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INTERVENTIONAL

Intracardiac cement embolism during percutaneous vertebroplasty: incidence, risk factors and clinical management

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Abstract

Objective To evaluate the incidence and risk factors for ICE during a PV.

Materials and methods Single-center retrospective analysis of 1512 consecutive patients who underwent 1854 PV procedures for osteoporotic (34 %), malignant (39.9 %) or other cause (26.1 %) of vertebral compression fractures (VCFs)/spine tumor lesions. Only thoracic or lumbar PVs were included. PVs were performed with polymethylmethacrylate (PMMA) low-viscosity bone cement under fluoroscopic guidance. Chest imaging (X-ray or CT) was performed the same day after PV in patients with high clinical suspicion of ICE. All post-procedural chest-imaging examinations were reviewed, and all ICEs were agreed upon in consensus by two radiologists.

Results ICEs were detected in 72 patients (92 cement embolisms). In 86.1 % of the cases, concomitant pulmonary artery cement leakage was detected. Symptomatic ICEs were observed in six cases (8.3% of all ICEs; 0.32% of all PV procedures). No ICE led to death or permanent sequelae. Multiple levels treated during the same PV session were associated with a higher ICE rate [OR: 3.59, 95% CI: (1.98-6.51); $p < 0.001$]; the use of flat panel technology with a lower ICE occurrence [OR: 0.51, 95% CI: (0.32-0.83); $p = 0.007$].

Conclusion Intracardiac cement embolism after PV has a low incidence (3.9 % in our study). Symptomatic complications related to ICE are rare (0.3%); none was responsible for clinical sequelae in our series.

Key Points

• *The incidence of intracardiac cement embolism (ICE) during PVP is low (3.9%).*
• *Having a high number of treated vertebrae during the same session is a significant risk factor for ICE.*
• *Symptomatic intracardiac cement embolisms have a low incidence (8.3% of patients with ICE).*

Keywords Percutaneous vertebroplasty · Leakage · Cement · Embolism · Cardiac · Complication

Abbreviations

AP	Anteroposterior
ICE	Intracardiac cement embolism
IV	Intravenous
PCE	Pulmonary cement embolism
PMMA	Polymethylmethacrylate
PV	Percutaneous vertebroplasty
RA	Right atrium
RAA	Right atrial appendage
RV	Right ventricle
VCF	Vertebral compression fracture

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Introduction

Percutaneous vertebroplasty (PV) has gained acceptance in the last 3 decades for the treatment of painful vertebral compression fractures [1]. This safe and mini-invasive technique is nowadays widely performed [2, 3] although major and minor complications may occur. Minor complications mainly include fever, transient back pain worsening, transient radicular pain, paravertebral bone cement venous migration and subcutaneous hematoma along the course of the bone needles [2, 4, 5]. Major complications consist in cauda equina/spinal cord compression related to bone cement migration into the spinal canal, nerve root compression by cement fragment, spondylitis, arterial bone cement migration, symptomatic pulmonary bone cement migrations and decompensation of comorbidities (cardiac or pulmonary failure) [4, 6–9]. Migration of bone cement in pulmonary arteries is mainly due to cement leakage in the paravertebral veins, secondarily migrating into the azygos venous system or directly into the vena cava and eventually migrating to the pulmonary arterial tree after having passed through the right cardiac cavities [10, 11]. Pulmonary cement embolisms during PV procedures have been extensively reported. Their incidence ranges from 2.1 to 26%; most of them are asymptomatic and have no clinical consequence [12–16].

Even though all pulmonary cement embolisms necessarily pass first through the heart cavities, some cement fragments may stay inside the heart cavities. This subtype of cement embolisms has been called “intracardiac cement embolisms” (ICEs). This specific PV complication has been poorly reported in the literature, mostly in case reports [17–20].

The purpose of our study was to evaluate the incidence of ICEs during a PV procedure and to evaluate their risk factors and clinical consequences.

Materials and methods

Study design

Single-center retrospective study from January 2004 to December 2011.

Patients

Patients’ demographics are summarized in Table 1.

During the study period, 1600 consecutive patients [female: n = 1057 (66%), male: n = 543 (34%); mean age = 68.8 ± 13.9 years (range: 18-108)] underwent PV (cervical, thoracic, lumbar and sacral) corresponding to 1982 procedures. Among them, we excluded 88 patients (5.5%) who underwent cervical (n = 44, 50%) or sacral (n = 44, 50%) procedures (Fig. 1).

One thousand five hundred twelve consecutive patients who had thoracic T1-T12 (n = 739, 39.9%), lumbar L1-L5 (n = 749, 40.4%) or both (n = 366, 19.7%) percutaneous vertebroplasties were thus finally included, corresponding to 1854 PV procedures and 3581 treated levels (mean = 1.9 ± 1.4 levels/procedure; range: 1-7).

