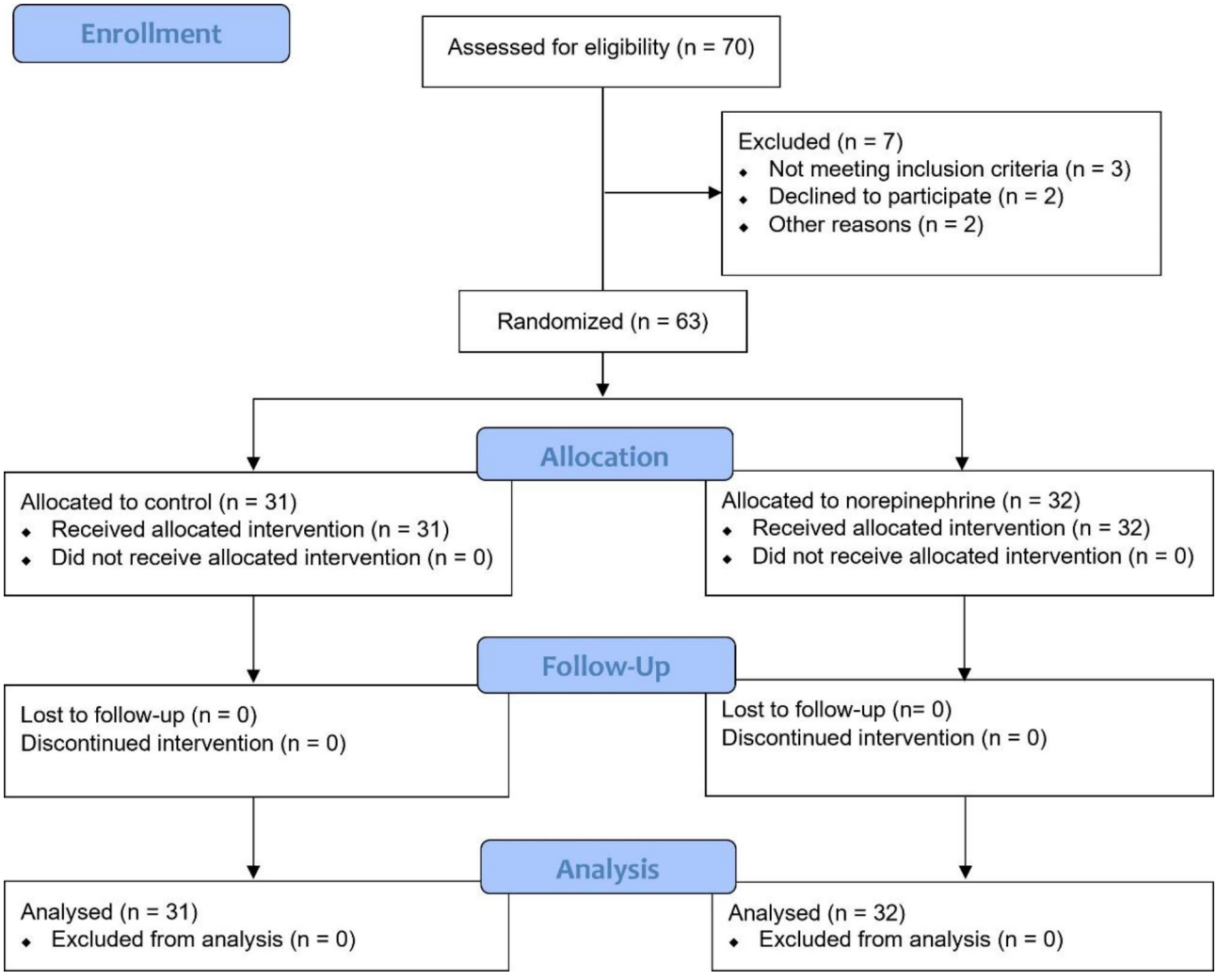

Fig. 1 CONSORT Flow Diagram of Study Recruitment

Table 1 Characteristics of the study subjects

	Control group (*n* = 31)	Norepinephrine group (*n* = 32)	*P* value
Patient Characteristics			
Age, years, median (IQR),	74 (69–79)	75 (71–79)	0.690
Gender [n (%)]			0.933
male	10 (32.3)	10 (31.3)	
female	21 (67.7)	22 (68.7)	
Height, median (IQR), cm	163 (155–168)	162 (160–168)	0.405
BMI, mean (SD)	23.1 (2.5)	23.2 (21.3)	0.831
ASA Physical Status Classification [n (%)]			0.722
I	0 (0)	0 (0)	
II	17 (54.8)	19 (59.4)	
III	14 (45.2)	13 (40.6)	
FRAIL score, median (IQR)	1 (0.25-2)	1.5 (0.5-2)	0.838
Preoperative pain VAS score, median (IQR)	3 (2–4)	3 (2–4)	0.615
Smoking status [n (%)]	4 (12.9)	3 (9.4)	0.675
Drinking status [n (%)]	3 (9.7)	3 (9.4)	0.969
Comorbidities [n (%)]			
Hypertension	12 (38.7)	14 (43.8)	0.885
Coronary artery disease	4 (12.9)	6 (18.8)	0.688
Chronic obstructive pulmonary disease	6 (19.4)	6 (18.8)	0.956
Diabetes	3 (9.7)	3 (9.4)	0.969
Anemia	4 (12.9)	3 (9.4)	0.675
Allergic disease	2 (6.5)	2 (6.3)	0.975
Antihypertensive medication [n (%)]			
β-Blocker	5 (16.1)	7 (21.9)	0.601
Calcium channel blocker	6 (19.4)	8 (25.0)	0.635
ARB/ACE inhibitor	3 (9.7)	4 (12.5)	0.737
Surgery segment, median (IQR)	L_1 (T_{12}–L_2)	L_1 (T_{12}–L_2)	0.725
Duration of surgery, median (IQR), min	55 (52–59)	57 (54–62)	0.343
Duration of anesthesia, median (IQR), min	76 (73–80)	74 (69–77)	0.280
Intraoperative fluid administration, mean (SD), mL	436 (72)	440 (58)	0.802
Intraoperative bleeding, median (IQR), mL	10 (10–15)	10 (10–15)	0.911
Intraoperative urinary output, mean (SD), (mL)	77 (31)	89 (24)	0.094

