Systematic Reviews /Meta-analyses

# Combination radiofrequency ablation and vertebral cement augmentation for spinal metastatic tumors: A systematic review and meta-analysis of safety and treatment outcomes

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A R T I C L E   I N F O

A B S T R A C T

*Background:* The treatment of spine metastases continues to pose a significant clinical challenge, requiring the integration of multiple therapeutic modalities to address the multifactorial aspects of this disease process. Radiofrequency ablation (RFA) and vertebral cement augmentation (VCA) are 2 less invasive modalities compared to open surgery that have emerged as promising strategies, offering the potential for both pain relief and preservation of vertebral stability. The utility of these approaches, however, remains uncertain and subject to ongoing investigation.

This systematic review and meta-analysis evaluates the available evidence and synthesize the results of studies that have investigated the combination of RFA and VCA for the treatment of spinal metastases, with the goal of providing a comprehensive and up-to-date assessment of the efficacy and safety of this therapeutic approach.

*Methods:* A literature search was conducted using the electronic databases PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus from their inception to May 4th, 2022 in accordance with PRISMA guidelines. Studies were included if they met the following criteria: 1) spine metastases treated with RFA in combination with VCA, 2) available data on at least one outcome (i.e., pain palliation, complications, local tumor control), 3) prospective or retrospective studies with at least 10 patients, and 4) English language. Meta-analyses were conducted in R (R Foundation for Statistical Computing; Vienna, Austria), using the *meta* package.

*Results:* In the 25 included studies, a total of 947 patients (females=53.9%) underwent RFA + VCA for spinal metastatic tumors. Out of 1,163 metastatic lesions, the majority were located in the lumbar region (585/1,163 [50.3%]) followed by thoracic (519/1,163 [44.6%]), sacrum (39/1,163 [3.4%]), and cervical (2/1,163 [0.2%]). 48/72 [66.7%] metastatic lesions expanded into the posterior elements. Preoperative pathologic vertebral fractures were identified in 115/176 [65.3%] patients. Between pre-procedure pain scores and postprocedure pain scores, average follow-up (FU) was $4.41\pm2.87$ months. Pain scores improved significantly at a short-term FU (1-6 months), with a pooled mean difference (MD) from baseline of 4.82 (95% CI, 4.48–5.16). The overall local tumor progression (LTP) rate at short-term FU (1–6 months) was 5% (95% CI, 1%–8%), at mid-term FU (6–12 months) was 22% (95% CI, 0%–48%), and at long-term FU (>12 months) was 5% (95% CI, 0%–11%). The pooled incidence of total complications was 1% (95% CI, 0%–1%), the most frequent of which were transient radicular pain and asymptomatic cement extravasation.

*Conclusions:* The findings of this meta-analysis reveal that the implementation of RFA in conjunction with VCA for the treatment of spinal metastatic tumors resulted in a significant short-term reduction of pain, with minimal total complications. The LTP rate was additionally low. The clinical efficacy and safety of this technique are established, although further exploration of the long-term outcomes of RFA+VCA is warranted.

## Introduction

The treatment of spine metastases poses a significant clinical challenge, requiring the integration of multiple therapeutic modalities to address the multifaceted nature of this complex disease. Spinal metastases, which arise from the dissemination of primary tumors to the vertebral column, can lead to debilitating pain, neurological deficits, and compromised structural integrity of the spine [1–3]. As cancer survival rates improve, the demand for effective and minimally invasive treatments has grown.

Radiofrequency ablation (RFA) and vertebral cement augmentation (VCA) are 2 promising strategies for managing spine metastases. Radiofrequency ablation is a minimally invasive technique that uses high-frequency electrical current to generate heat and cause coagulative necrosis of targeted tumor cells, providing significant pain relief [4,5]. VCA, which includes vertebroplasty and kyphoplasty, involves the percutaneous injection of bone cement into the affected vertebra, stabilizing the vertebral body and alleviating pain [6–9].

The combination of RFA and VCA has the potential to offer synergistic benefits in the treatment of spine metastases, with RFA providing targeted tumor ablation and pain relief, while VCA offers additional vertebral stabilization [10–12]. This dual approach may be particularly beneficial in patients with extensive vertebral involvement, where the combined effect of tumor destruction and vertebral reinforcement may result in more effective pain relief and preservation of spinal function [13–19].

Despite the theoretical advantages of combining RFA and VCA, the utility of these approaches in clinical practice remains uncertain and subject to ongoing investigation. The current body of literature on this topic is characterized by heterogeneity in study design, patient populations, and reported outcomes, complicating the interpretation of existing evidence.