Table 1 Patient demographics/lesion characteristics

Patient demographics/lesion characteristics	
Age (years; m ± SD [range])	68.8 ± 13.9 [18-108]
Gender	
Female (n, %)	998 (66%)
Male (n, %)	514 (34%)
Type of vertebral compression fracture/lesion	
Osteoporotic (n, %)	513 (34%)
Malignant (n, %)	603 (39.9%)
Hematologic malignancies (myeloma, plasmocytoma, lymphoma, leukemia) *(n, %)*	94 (15.6%)
Primitive bone tumors (synovialosarcoma, giant cell tumors) *(n, %)*	3 (0.5%)
Metastatic tumors *(n, %)*	506 (83.9%)
Breast *(n, %)*	239 (47.2%)
Unknown *(n, %)*	74 (15%)
Lung *(n, %)*	61 (12%)
Prostate *(n, %)*	31 (6.1%)
Kidney *(n, %)*	28 (5.5%)
Thyroid *(n, %)*	16 (3.1%)
Colorectal *(n, %)*	11 (2.1%)
Bladder *(n, %)*	11 (2.1%)
Womb *(n, %)*	10 (1.9%)
Head and neck *(n, %)*	9 (1.8%)
Ovarian *(n, %)*	7 (1.4%)
Liver *(n, %)*	3 (0.6%)
Melanoma *(n, %)*	2 (0.4%)
Esophagus *(n, %)*	2 (0.4%)
Gastric *(n, %)*	1 (0.2%)
Pancreatic *(n, %)*	1 (0.2%)
Traumatic (n, %)	154 (10.1%)
Other causes: hemangioma, bone cyst, unknown, ... (n, %)	242 (16%)

m: mean, SD: standard deviation, n: number

Thirty-four percent of the patients (513/1512) had osteoporotic VCF; 39.9% of the patients (603/1512) had malignant vertebral lesion(s). Among them, 83.9% (506/603) had metastatic tumor lesions; 16.1% (97/603) had lesions from a primitive bone tumor (details about the primitive cancer/hematologic malignancies responsible for spine lesions are listed in Table 1). Finally, 10.1% (154/1512) had traumatic VCF and 16% (242/1512) had a spine lesion from another cause (benign tumor lesion, unknown, etc.) (Table 1).

Inclusion criteria

Inclusion criteria were: age above 18 years, intractable pain due to VCFs secondary to osteoporosis, or malignant or benign vertebral tumor or other cause.

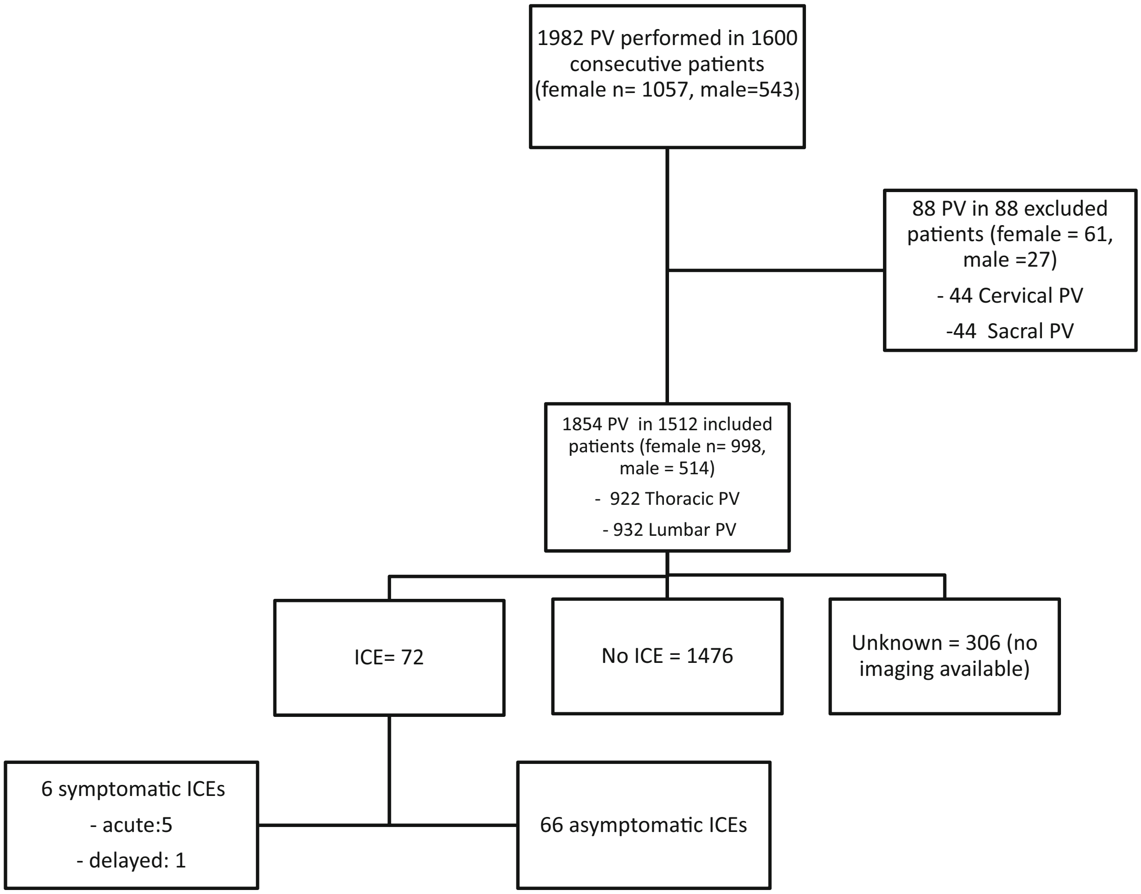

Fig. 1 Recruitment flow chart. *ICE*: intracardiac cement embolism; *PV*: percutaneous vertebroplasty

Exclusion criteria were: cervical percutaneous vertebroplasty or cement sacroplasty, local cutaneous or subcutaneous infection, active systemic infection, leukopenia, coagulation disorder or past history of allergy to polymethylmethacrylate (PMMA) bone cement used for vertebroplasty.