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; VAS, visual analog scale; ARB, angiotensin II receptor blocker; ACE, angiotensin-converting enzyme

Continuous variables presented as mean (SD) were compared using the independent sample *t* test or median (IQR) were compared using the Mann–Whitney *U* test

Categorical variables presented as number (percentage) were compared using χ^2 or Fisher's exact test, as appropriate

Table 2 Incidences of hemodynamic instabilities after implantation of bone cement

	Control group (*n* = 31)	Norepinephrine group (*n* = 32)	*P* value
Incidence of hypotension [n (%)]	14 (45.2)	4 (12.5)	0.005*
Number of hypotensive episodes, median (IQR)	0 (0–2)	0 (0–0)	0.005*
Number of vasopressors, median (IQR)	0 (0–1)	0 (0–0)	0.004*
Tachycardia [n (%)]	2 (6.5)	1(3.1)	0.545
Bradycardia [n (%)]	13 (41.9)	11 (34.4)	0.627

Continuous variables presented as median (IQR) were compared using the Mann–Whitney *U* test

Categorical variables presented as number (percentage) were compared using χ^2 or Fisher's exact test, as appropriate

Compared with the control group, *$P<0.05$

into two groups: the control group ($n=31$; median [IQR] age, 74 [69–79] years; male/female, 10/21) and the norepinephrine group ($n=32$; median [IQR] age,75 [71–79] years; male/female, 10/22) (Table 1).

The demographic data in terms of height, BMI, ASA classification, FRAIL score, comorbidities, antihypertensive medication, preoperative pain VAS score, smoking status, and drinking status were similar in the two groups. Furthermore, there were no significant differences between the groups in terms of surgical segments, duration of surgery and anesthesia, intraoperative fluid administration, estimated blood loss, or urinary output (Table 1).