This systematic review and meta-analysis aims to critically evaluate the available evidence and synthesize the results of studies investigating the combination of RFA and VCA for the treatment of spinal metastases. By pooling data from diverse clinical studies, this review seeks to provide a comprehensive assessment of the efficacy, safety, and potential benefits of this therapeutic approach in managing spine metastases. This analysis will address existing gaps in knowledge, guide future research, and ultimately inform clinical decision-making, improving care for patients with spinal metastases.

## Methods

Guidelines from the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement were used to conduct this systematic review.

### Search strategy

A literature search was conducted using the electronic databases PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus from their inception to May 4th, 2022. The keywords and medical subject headings (MeSH) terms included the following search terms: "radiofrequency ablation AND spine AND metas*". Identified studies were uploaded into a reference management software (ie, Endnote) and duplicates were removed.

### Study screening

Two authors (A.L.C. and N.S.S.) independently screened the titles and abstracts of all articles based on the prespecified inclusion and exclusion criteria. Articles that met the inclusion criteria were then full-text reviewed independently by the same 2 authors and eligible articles were selected based on the set criteria. Disagreements between the 2 authors were resolved via involvement of the senior author (S.V.). References of relevant articles were also reviewed in case any were missed via the electronic search.

### Assessment of study eligibility

The research question and selection criteria were determined prior to commencement of this study. Studies were included if they met the following criteria: 1) spine metastases treated with RFA in combination with VCA, 2) available data on at least one outcome (ie, pain palliation, complications, local tumor control), 3) prospective or retrospective studies with at least 10 patients, 4) English language. Exclusion criteria were defined as follows: 1) RFA or VCA in anatomical regions besides the spine or sacrum, 2) studies reporting mixed clinical outcomes from 2 or more different treatment modalities, 3) meta-analyses, narrative reviews, editorials, animal and experimental laboratory studies.

### Data extraction

Three authors (A.L.C., Y.R., and S.D.) initially extracted the data from the studies. This data was independently confirmed by 2 other authors (N.S.S. and S.V.). For each study, the following variables were extracted: 1) study and demographic characteristics including study design, sample size, gender, age, spinal levels affected, tumor characteristics (location within spine, presence of epidural expansion, radiograph characteristics, primary histology), 2) procedure-related variables (imaging guidance, anesthetic protocol, imaging follow-up, preoperative vertebral fractures, presence of multiple vertebral lesions per patient, tumor epidural expansion, ancillary thermo-protective measures), 3) patient-reported outcome measures (PROMs) for pain at pre- and postoperative time points including pain scale used and time between pre- and postoperative pain scores, 4) local tumor control, defined as locally stable or improved disease on imaging at the last follow-up, 5) complications (classified according to the Common Terminology Criteria for Adverse Events (CTCAE, version 5.0)). Complications were assessed and classified into major (CTCAE grade 3–5) and minor (CTCAE grade 1–2), and 6) other relevant information including VCA access site compared to RFA, chemotherapy or radiotherapy utilized in addition to RFA and VCA, improvement of clinical symptoms, vertebral stability post operation.

### Quality assessment

Given that all included studies had a non-randomized, cohort design, the risk of bias assessment was carried out using the Newcastle Ottawa Scale (NOS). The NOS for cohort studies utilizes a star-based system for rating the methodological quality of the study and is comprised of 3 major domains: selection, comparability, and outcome. Two reviewers (A.L.C and N.S.S.) independently assessed the quality of each study with disagreements resolved via involvement of a third author (S.V.) (Supplementary Table 1). Articles scoring at least 5 stars were retained in our analysis.

### Data analysis

Studies reporting changes in pain scores following RFA in combination with vertebroplasty were calculated according to a 0- to 10-point numeric rating scale (NRS). Single-arm meta-analyses were conducted to calculate the pooled mean difference (MD) from baseline in pain scores at 12 to 24-month and >24-month follow-ups. Meta-analyses were conducted in R (R Foundation for Statistical Computing; Vienna, Austria), using the *meta* package. The 95% confidence interval (CI) was calculated for each meta-analysis. Heterogeneity between studies was assessed using the $I^2$ statistic, where $I^2$ values greater than 40% indicated statistically significant heterogeneity. The results of both the fixed- and random-effects models were presented in the forest plot. When

significant heterogeneity was present, publications bias was evaluated by creating a funnel plot. The standard error of each study was plotted against the mean difference of the pain outcomes. The presence of asymmetry in the funnel plot indicates occurrence of publication bias. Other outcomes including demographics, nidus size, local tumor control, complications, and procedure-related parameters were descriptively reported due to significant heterogeneity across studies.