Technique

PV procedures were performed using fluoroscopic guidance with a monoplane C-arm (Angiostar; Siemens) from 2004 to 2007; PVs performed after 2007 were treated using a monoplane C-arm flat panel (Axiom, Siemens). All patients were treated in the prone position under conscious sedation that was achieved with IV administration of propofol (Diprivan; AstraZeneca) alone or in combination with IV alfentanil (Rapifen; Janssen-Cilag) and midazolam hydrochloride (Hypnovel; Roche Products). Local anesthesia (1% lidocaine, xylocaine; AstraZeneca) was administered subcutaneously under fluoroscopic guidance, and 1 g intravenous cefazolin (or other broad-spectrum antibiotic) was also administered according to the protocol for orthopedic surgery to minimize any risk of infection. Patients were treated using a bipedicular approach with beveled 11-G bone needles (Thiebaud) under monoplane fluoroscopic guidance, except in cases of osteolysis of the pedicle or when the patient had previously undergone posterior surgical fixation. In the latter cases, the bone needle was inserted into the vertebral body using a parapedicular approach. The cement used was polymethylmethacrylate (PMMA) low-viscosity bone cement. All procedures were performed in sterile conditions with strict adherence to aseptic measures.

When the imaging findings were not conclusive as to the cause of the lesion, a bone biopsy was performed before PMMA injection using a coaxial system with a 13-G long bone biopsy needle (Thiebaud). Then, the PMMA cement, mixed with a tungsten powder (Balt) used to enhance the cement's radioopacity, was injected under fluoroscopic guidance until homogeneous filling of the target lesion was achieved.

From January 2004 to April 2006, Osteopal V Bone Cement (Heraeus Medical) or Simplex P Bone Cement (Stryker) low-viscosity cements were alternatively used, and after April 2006, Biomet V Bone Cement (Biomet Orthopedics), a low-viscosity cement, was then used.

All PVs were performed by four different physicians, three of them with more than 2 years' experience and thus considered "experienced" operators. Technique of PV did not change during the study period, except the change to flap panel technology guidance.

Technical details of the PVs are summarized in Table 2.

A chest imaging (plain X-ray or CT) was systematically performed immediately after the PV procedure, except when the operator was confident that no perivertebral venous leakage had occurred. Thus, in 83.5% (1548/1854) of the PVs, a post-procedure chest imaging was performed. In 41.8% of the cases, only a chest X-ray in anteroposterior (AP) projection was performed; in 49.9% of the cases an unenhanced chest CT scan (lung and mediastinum windowing) was directly performed, and in 8.3% of the cases both a chest X-ray and chest CT scan were performed the same day (Table 3). When an opacity suggestive of pulmonary/cardiac cement migration was seen on the AP chest X-ray, a chest CT scan was performed the same day as the PV procedure to confirm the diagnosis of pulmonary and/or cardiac cement migration (*n* = 128/1548, 6.9%) (Table 3).

All chest examinations were reviewed on our picture-archiving and communication system (CarestreamVue PACS, CarestreamHealth) by a radiologist with 2 years' experience. A chest CT was mandatory for diagnosis confirmation using the following criteria, adapted from a previous study on pulmonary cement embolisms [16]: ICE had to be located inside right cardiac cavities (right atrial appendage and/or right atrium and/or right ventricle), and ICE had to be hyperdense with an attenuation > 500 HU (Figs. 2, 3 and 4).

Table 2 Percutaneous vertebroplasty procedures

Number of treated vertebrae	3581
Mean	1.9 ± 1.4 levels/procedure
Range	1 to 7 level(s)/procedure
Multiple levels (*n*, %)	1028 procedures (55.4%)
Thoracic vertebrae (*n*, %)	739 (39.9%)
Lumbar vertebrae (*n*, %)	749 (40.4%)
Mixed (thoracic and lumbar) (*n*, %)	366 (19.7%)
Bone biopsy	
Yes (*n*, %)	752 (40.6%)
No (*n*, %)	953 (51.4%)
Unknown (*n*, %)	149 (8%)
Malignant VCF (*n*, %)	744 (40%)
Osteolytic type (*n*, %)	435 (58.5%)
Osteoblastic type (*n*, %)	61 (8.2%)
Mixed type (*n*, %)	160 (21.5%)
Unknown (*n*, %)	88 (11.8%)
Operators (*n*)	4
1 (*n*, %)	1211 PV (65.3%)
2 (*n*, %)	554 PV (29.9%)
3 (*n*, %)	55 PV (3%)
4 (*n*, %)	34 PV (1.8%)
Flat panel technology (*n*, %)	1127 procedures (60.8%)

m: mean, *n*: number, PV: percutaneous vertebroplasty, VCF: vertebral compression fracture

Table 3 Imaging findings of ICEs, characteristics of the patients with symptomatic ICEs

Chest imaging available (*n*, %)	1548 (83.5%)
Chest X-ray (*n*, %)	648 (41.8%)
Chest CT (*n*, %)	772 (49.9%)
Both (*n*, %)	128 (8.3%)
Patients with intracardiac cement embolism	
Number of patients (*n*, %)	72 (3.9%)
Multiple ICE (*n*, %)	18 (25%)
2 fragments (*n*, %)	16 (88. 9%)
3 fragments (*n*, %)	2 (11.1%)
Number of fragments (m ± SD)	92 (1.2 ± 0.51, range: 1-3)
Location	
RA	29 (31.6%)
RAA	28 (30.4%)
RV	35 (38%)
Associated pulmonary cement embolism (*n*, %)	62 (86.1%)
Symptomatic ICE (*n*, %)	6 (8.3%)
Female (*n*, %)	4 (66.6%)
Age (m ± SD)	65.7 ± 15.6 years (range: 33-83)
Type of VCF/vertebral lesion	
Malignant lytic fracture (myeloma, lymphoma, lung cancer)	3
Other cause (Waldenström disease, drepanocytosis)	2
Osteoporosis	1
Associated pulmonary cement embolism (*n*, %)	6 (100%)
Cardiorespiratory arrest (*n*, %)	1 (16.7%)
Acute dyspnea (*n*, %)	4 (66.6%)
Late pericardial effusion (*n*, %)	1 (16.7%)
Fatal outcome	0