The norepinephrine group had a lower overall incidence of hypotension after bone cement implantation (12.5% vs. 45.2%; relative risk [RR], 3.61 [95% CI, 1.13–15.07]; $P=0.005$) than the control group had. Moreover, the number of hypotensive episodes (0 [0–0] vs. 0 [0–2]; $P=0.005$) and the total number of vasopressors (0 [0–0] vs. 0 [0–1]; $P=0.004$) in the norepinephrine group were significantly lower than those in the control group (Table 2). Furthermore, compared with the baseline, the MAP significantly decreased at 1 min ($P=0.007$) and 3 min ($P<0.001$), the HR decreased at 3 min ($P=0.002$), and the CO also decreased at 3 min ($P=0.002$) after implantation of bone cement in the control group (Fig. 2). In contrast, the MAP at different time points in the norepinephrine group did not decrease significantly compared with the baseline after bone cement implantation. However, at 3 min after implantation of bone cement, the MAP in the control group was significantly lower than that in the norepinephrine group ($P<0.001$). There were no significant differences in SV, SVR, and SVV at different time points between the two groups (Fig. 2).

There were no significant differences between the groups regarding PO_2, PCO_2, base excess, or lactic acid in the PACU. Furthermore, there were no significant

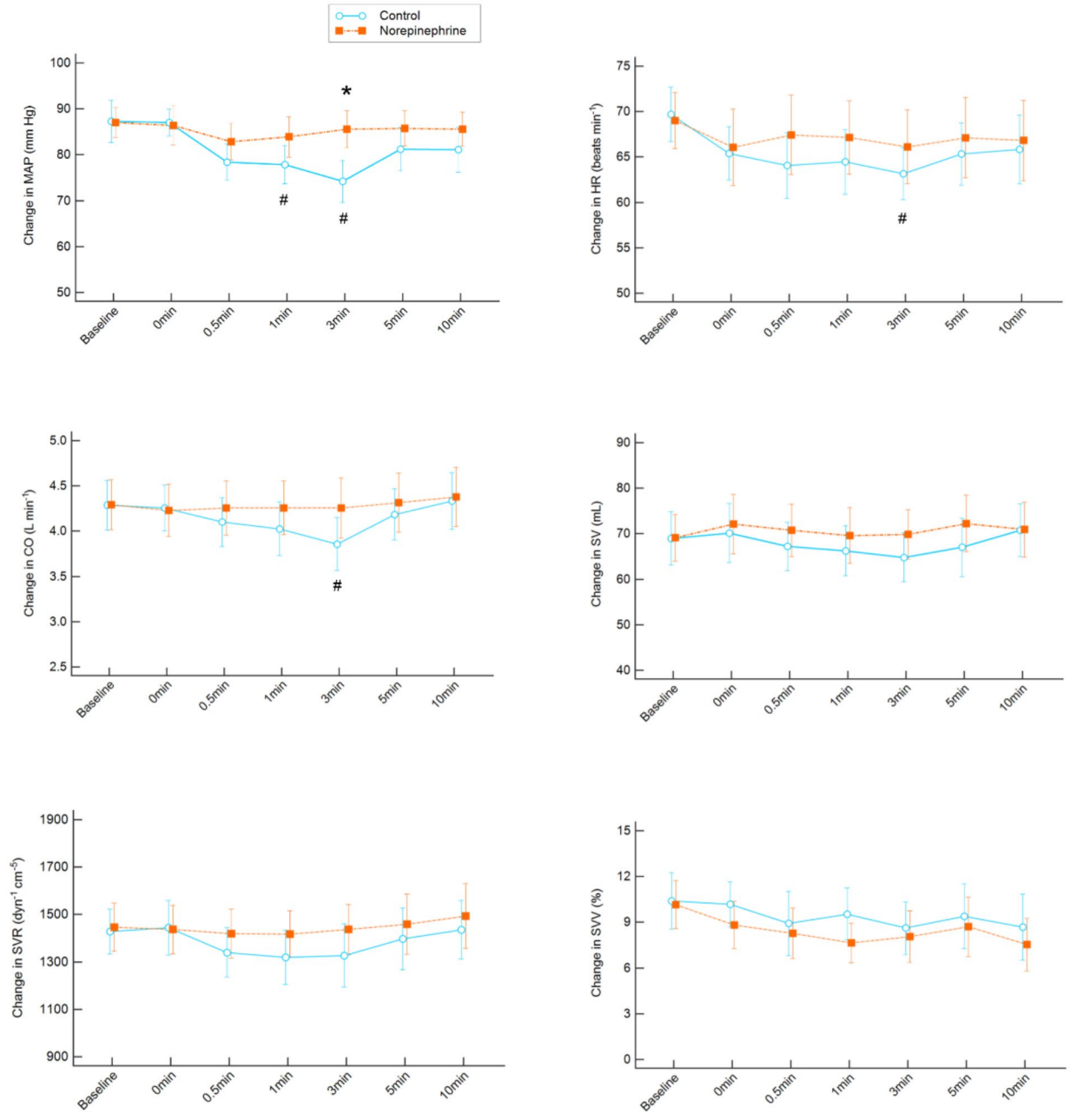

Fig. 2 Hemodynamic Parameters Before and After Implantation of Bone Cement. Abbreviations: MAP, mean arterial pressure; HR, heart rate; CO, cardiac output; SV, stroke volume; SVR, systemic vascular resistance; SVV, stroke volume variation. Compared with the control group, $^{*}P < 0.05$; Compared with the baseline, $^{\#}P < 0.05$

differences between the groups in terms of arrhythmia, nausea and vomiting, or postoperative pain VAS score (Table 3).

Multivariable logistic regression was used to assess the risk factors associated with hypotension after implantation of bone cement, and these were found to include age (OR, 1.08; 95% CI, 0.96–1.23), BMI (OR, 0.90; 95% CI, 0.65–1.24), FRAIL score (OR, 2.29; 95% CI, 1.21–4.31), preoperative hypertension (OR, 2.00; 95% CI, 0.50–7.99), preoperative pain VAS score (OR, 1.09; 95% CI, 0.68–1.76), and norepinephrine use (OR, 0.13; 95% CI, 0.03–0.56) (Fig. 3).

Table 3 Postoperative outcomes in the PACU

	Control group (*n* = 31)	Norepinephrine group (*n* = 32)	*P* value