## Results

### Study selection

The initial literature search yielded 421 articles (PubMed: 122, Scopus: 299, CENTRAL: 0 for now). After the removal of 100 duplicates, there were 321 articles. A total of 288 studies were excluded based on screening of the title and abstract. A total of 33 full-text articles were then assessed for inclusion. Of these, 8 articles failed to meet inclusion criteria and were subsequently excluded. A total of 25 nonrandomized studies (21 retrospective, 4 prospective) published between 2008 and 2022 were included based on the inclusion/exclusion criteria (Supplementary Fig. 1) [5,15-17,19,20,24-42]. All included studies reported exclusively on metastatic spinal tumors. Based on the Newcastle-Ottawa Scale, most of the studies were rated to have 3 stars in the "selection" domain, zero stars in the "comparability" domain, and 3 stars in the "outcome" domain (Supplementary Table 1). Adequate length of follow-up was determined to be at least 1-month postprocedure and 2 of the studies had significant loss to follow-up defined as more than 20% of the preprocedure patient population. Otherwise, loss to follow-up in the rest of the studies was either absent or minimal. Publication bias was evaluated by creating a funnel plot. Data were distributed uniformly between the left and right side of the plot indicating that no major asymmetry was present and that the heterogeneity between studies was most likely not caused by publication bias (Supplementary Fig. 2).

### Study population

A total of 947 patients (395 males, 462 females with available data; mean age ranging from 51.4 to 69.5 years) were included across 23 studies. Out of 1,163 metastatic lesions, the majority were located in the lumbar region (585/1,163 [50.3%]) followed by thoracic (519/1,163 [44.6%]), sacrum (39/1,163 [3.4%]), and cervical (2/1,163 [0.2%]). Multiple vertebral lesions occurred in 175/525 [33.3%] patients across 12 studies. Preoperative vertebral fractures occurred in 115/176 [65.3%] patients across 6 studies. A total of 48/72 [66.7%] metastatic lesions expanded into the epidural region across 3 studies. Patient demographics and clinical characteristics are further outlined in Table 1.

### Procedure-related results

Image guidance for RFA procedures exclusively involved fluoroscopy and computed tomography (CT) in all studies. With regards to the anesthetic protocol across 18 studies, general anesthesia was used in 158/839 [18.8%] patients. Conscious sedation and local anesthetic were used in 681/839 [81.2%] patients. Ancillary protective measures to prevent thermal-mediated injuries to the spinal cord and nerve roots (eg, epidural air insufflation, thermocouples, or neuroprotective sterile water infusion) were mentioned in 14/25 [56%] studies (Table 2).

### Pain outcomes

Analgesic efficacy of RFA plus VA on spinal metastatic tumors was assessed by comparing pre- and postoperative pain scores in 22 of the 25 studies. Average follow-up (FU) was 4.41±2.87 months. A meta-analysis of the mean difference (MD) in pain scores following RFA + VA demonstrated statistically significant heterogeneity ($I^2$=94%, p<.01). In the

random effects model, the pooled MD in pain scores from baseline on the 0 to 10 NRS was 4.82 (95% CI, 4.48–5.16) (Fig. 1). Pain outcomes are further delineated in Table 3.

### Local tumor progression

The overall local tumor control rate was 91% (260/286 patients). At short-term (1–6 months) follow-up, random effects meta-analysis demonstrated a pooled local tumor progression rate of 5% (95% CI, 1%–8%) across 8 studies ($I^2$=49%; p=.06). At the mid-term (>6–12 months), random effects meta-analysis showed a pooled local tumor progression rate of 22% (95% CI, 0%–48%) across 3 studies ($I^2$=90%; p<.01). Lastly, at a long-term (>12 months) follow-up, similar to the short-term follow-up, a pooled local tumor progression rate of 5% (95% CI, 0%–11%) was observed across 4 studies ($I^2$=84%; p<.01) (Fig. 2). Patients with tumor progression were subsequently and successfully treated by intralesional resection and/or repeat RFA.

### Safety

Overall, complications occurred in 55 patients (55/908 [6.0%]). Major complications occurred in 5 patients (5/908 [0.5%]): 2 patients contracted sepsis, 2 patients were hospitalized for respiratory distress, and 1 patient had thermal damage to the spinal cord resulting in bilateral lower extremity weakness, difficulty in urination, and inability to have an erection. Minor complications occurred in 50 patients (50/908 [5.5%]), which mostly included asymptomatic bone cement extravasation in 38 patients (38/908 [4.2%]). Complications are further outlined in Table 4. The overall pooled incidence of total complications using the random-effects model was calculated at 1% (95% CI, 0%–1%), with insignificant heterogeneity between studies observed ($I^2$=19%, p=.2; Fig. 3). Additional information regarding patient population, procedure characteristics, and outcomes can be found in Table 5.