ICE: intracardiac cement embolism, m: median, *n*: number, RA: right atrium, RAA: right atrial appendage, RV: right ventricle, SD: standard deviation, VCF: vertebral compression fracture

All cases of ICE were assessed in consensus with a senior radiologist (8 years' experience).

All patients were reviewed by the operator 1 month after vertebroplasty to evaluate the effectiveness of PV and potential delayed PV-related complications. Only medical charts (computer and papers files) of patients with ICE were reviewed to detect early and late complication.

Objectives

The primary objective of our study was to evaluate the incidence of ICEs during a PV procedure. The secondary objective was to identify independent risk factors of such intracardiac cement embolisms. The third objective was to evaluate clinical consequences of ICEs.

Fig. 2 ***Method for ICE detection.*** **a** Post-PV anteroposterior (AP) plain X-ray focused on T11 level in a 62-year-old female who underwent PV for symptomatic hemangioma. Satisfactory filling of the vertebra is seen. Additionally, multiple paravertebral cement venous leakages are detected (arrows). **b** Post-PV AP chest X-ray in the same patient, showing multiple pulmonary cement embolisms in right pulmonary lobes (arrowheads) and two opacities in projection of the cardiac silhouette suggesting multiple cardiac embolisms (open arrows). **c**, **d** Post-PV chest CT scan, axial slices, in the same patients showing a spontaneous hyperdensity, measured at 887 HU, within the right atrium corresponding to an ICE (arrow)

Statistical analysis

Data analysis was performed using the Stata software (Stata/IC 13.1 for Mac; StataCorp LP). Results are presented as means ± standard deviations and ranges or medians with their interquartile range (IQR). Comparison of distribution was performed with a X^2 or Fisher's exact test, depending on the sample size. Comparison of means was performed using a Student's *t* test or Wilcoxon test according to data distribution. Univariate then multivariate analysis (logistic regression using dichotomized variables) was performed to evaluate the influence of the following criteria on the occurrence of cardiac PMMA cement embolism: age, sex, number of treated levels during the same session, use of flat panel technology for the fluoroscopic guidance, malignant nature of the lesion, lesion's location (i.e., thoracic or lumbar) and experience of the operator (long experience was defined as performing PV for 2 years or more). Results were considered statistically significant when $p < 0.05$.

Ethical statement

Neither approval of the institutional review board nor patient informed consent is required by the ethics committee of our

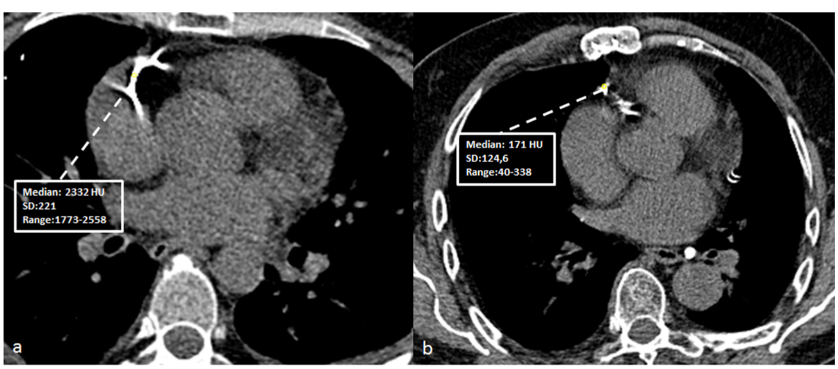

Fig. 3 ***Distinction between ICE and coronary calcifications.*** **a** Post-PV non-gated unenhanced chest CT, axial slice, in a 73-year-old female with osteoporotic VCF showing a spontaneous hyperdensity, measured at 2332 HU, within the right atrial appendage corresponding to an ICE. **b** Post-PV non-gated unenhanced chest CT, axial slice, in a 82-year-old male with osteoporotic VCF, showing spontaneous hyperdensity located outside the heart cavities along the expected course of the right coronary artery, with lower density (171 HU), corresponding to a coronary calcification