Arterial blood gas			
pH, median (IQR)	7.41 (7.40–7.41)	7.41 (7.39–7.41)	0.708
PO_2, median (IQR), mmHg	92 (90–96)	92 (90–97)	0.852
PCO_2, median (IQR), mmHg	39 (34–41)	38 (33–41)	0.557
Base excess, median (IQR), mM	2.1 (-0.6-2.3)	1.3 (0-2.3)	0.430
Lactic acid, median (IQR), mM	0.8 (0.6–1.8)	0.8 (0.6–1.4)	0.426
Arrhythmia [n (%)]	0 (0.0)	1 (3.1)	0.325
Nausea and vomiting [n (%)]	7 (22.6)	6 (18.8)	0.738
Postoperative pain VAS score, median (IQR)	2 (1–3)	2 (1–2)	0.959

Continuous variables presented as median (IQR) were compared using the Mann–Whitney *U* test

Categorical variables presented as number (percentage) were compared using χ^2 or Fisher's exact test, as appropriate

Discussion

Our study demonstrated that a hypotensive response appeared at 1 min, and especially at 3 min, after PMMA injection in senior patients with vertebral compression fracture. However, prophylactic infusion of norepinephrine reversed the PMMA-induced hypotension in patients receiving vertebroplasty.

In this study, the gradual fall in baseline MAP observed in the control group was predominantly linked with a decline in CO, indicating that the decrease in MAP was primarily due to CO. The present study revealed that MAP decreased significantly at 1 and 3 min after injection of PMMA, the decrease was the most obvious at 3 min, consistent with a previous study [19], and the MAP returned to the baseline level at 5 min after injection. At the same time, the HR showed a significant decrease at 3 min after PMMA injection, and returned to the baseline level at 5 min. However, prophylactic infusion of norepinephrine attenuated these changes in MAP, CO and HR in patients receiving vertebroplasty with bone cement implantation. One study reported that the incidence of hypotension was 28% among patients undergoing hip arthroplasty with implantation of bone cement [20]. However, hypotension occurs frequently in senior patients undergoing vertebroplasty; its incidence increased to 45.2% in this study. Our results showed a higher incidence of hypotension, possibly due to the elderly status and prone position. None of the patients experienced serious complications in our trial. Our results indicated that transient and slight hemodynamic changes appear after the injection of PMMA, which is easy for clinicians to ignore.