## Discussion

The results of this systematic review and meta-analysis provide valuable insights into the clinical efficacy and safety of the combined use of radiofrequency ablation (RFA) and vertebral cement augmentation (VCA) as a minimally invasive treatment strategy for patients with spinal metastases. The analysis included 25 studies with a total of 942 patients, demonstrating a significant improvement in pain scores at short-term follow-up, low local tumor progression rates, and a relatively low incidence of complications. These findings suggest that the combination of RFA and VCA may be a viable and promising therapeutic option for managing spine metastases. Our analysis demonstrated a significant reduction in pain across all meta-analyzed studies at an average follow-up of 4.4 months, emphasizing the potent analgesic properties of the RFA and VCA combination in a mid-term period. Pain management is a critical aspect of spinal metastases treatment, as uncontrolled pain significantly impairs patients' quality of life [10–12]. The synergistic effect of RFA and VCA offers substantial pain relief, potentially enhancing patients' overall well-being. The analgesic efficacy of RFA and VCA can be attributed to several factors. RFA eradicates tumor cells and disrupts pain-conducting nerve fibers, resulting in immediate and lasting pain relief [4,5]. Concurrently, VCA stabilizes the affected vertebrae by filling the tumor cavity with cement, mitigating further compression and movement-induced pain [6–9]. A systematic review by Cazzato et al. supports the analgesic potential of RFA and VCA. In their study, 5 out of 8 included studies reported highly effective pain management, with pain reduction of at least 4 points between baseline and the last timepoint available [20]. Additionally, 2 studies reported moderate results, with a 2-point pain reduction. Their findings suggest that RFA, combined with VCA in most cases, effectively and safely achieves short- to mid-term analgesia in patients with painful spinal metastases [21,22]. Furthermore, a study by Abdelgawaad et al. [19] involving 60 patients