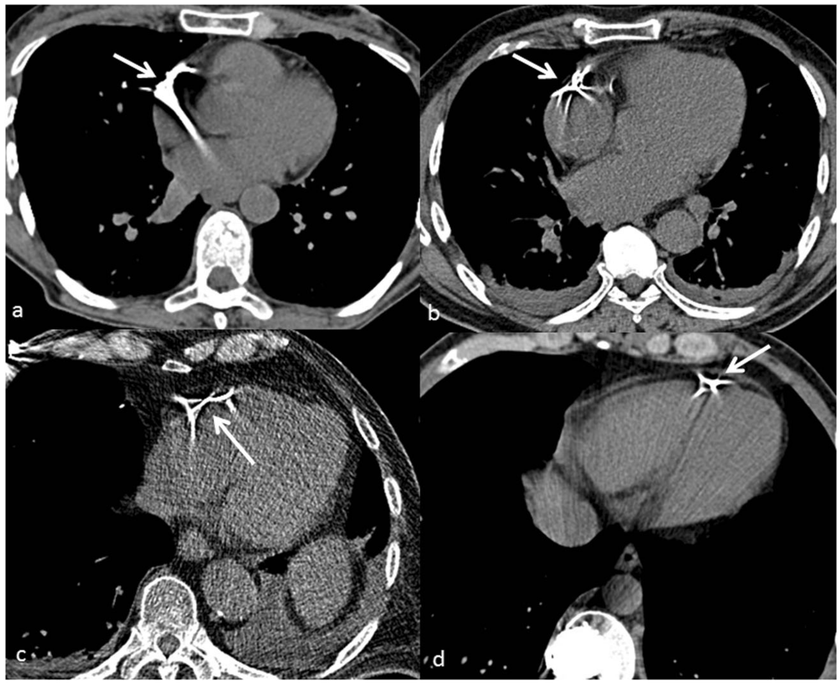

Fig. 4 ***Examples of ICEs in four different patients.*** Post-PV non-gated unenhanced chest CTs, axial slices, demonstrating spontaneous hyperdensities (arrows) located in the right atrium (**a**,**b**) or right ventricle (**c**,**d**) corresponding to ICEs

institution for retrospective analyses of patients' records and imaging data.

Results

Incidence and characteristics of intracardiac cement embolisms

Intracardiac cement embolisms were identified in 72 patients (3.9%) corresponding to a total of 92 cement fragments. Eighteen patients (25%) had multiple ICEs, two intracardiac fragments in 16 patients and three in two patients (average number of ICEs = 1.2/patient) (Table 3).

In 15.3% of the cases (11/72), intracardiac embolisms were isolated, whereas in 84.7% (61/72) ICEs were associated with pulmonary artery cement embolisms (Table 3). The overall incidence of pulmonary cement embolisms in our series was 24 % (450/1854). Among the 92 intracardiac cement fragments detected, 29 (31.6%) were located in the right atrium (RA), 28 (30.4%) in the right atrial appendage (RAA) and 35 (38%) in the right ventricle (RV) (Table 3).

No paradoxical cement embolism in the arterial systemic circulation related to patent *foramen ovale* was recorded.

Risk factors for ICE

Results from the univariate analyses showed that the risk of ICE increased when multiple levels were treated during the same session of PV ($p < 0.001$) and when the lesion was located in a thoracic vertebra ($p < 0.047$). On the other hand, the risk of ICE decreased with the use of flat panel technology ($p = 0.004$). There was no statistically significant difference according to age, gender, type of vertebral lesion and operator's experience.

According to the multivariate analysis, there was an increased OR for ICE in patients treated for multiple levels during the same PV procedure [OR = 3.59, CI 95% (1.98-6.51), $p < 0.001$]. Interestingly, the risk of ICE did not increase proportionally with the number of treated levels during the same session. Additionally, the use of flat panel technology was significantly associated with a low risk of ICE [OR = 0.51, CI 95% = (0.32-0.83), $p = 0.007$]. Finally, there was no significant difference according to age, gender, type of vertebral fracture and lesion location (thoracic or lumbar). Moreover, greater operator experience in PV did not influence the risk of ICE. Results from the multivariate analysis of intracardiac cement leakage occurrence are presented in Table 4.

Clinical outcome

All patients with ICE had a clinical follow-up with a mean delay of 8.1 ± 19 months (range 0.1-108) to detect early and late complications.

Five patients (0.33% of the overall population; 6.9% of patients with ICE) presented potentially ICE-related symptoms within the 24 h after the procedure. One patient (20%) presented a cardiorespiratory arrest immediately after the PV procedure and four patients (80%) presented acute dyspnea. Patients' characteristics and clinical outcome are summarized in Table 5. One patient (20%) presented a cardiorespiratory arrest during the switching position from prone to the supine

Table 4 Multivariate analysis evaluating the influence of various risk factors for the occurrence of an intracardiac cement embolism during percutaneous vertebroplasty

	Odds ratio	[95% Conf. interval]	*p*
Age	0.74	[0.45-1.22]	0.237
Gender	0.89	[0.54-1.48]	0.677
Multiple levels	3.59	[1.98-6.51]	< 0.001*
Operator experience	1	(Not retained for the analysis)	
Malignant VCF	1.09	[0.66-1.80]	0.730
Flat panel	0.51	[0.32-0.83]	0.007 *
Thoracic level	1.59	[0.94-2.68]	0.081

VCF: vertebral compression fracture; Conf.: confidence

*Statistically significant difference

position at the end of the procedure. He was resuscitated in emergency and was admitted to the intensive care unit for multiorgan failure with acute right heart failure. The post-procedural unenhanced chest CT revealed two fragments of ICE (one in the RA and one in the RV), bilateral pleural effusion and partial consolidation of the lower lobes. He was treated conservatively, without any anticoagulation treatment. Eventually, the patient had a satisfactory clinical outcome and was discharged at day-12 without sequelae. Four patients (80%) presented acute dyspnea, which occurred in the immediate postoperative period and resolved with symptomatic management (Fig. 5). None of these patients received anticoagulation therapy. Interestingly, all patients with symptomatic complications had pulmonary artery cement leakage(s) associated with the ICE.