Vertebroplasty is safe and effective, which reduces the demand for analgesics, and a relatively common technique for the treatment of vertebral compression fractures [21]. The number of performed this type of surgery is growing; however, there have been few studies investigating the hemodynamic changes associated with PMMA. Hemodynamic changes related to PMMA have

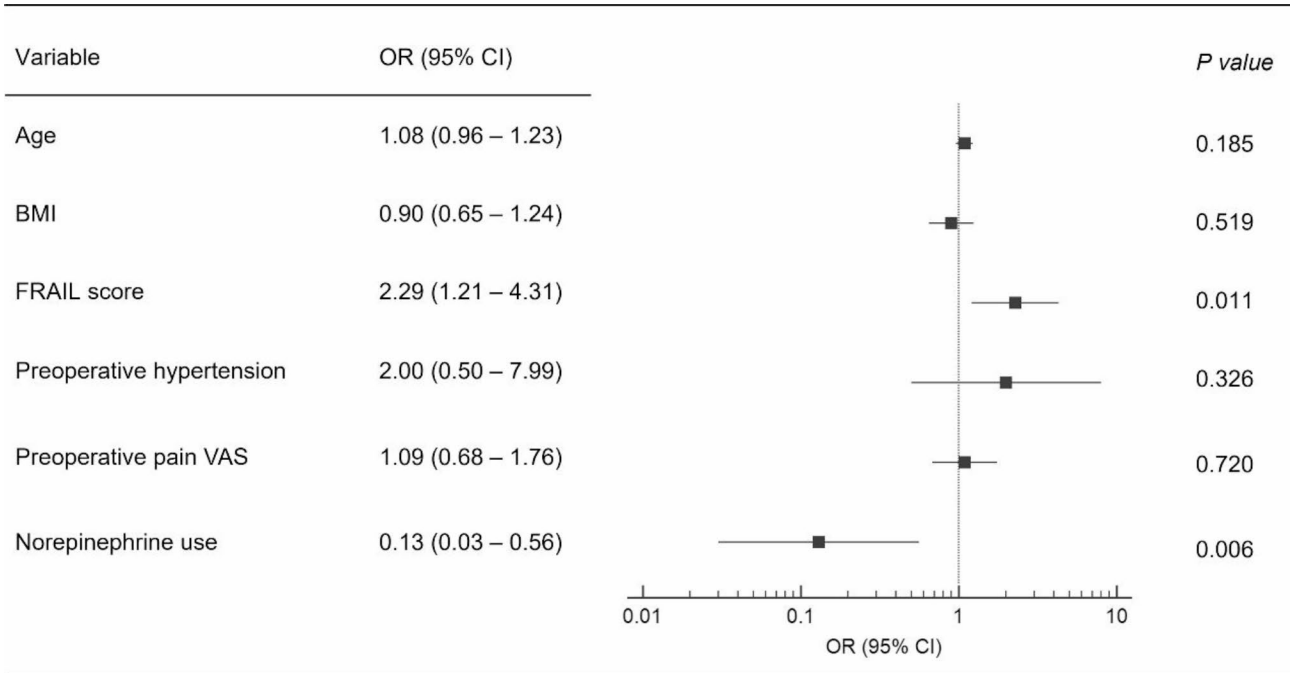

Fig. 3 Forest Plot of Factors Analyzed for Association with Incidence of Hypotension in Multivariable Logistic Regression. Abbreviations: BMI, body mass index; VAS, visual analog scale; OR, odds ratio

also been well documented during hip arthroplasty [22]. The mechanisms underlying PMMA-induced hemodynamic changes (which may occur because an early injection in the liquid phase can cause bone cement extravasation into the venous system, as well as into the lungs) may involve potential toxic, vasodilating, or allergic effects, as well as possible bone marrow microemboli. One study showed that regardless of what type of PMMA material is used, deteriorating baseline MAP may be associated with the pressurization of the vertebral bodies rather than with the use of PMMA during vertebroplasty [9]. However, because bone is replaced by fat in osteoporotic vertebral bodies, the augmentation of an osteoporotic vertebral body with bone cement could cause the release of an even greater quantity of fat emboli, especially during the prophylactic augmentation of more than one vertebral body. Hence, in the present study, we speculated that these hemodynamic changes during vertebroplasty mainly involved an increase in intraosseous pressure, which can induce a neural reduction in sympathetic tone and the release of bone marrow contents into the circulation. Some scholars suggest that the solvent and monomers of bone cement may stimulate the sensory nerve endings of vertebral bodies, resulting in reflex hypotension. As far as the clinician is concerned anesthetic techniques that intervene in afferent nerve pathways from the medullary cavity represent a possible approach that should be used [23].