**Table 1**
Demographics and Clinical Characteristics

| Article author and year | Study design | Patients or lesions treated with RFA + VCA | M, F | Mean age | Spine level affected | Tumor anatomic location within vertebra | Lesions with epidural extension | Radiographic characteristic of tumor | Primary histology |
|---|---|---|---|---|---|---|---|---|---|
| Anchala et al 2014 | R | 34 patients (66 Lesions) | 13,21 | 60 (35–84) | 35 Thoracic, 27 Lumbar, 8 Sacrum | Posterior Vertebral body in 21 patients | n/s | n/s | Lung (27%), Breast (16%), Sarcoma (9%) |
| Bagla et al 2016 | P | 50 Patients (66 Lesions) | 26,24 | 61 (23–83) | 30 Thoracic, 39 Lumbar | 69 Vertebral body | n/s | n/s | 11 Kidney, 10 Breast, 9 Lung, 3Lliver, 2 Bladder, 15 other |
| Cazzato et al 2018 | R | 11 Patients | 5,6 | 61 (40–77) | 2 Thoracic, 8 Lumbar, 1 Sacrum | 11 Vertberal body | n/s | 7 Lytic, 4 Mixed | 4 Lung, 2 Breast, 2 Liver, 1 Colorectal, 1 Bladder, 1 Cartilage |
| David et al 2017 | R | 26 Patients (39 Lesions) | 15,11 | 69.5 | n/s | n/s | n/s | n/s | 11 Prostate, 4 Kidney, 8 Multiple Myeloma, 3 Breast, 3 Colorectal, 3 Lung, 2 Cervical, 1 Bladder, 4 Osteoporosis |
| Hoffman et al 2008 | P | 15 Patients (18 Lesions) | 9,6 | 64 (41–86) | 6 Thoracic, 10 Lumbar, 2 Sacrum | 18 Vertebral body | n/s | n/s | 3 Kidney, 4 Multiple Myeloma, 3 Lung, 3 Breast, 2 unknown |
| Jain et al 2020 | R | 34 Patients | 19,16 | 63 | n/s | n/s | n/s | n/s | Multiple Myeloma (20%), Lung Adenocarcinoma (12.5%) |
| Levy et al 2020 | P | 100 patients (130 Lesions) | 44,56 | 64.6 (30–89) | 44 Thoracic, 33 Lumbar, 10 Thoracic + Lumbar, 4 Periacetabulum, 3 Sacrum, 2 Lumbar +Iliac crest, 1 Iliac crest, 1 Sacrum + Iliac crest, 1 Lumbar + Sacrum, 1 Thoracic + Sacrum | n/s | n/s | No osteoblastic | 25 Lung, 21 Breast, 10 Kidney, 6 Prostate, 5 Colon, 4 Liver, 3 Lymph Node, 2 Endometrium, 2 Pancreas, 2 Skin, 1 Bone, 1 Gastrointestinal System, 1 Thyroid, 1 Noncancerous, 16 others |
| Lu et al 2019 | R | 51 Patients | n/s | n/s | n/s | n/s | n/s | n/s | Renal (14%), Lung (23%), Breast (20%), Liver (22%), Gastric (7%), Colon (10%), Cervical Carcinoma (7%)_ |
| Lv et al 2020 | R | 35 Patients (47 Lesions) | 21,14 | 51.4 +/- 9.3 | 26 Thoracic, 21 Lumbar | 37 Vertebral body | n/s | Mainly osteolytic or mixed | 21 Lung, 7 Breast, 2 Prostate, 1 Kidney, 2 Liver, 1 Lymphatic, 1 Thyroid Gland |
| Madani et al 2022 | R | 18 Patients (24 Lesions) | 9,9 | 53.9 +/_ 13.5 | 14 Thoracic, 10 Lumbar | n/s | 24/24 | 17 Osteolytic, 7 Mixed | 1 Breast, 1 Melanoma, 2 Medullary Thyroid, 6 Clear Cell Renal Carcinoma, 3 Intracanalicular Breast, 1 Adrenocortical, 1 Leiomyosarcoma, 4 Pulmonary Adenocarcinoma, 1 Anal Aquamous Cell, 1 Colon, 2 Biliary Adenocarcinoma, 1 Pheochromocytoma |
| Maugeri et al 2017 | R | 18 Patients (18 Lesions) | 11,7 | 55.72 (34–69) | 7 Thoracic, 11 Lumbar | 18 Vertebral body | n/s | All osteolytic | 2 Kidney, 6 Breast, 7 Lung, 1 Melanoma, 2 Bladder |
| Mayer et al 2021 | R | 31 Patients (37 Lesions) | 11,20 | 62.4 (40–78) | 1 Cervical, 13 Thoracic, 22 Lumbar, 1 Sacral | n/s | 15/37 | 25 Lytic, 12 Mixed | 11 Breast, 9 Lung |
| Pusceddu et al 2021 | R | 35 Patients (41 Lesions) | 13,22 | n/s | 19 Thoracic, 21 Lumbar, 1 Sacral | 41 Vertebral body | n/s | No osteblastic | 16 Breast, 5 Lung, 4 Colon, 3 Prostate, 2 Kidney, 1 Melanoma, 1 Multiple Myeloma, 1 Thyroid, 1 Sarcoma, 1 Adrenal Gland |
| Ragheb et al 2022 | R | 23 Patients | 0,23 | 57.1 (33–86) | 30 Thoracic, 20 Lumbar | 50 Vertebral body | n./s | n/s | 23 Breast (18 Invasive Ductal, 2 Lobular, 1 Inflammatory, 2 unknown) |
| Reyes et al 2018 | R | 49 Patients (79 Lesions) | 15,34 | 64.3 +/- 12.6 | 33 Thoracic, 38 Lumbar, 1 Sacral | n/s | n/s | 50 Lytic, 8 Mixed lytic/sclerotic, 2 Sclerotic | 21 Breast, 18 Lung, 2 Pancreatic, 2 Renal, 2 Prostate, 1 Colon, 1 Sarcoma, 1 Melanoma, 1 Urinary Bladder |

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**Table 1** (*continued*)