Only one patient with cardiac embolism (0.06% of the overall population; 1.4% of patients with ICE) had a delayed complication (i.e., after discharged). The patient presented cough and fever 3 years and 7 months after the PV procedure. She was treated for a lymphoma, and the chest CT revealed a pericardial hematoma close to the right cardiac cavities in front of the cement fragment located in the RA. A cardiac MR examination was subsequently performed, and the diagnosis was confirmed (Fig. 6). As the patient was barely symptomatic (i.e., no cardiopulmonary symptoms), she was treated conservatively; no surgical treatment was performed. At last follow-up (7 years and 11 months after PV), no cardiopulmonary symptoms were recorded.

All asymptomatic patients with ICE were treated conservatively. Only two patients (3%) were treated with oral anticoagulation.

Influence of number and location of ICEs

Among the patients with symptomatic complications potentially related to ICE, 33.3% (2/6) had multiple ICEs versus 24.2% (16/66) in patients with asymptomatic ICE. However, this difference was not statistically significant [$p = 0.63$, OR = 1.55 CI 95% (0.13; 12.0)].

In 66.6% (4/6) of the patients with symptomatic complications potentially related to ICE, a right ventricle fragment was detected versus 42.4% (28/66) in asymptomatic ICE patients. However, this difference was also not statistically significant [$p = 0.39$, OR = 2.68 CI 95% (0.35; 31.5)].

Discussion

In our study, the incidence of intracardiac cement embolism during PV was low: 3.9%. To the best of our knowledge, no previous studies have reported the incidence of ICE after PV. Moreover, this study was based on one of the largest vertebroplasty population since the EVEREST cohort [2], with more than 1500 patients and 1854 PV procedures. We detected 72 patients with intracardiac cement embolisms, the largest population with this complication ever studied. Indeed, only case reports have been published in the literature so far [17–20], and Hatzantonis et al [21], in their systematic review of the literature, only collected 18 cases.

Our study also showed that having a higher number of treated vertebrae during the same PV procedure is an independent risk factor for occurrence of ICE (asymptomatic or not). It can be explained by the use of a larger amount of cement, more difficult technical conditions (difficulties to file numerous vertebrae during the same cement injection period) or a longer operation duration (patient staying a longer time in the prone position, potentially modifying the venous circulation regimen), all of these factors increasing the risk of cement venous leakage.

In this study, the risk of ICE seems to have been lower since the use of flat panel technology for guidance (after 2007). This association is in accordance with previous studies on PCE [11, 16], which showed that high-quality fluoroscopic guidance is mandatory to detect venous leakage and prevent PCE. However, the fact that the ICE rate was lower during the study period when flat panel technology was used does not imply a causal link. Indeed, many other mechanisms are plausible and potentially confounding.

Table 5 Symptomatic patient characteristics

	Age (years)	Gender	Symptoms	Number of treated vertebrae	Level of treated vertebrae	Number of fragments	Fragment location	Chest CT findings	Management	Outcome
Patient 1	83	Male	Acute: Cardio-respiratory arrest, right heart failure	3	L3-L4-L5	2	RAA, RV	Moderate pleural effusion and partial consolidation of lower lobes	Conservative No anticoagulation	Uneventful outcome at 20-month follow-up
Patient 2	78	Male	Acute: dyspnea	2	T12-L2	1	RV	Moderate left pleural effusion	Conservative No anticoagulation	Deceased from unknown cause 10 days after PV
Patient 3	58	Female	Acute: dyspnea	4	T8-T12-L1-L2	1	RAA	Bilateral partial consolidation of lower lobes	Conservative No anticoagulation	Uneventful outcome at 3-year follow-up
Patient 4	33	Female	Acute: dyspnea	4	L2-L3-L4-L5	1	RV	Bilateral partial consolidation of lower lobes	Conservative No anticoagulation	Uneventful outcome at 9-year follow-up
Patient 5	60	Female	Acute: dyspnea	3	T5-T7-T10	1	RA	Bilateral pleural effusion and small pericardial effusion	Conservative No anticoagulation	Uneventful outcome at 1-month follow-up
Patient 6	47	Female	Delayed: cough and fever 3 years 7 months after PV	4	T9-T10-T11-T12	2	RA, RV	Pericardial hematoma next to right cavities, pleural effusion	Conservative No anticoagulation	Uneventful outcome at 7-year 11 month follow-up

PV: percutaneous vertebroplasty, RA: right atrium, RAA: right atrial appendage, RV: right ventricle

Interestingly, in our study, we found that greater operator experience did not prevent ICE. However, more than 90% of PVs were performed by highly skilled operators.