Vertebral compression fractures are common in the aged population [5], which showed a higher incidence of hypotension, especially in patients with preoperative hypovolemia and cardiovascular disease. In the present study, we enrolled patients over 65 years old who had an ASA physical status classification of II or higher. Multivariable logistic analysis showed that preoperative frailty and norepinephrine use were associated with the occurrence rate of hypotension. Frailty is an age-associated syndrome featuring multiorgan loss of reserve and resiliency, and increased vulnerability to stressors, with a prevalence ranging from 10 to 65% [24], which is tightly related to and even predictive of hospitalization and death [25]. It has been shown that during most surgeries, intraoperative hypotension is a marker of severity, patient frailty, or both rather than a mediator of postoperative complications [26]. Our study also demonstrated that frailty was prevalent in older patients undergoing vertebroplasty and may be a risk factor for PMMA-induced hypotension. A recent study reported that frailty is associated with an increased risk of cardiovascular events and is a marker of high cardiovascular risk; however, patients with frailty still experience benefits from intensive blood pressure control without an increased risk of serious cardiovascular events [27]. A narrative review summarized what is known about the association between blood pressure and frailty, the clinical management of blood pressure in frailty and the association between blood pressure, cognitive decline and dementia, avoiding hypotension is likely to be crucial for older people with frailty or cognitive vulnerability [28].

The mechanism of PMMA-induced hypotension is unclear, and only symptomatic treatment is needed. It has been shown that the hemodynamic profile offered by norepinephrine during cesarean delivery is superior to that of phenylephrine due to less fluctuation in HR [29]. Our data showed that prophylactic infusions of norepinephrine can stabilize hemodynamics in patients undergoing vertebroplasty with PMMA. What is more important, the procedure of bone cement implantation needs to be performed under continuous fluoroscopy. In some cases, the anesthesiologist is not at the bedside of the patient, and the vasopressor cannot be administered in time when the blood pressure drops; hence, prophylactic infusion of norepinephrine may prevent PMMA-induced hypotension. We speculate that younger patients undergoing vertebroplasty with PMMA might also benefit from this method.

Most case of PMMA-induced hypotension in patients undergoing vertebroplasty may resolve automatically by fluid resuscitation therapy; some patients may need to use vasopressors, and a few patients may suffer from bone cement implantation syndrome, which involves refractory hypotension, pulmonary edema, hypoxemia, arrhythmia and even cardiac arrest. One study reported that bone cement leakage into the paravertebral venous system may lead to embolization of cement particles into the right cardiac chambers and pulmonary artery [30]. Another study revealed that the risk of pulmonary embolism ranges from 3.5 to 23% for patients with osteoporotic fractures [31]. If paravertebral vein filling is observed by fluoroscopy, the injection of bone cement should cease and be staged. If the clinician is unaware of this procedure-related risk, hypotension in a senior patient undergoing vertebroplasty under general anesthesia could easily be misinterpreted and ascribed to supposed postural hypotension or 'cardiopulmonary comorbidity' [32].

The present study has certain limitations. First, only elderly people with vertebral compression fractures were enrolled. Second, the prone position tends to induce hypotension. Last, while the number of cases is small, the sample size was calculated from the results of a preliminary study, and thus it is possible that the current study was not large enough to identify a true difference in the incidence of perioperative complications.

Conclusion

Previous research showed that risk factors for intraoperative hypotension are associated with lower pre-induction MAP, older age, emergency surgery, and ASA III ~ V [33]. In this study, although PMMA-induced hypotension is not severe, it requires clinical attention. Prophylactic infusion of norepinephrine can stabilize hemodynamics and reduce the incidence of hypotension after bone cement implantation.

Abbreviations

PMMA	Polymethylmethacrylate
ASA	American Society of Anesthesiologist
BMI	Body mass index
VAS	Visual analog scale
MAP	Mean arterial pressure
HR	Heart rate
CO	Cardiac output
SV	Stroke volume
SVR	Systemic vascular resistance
SVV	Stroke volume variation
PACU	Postanesthesia care unit

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This research was performed mainly at the department of Anesthesiology, Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine in China.

Author contributions

QF, DLT, and YJ made the conception and design, and wrote the manuscript. SAL, YQS, and MJ performed most of the data collection and date analysis. All authors reviewed the manuscript.

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Data availability

The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study has been approved by the Ethics Committee of the Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine in China. Written informed consent was obtained from each patient prior to the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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