| Article author and year | Study design | Patients or lesions treated with RFA + VCA | M, F | Mean age | Spine level affected | Tumor anatomic location within vertebra | Lesions with epidural extension | Radiographic characteristic of tumor | Primary histology |
|---|---|---|---|---|---|---|---|---|---|
| Sayed et al 2019 | P | 28 Patients | 19,11 | 62.9 +/- 13.45 | 13 Thoracic, 21 Lumbar | 30 Vertebral body | n/s | n/s | 7 Renal, 6 Breast, 5 Lung, 2 Liver, 2 Bladder, 2 Melanoma, 1 Adenocarcinoma, 1 Multiple Myeloma, 1 Maxillary Sinus, 1 Prostate, 1 Thyroid, 1 Colon |
| Senol et al 2022 | R | 41 Patients (41 Lesions) | 22,19 | 67 (45–87) | 26 Thoracic, 29 Lumbar | n/s | n/s | n/s | 7 Lung, 9 Prostate, 7 Plasmacytoma, 3 Multiple Myeloma, 2 Breast, 2 Kidney, 2 Endometrium, 9 other |
| Shawky Abdelgawaad et al 2021 | n/s | n/s | n/s | n/s | n/s | n/s | n/s | n/s | n/s |
| Tomasian et al 2018 | R | 27 Patients (33 Lesions) | 17,10 | (23–86) | 12 Thoracic, 20 Lumbar, 1 Sacral | 31 Vertebral body and/or pedicle, 1 Pedicle only | n/s | No osteoblastic | 10 Non Small Cell Lung Cancer, 6 Sarcoma, 4 Renal Cell Carcinoma, 3 Melanoma, 2 Multiple Myeloma, 2 Epithelioid Hemangioendothelioma, 1 Heaptocellular Carcinoma, 1 Head and Neck Squamous Cell, 1 Breast Adenocarcinoma, 1 Bladder, 1 Prostate Adenocarcinoma, 1 Germ Cell Tumor |
| Tomasian et al 2021 | R | 166 Patients (242 lesions) | 77,89 | n/s | 1 Cervical, 110 Thoracic, 137 Lumbar, 18 Sacral, | n/s | n/s | No ostebolastic | 45 Lung, 32 Genitourinary, 23 Sarcoma, 21 bBeast, 13 GI, 10 Melanoma, 6 Pancreaticobiliary, 6 Multiple Myeloma, 4 Head and Neck Squamous Cell, 3 Thyroid, 2 Malignant Peripheral Nerve Sheath, 1 Myogenic Hemangioendothelioma |
| Wallace et al 2015 | R | 72 patients (105 Lesions) | 28,44 | 68.4 +/- 18.8 | 54 Thoracic, 56 Lumbar | 89 Posterior vertebral body, 32 Erosion of posterior vertebral body cortex, 49 pedicles | n/s | No ostebolastic | 11 Breast, 17 Non Small Cell Lung Cancer, 3 Small Cell Lung Cancer, 13 Sarcoma, 9 Renal Cell Carcinoma, 4 GI Adenocarcinoma, 4 Multiple Myeloma, 4 Melanoma, 7 other |
| Wallace et al 2016 | R | 55 Lesions | n/s | n/s | 26 Thoracic, 29 Lumbar | 40 Posterior vertebral body, 17 Erosion of posterior vertebral body cortex, 26 Pedicles | n/s | No ostebolastic | 15 Sarcoma, 9 Non-Small Cell Lung Cancer, 6 Renal Cell Carcinoma, 4 Melanoma, 7 Breast Adenocarcinoma, 5 Papillary Thyroid, 2 Hepatocellular, 2 Head and Neck Squamous Cell Carcinoma, 2 Multiple Myeloma, 2 Malignant Peripheral Nerve Sheath Tumor, 1 GI Adenocarcinoma |
| Wang et al 2022 | R | 15 Patients (17 Lesions) | 9,6 | | | | | | |
| s | n/s | 8 Thoracic, 9 Lumbar | n/s | n/s | n/s | 5 Lung, 4 Liver, 2 Kidney, 4 Esophagus; | | | |
| Yildizhan et al 2021 | R | 40 Patients | n/s | n/s | n/s | n/s | n/s | n/s | 14 Multiple Myeloma |
| Zheng et al 2014 | R | 26 Patients | 12,14 | 59.31 (32-80) | 11 Thoracic, 24 Lumbar, 3 Sacrum | 38 Vertebral body | n/s | n/s | 5 Prostate, 2 Liver, 2 Lymphoma, 1 Mesenchymal Malignant Tumor, 2 Sacrum, 6 Breast, 3 Lung, 1 Thyroid, 1 Esophagus, 1 Adenocarcinoma, 2 Kidney |

RFA = Radiofrequency Ablation, VCA = Vertebral Cement Augmentation, R = Retrospective, P = Prospective