Most patients with ICE (93%) detected in our series were asymptomatic. We reported only 5 out of 72 patients with ICE (7%) who presented acute cardiopulmonary symptoms potentially related to the cardiac cement embolism. None of them died from these symptomatic ICEs. Only one case of ICE leading to death was reported in the literature by Lee and al. [17], who reported the case of a patient presenting a cardiac tamponade and right ventricle perforation by a spike of PMMA 3 months after PV. The patient was treated by open-heart surgery but died 5 days after admission from an acute respiratory distress syndrome. Interestingly, in our series, all patients with symptomatic ICE had concomitant cement embolism in the pulmonary arteries. In Hatzantonis et al's systematic review of the literature [21], ICE-related clinical manifestations varied from asymptomatic (5.5% vs. 93% in our series) to mild symptoms such as chest pain, syncope or moderate dyspnea (72% vs. 5.5% in our series) to life-threatening conditions such as acute respiratory distress or cardiac tamponade (22.2% vs. 1.4% in our series). In our study, most of the acute symptomatic patients (80%) had mild to moderate symptoms, mainly dyspnea, and they all had pleural effusion and/or lung abnormalities on chest CT scans (Table 5, Fig. 5). One patient (1.4% of patients with ICE; 20% of acute symptomatic patients) had a life-threatening symptom (cardiorespiratory arrest early resuscitated) with good clinical outcome. A direct relationship between the ICE and cardiorespiratory arrest remains uncertain in the latter case; associated pulmonary cement embolisms or other unrelated causes such as allergic reaction to bone cement could have been responsible for this severe complication. One patient (20%) with moderate acute dyspnea died 10 days after PV from unknown cause. He had a lung tumor invading the mediastinum and the right pulmonary artery. No case of tamponade, cardiac perforation, acute valvular damage or paradoxical cerebral embolism was recorded in our series, although described in literature [17, 20, 22–24]. All of the above-mentioned five patients were treated conservatively. In Hatzantonis et al's systematic review on this topic [21], since numerous patients were symptomatic, most of them were treated by open heart surgery or percutaneous retrieval with uneventful recovery except for one death. Only 1 out of 18 patients was treated conservatively in the above-mentioned review of the literature, with full recovery. To date, there is no consensus in the literature on the best management of ICE. Current treatment options are: conservative management with symptomatic treatment, oral anticoagulation for 3 to 6 months until PMMA endothelializes and stops being thrombogenic [25, 26], percutaneous retrieval (especially for right atrium leakage) or open-heart surgery. Usually, asymptomatic patients are treated conservatively. Patients with moderate to life-threatening symptoms are most likely to be

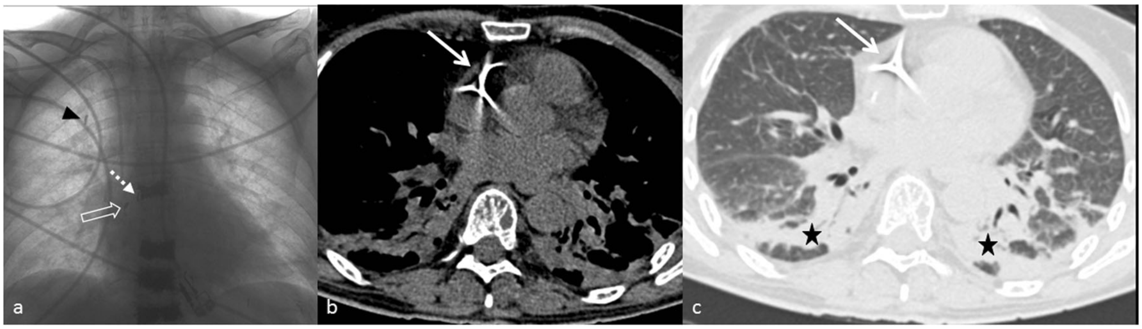

Fig. 5 ***Example of acute ICE-related complication.*** A 58-year-old female with multiple myeloma treated for T8, T12, L1 and L2 lesions during the same PV session, who developed acute moderate dyspnea within the 24 h after the procedure. **a** Post-PV AP chest plain X-ray showing paravertebral T8 cement venous leakages (dotted arrow), pulmonary cement leakage in the upper right lobe (arrowhead) and linear opacity in projection of the right heart cavities suggesting an ICE (open arrow). **b** Post-PV non-gated unenhanced chest CT, axial slice, mediastinum windowing, showing an ICE located in the right atrium (arrow). **c** Post-PV non-gated unenhanced chest CT, axial slice, lung windowing, showing bilateral partial consolidation of lower lobes (stars)

surgically treated even if there is no strong evidence for the value of this strategy.

In our study, a single intracardiac fragment was detected in 75% of patients with ICE versus 50% of cases in the literature [21, 24]. A possible explanation is that most cases described in the literature are dealing with severe symptomatic patients who underwent open cardiac surgery or percutaneous retrieval and that a larger amount of cement within the right cardiac cavities may increase the risk of severe symptomatic ICE-related complications. Our results show the same tendency, as multiple fragments were more frequently detected in symptomatic patients, although the difference was not statistically significant.

As described by Hatzantonis et al [21], cement location in the right ventricle can also be an important factor in cardiac complications as cement leakage into the right ventricle was more frequently associated with pericardial effusion,