**Table 2**
Procedure-Related Variables

| Article author and year | Imaging guidance | Anesthesia protocol | Local tumor control rate | Mean imaging follow-up (months) | Pre-operative vertebral fractures (Y/N) | Multiple vertebral lesions (Y/N) | Ancillary protective measures |
|---|---|---|---|---|---|---|---|
| Anchala et al 2014 | Flouroscopy and CT | Conscious sedation | 10/13 patients | 3 | n/s | Y | Epidural/Neuroforaminal thermocouple, CO2 injection, Cooled 5% dextrose water injection |
| Bagla et al 2016 | CT | Conscious sedation (35 patients), General anesthesia (15 patients) | n/s | 3 | N | Y (16/50 patients) | Thermocouple |
| Cazzato et al 2018 | CT | General anesthesia | 4/6 patients | 3.5 (1.2-8.2) | Y (1/11 patients) | N | Thermocouple and Hydrodissection (8/11 patients), Thermocouple (2/11 patients) |
| David et al 2017 | Fluoroscopy and CT + Fluoroscopy | Conscious sedation | n/s | n/s | Y (4/39 lesions) | Y | n/s |
| Hoffman et al 2008 | CT Fluoroscopy | Conscious sedation | 10/15 patients | 7.7 (3-15) | n/s | Y (3/15 patients) | n/s |
| Jain et al 2020 | Fluoroscopy | Conscious sedation | n/s | n/s | Y (34/34 patients) | n/s | n/s |
| Levy et al 2020 | Flouroscopy and CT | General anesthesia (52 patients), Local conscious sedation (30 patients), Monitored anesthesia care (18 patients) | n/s | n/s | n/s | Y (32/100 patients) | Thermocouple |
| Lu et al 2019 | n/s | Local anesthesia | n/s | n/s | n/s | n/s | n/s |
| Lv et al 2020 | Fluoroscopy | Local anesthesia | 31/35 patients | 6 | N | Y | n/s |
| Madani et al 2022 | Flouroscopy and CT | n/s | 17/18 patients | 17.3 +/- 11.5 | Y (7/24 lesions) | Y (5/18 patients) | n/s |
| Maugeri et al 2017 | Fluoroscopy | General anesthesia | n/s | n/s | n/s | N | Thermocouple |
| Mayer et al 2021 | Cone-Beam CT and CT + Flourscopy | General anesthesia | 5/5 patients | 5 +/- 4.6 | n/s | Y | Thermocouple and Hydrodissection |
| Pusceddu et al 2021 | CT Flourscopy | Conscious sedation with local anesthesia | 35/35 patients | 12 | n/s | Y (21 patients had 1 or 2 lesions, 14 patients had >2 lesions) | Thermocouple |
| Ragheb et al 2022 | n/s | n/s | 22/23 patients | 39.3 | Y (23/23 patients) | Y (13/23 patients) | n/s |
| Reyes et al 2018 | Flouroscopy | Conscious sedation | 16/17 patients | 1 | Y (19/41 patients) | Y (21/49 patients) | Thermocouple |
| Sayed et al 2019 | n/s | n/s | n/s | n/s | n/s | Y (4/30 patients) | Thermocouple |
| Senol et al 2022 | Flouroscopy | Conscious sedation | n/s | n/s | Y (12/41 patients) | Y (7/41 patients) | n/s |
| Shawky Abdelgawaad et al 2021 | n/s | n/s | n/s | 13.2 +/- 6.3 | n/s | n/s | n/s |
| Tomasian et al 2018 | Flouroscopy | Conscious sedation | 23/23 patients | Median: 4 (IQR= 7.4) | n/s | Y | Thermocouple |
| Tomasian et al 2021 | Flouroscopy and CT | Conscious sedation (161 patients), General anesthesia (5 patients) | 180/228 lesions | Median: 6.7 (IQR = 4.7–15.5) | n/s | Y | Thermocouple, Somatosensory and motor-evoked-potential monitoring, Neuroforaminal with or without epidural injection of carbon dioxide or dextrose 5% in water for thermal insulation |
| Wallace et al 2015 | Flouroscopy and CT | Conscious sedation | n/s | n/s | n/s | Y (27/72 patients) | Thermocouple |
| Wallace et al 2016 | Fluoroscopy and CT | Conscious sedation | 21/30 patients | 6-12 | Y (34/55 lesions) | n/s | Thermocouple |
| Wang et al 2022 | C-Arm Fluoroscopy and Cone-Beam CT | Local anesthisa with Conscious sedation | n/s | 1-6 | n/s | Y | n/s |
| Yildizhan et al 2021 | C-Arm Fluoroscopy | Local anesthesia with Conscious sedation | 40/40 patients | 6 | Y (26/26 patients) | Y (20/66 patients) | n/s |
| Zheng et al 2014 | CT | General anesthesia | 26/26 patients | 6 | N | Y (13/26 patients) | Thermocoagulation |

CT = computed tomography.