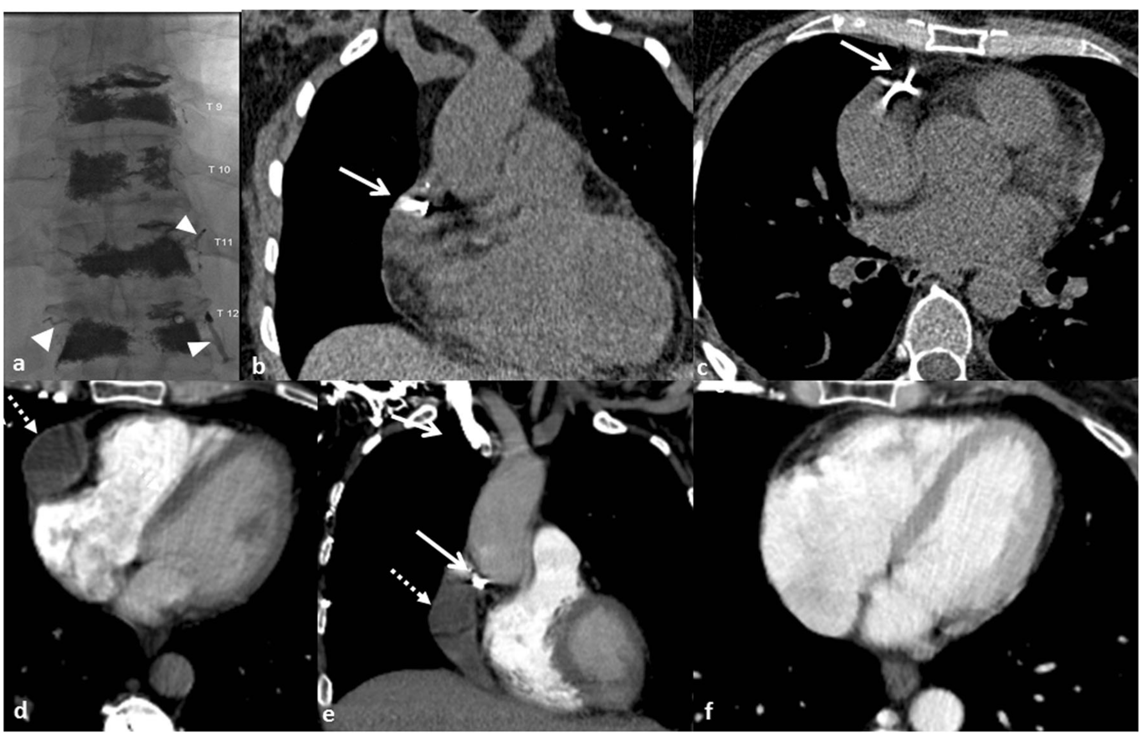

Fig. 6 ***Example of delayed ICE-related complication.*** **a** Post-PV AP plain X-ray focused on T9-T12 levels in a 47-year-old female treated for thoracic spine lesions from lymphoma, showing the filling of vertebrae and multiple paravertebral cement leakages (arrowheads). The same day, a few hours after the PV procedure, a chest CT scan was performed: **b** coronal reconstruction and **c** axial slice. ICE within the right atrium (arrows) was detected. Three years seven months after the PV procedure, a contrast-enhanced chest CT scan was performed for cough and fever: **d** axial slice and **e** coronal reconstruction. A spontaneous hyperdense collection with liquid-liquid level (dotted arrows) close to the intracardiac cement fragment (arrow) was detected, corresponding to a probable pericardial hematoma. **f** Seven years 11 months after the PV procedure, contrast-enhanced chest CT (axial slice) showed a complete resorption of the pericardial hematoma

hemopericardium and cardiac wall perforation. Indeed, in this review, all patients with severe symptoms (i.e., cardiac collapse or tamponade) had a right ventricle cement fragment. On the contrary, cement leakages into the right atrium were mostly asymptomatic or mildly symptomatic with no pericardial effusion and a normal ejection fraction at echocardiography [21]. Again, our results go along with this trend, as symptomatic patients tend to have more ICE located into the right ventricle than asymptomatic patients, though the difference was not statistically significant. Besides, the most severe symptomatic patient with life-threatening symptoms had two fragments, one being located in the right ventricle.

PMMA viscosity has been demonstrated to be a major risk factor for cement leakages [27]. Indeed, experimental studies have shown that low- or medium-viscosity PMMAs favor the interdigitation of cement into the trabecular bone but increase the risk of extravasation [28–31]. On the contrary, high-viscosity PMMA spreads uniformly in the vertebrae, potentially leading to a more efficient vertebral stabilization and reducing the risk of leakage and complications [31]. In our study, only low-viscosity cement was used. It can be suggested that the incidence of ICE would have been even lower with the use of high-viscosity cement.

Limitations of the study

Our study has several limitations. First, this is a retrospective monocentric study. Second, chest imaging was not available in all patients (16.4% of the patients did not undergo any chest imaging), which could lead to an underestimation of the ICE rate during PV.

Second, we were not able to collect data regarding the average cement volume used, which may have an influence on ICE occurrence.

Additionally, diagnosis of ICE was made on non-gated unenhanced chest CT scans, based on criteria established in a previous study focused on pulmonary cement embolisms [32]. The positive diagnosis of ICE was sometimes difficult to confirm, especially in patients with coronary calcifications, which can be mistaken for cement embolisms (Fig. 3), especially with non-gated CT acquisition. Careful analysis is essential to determine if the dense opacity is located within the right cavities or along the expected course of a coronary artery. To overcome this drawback, density measurement can also be helpful since coronary calcifications usually have lower attenuation than bone cement. It is noteworthy that exogenous devices such as central venous catheters or pacemakers may cause streaking artifacts, limiting the analysis of heart cavities.

Although acute cardiorespiratory complications were easily detected by the review of the patients' medical charts, delayed complications were more difficult to assess retrospectively. Indeed, the average late follow-up was 8.1 months, and only 26.4% of the patients had a late follow-up over 1 month. In the literature, some of the cardiorespiratory complications related to ICE were delayed, ranging from several months up to 5 years [21, 24]. Consequently, cardiorespiratory complications, especially delayed ones, could have been underestimated in our series.

Conclusion

In this study we found a low incidence of intracardiac cement embolism after PV; most were asymptomatic. Limiting the number of treated vertebrae during the same session may prevent these inopportune ICEs. Multicentric prospective series are warranted to further confirm our findings.

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Compliance with ethical standards

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was not required because French law states that no approval from a local IRB is necessary for retrospective analysis of patients' charts.

Methodology
• retrospective
• observational
• performed at one institution

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