## Meta-Analysis Forest Plot Showcasing the Average Decrease in Pain Score After Treatment
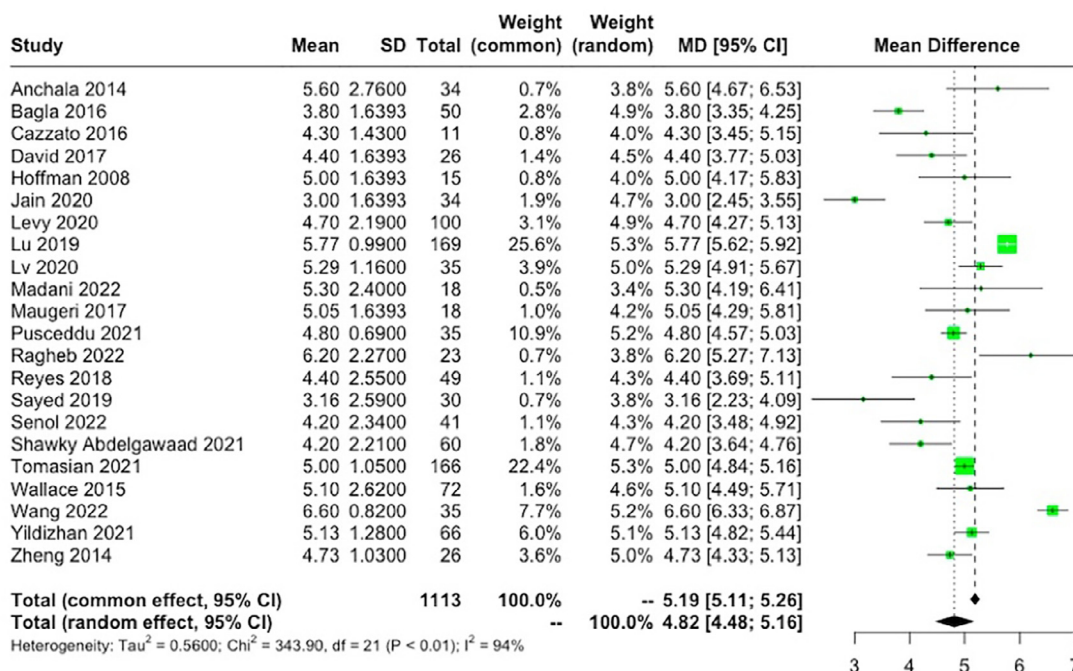
| Study | Mean | SD | Total | Weight (common) | Weight (random) | MD [95% CI] |
|---|---|---|---|---|---|---|
| Anchala 2014 | 5.60 | 2.7600 | 34 | 0.7% | 3.8% | 5.60 [4.67; 6.53] |
| Bagla 2016 | 3.80 | 1.6393 | 50 | 2.8% | 4.9% | 3.80 [3.35; 4.25] |
| Cazzato 2016 | 4.30 | 1.4300 | 11 | 0.8% | 4.0% | 4.30 [3.45; 5.15] |
| David 2017 | 4.40 | 1.6393 | 26 | 1.4% | 4.5% | 4.40 [3.77; 5.03] |
| Hoffman 2008 | 5.00 | 1.6393 | 15 | 0.8% | 4.0% | 5.00 [4.17; 5.83] |
| Jain 2020 | 3.00 | 1.6393 | 34 | 1.9% | 4.7% | 3.00 [2.45; 3.55] |
| Levy 2020 | 4.70 | 2.1900 | 100 | 3.1% | 4.9% | 4.70 [4.27; 5.13] |
| Lu 2019 | 5.77 | 0.9900 | 169 | 25.6% | 5.3% | 5.77 [5.62; 5.92] |
| Lv 2020 | 5.29 | 1.1600 | 35 | 3.9% | 5.0% | 5.29 [4.91; 5.67] |
| Madani 2022 | 5.30 | 2.4000 | 18 | 0.5% | 3.4% | 5.30 [4.19; 6.41] |
| Maugeri 2017 | 5.05 | 1.6393 | 18 | 1.0% | 4.2% | 5.05 [4.29; 5.81] |
| Pusceddu 2021 | 4.80 | 0.6900 | 35 | 10.9% | 5.2% | 4.80 [4.57; 5.03] |
| Ragheb 2022 | 6.20 | 2.2700 | 23 | 0.7% | 3.8% | 6.20 [5.27; 7.13] |
| Reyes 2018 | 4.40 | 2.5500 | 49 | 1.1% | 4.3% | 4.40 [3.69; 5.11] |
| Sayed 2019 | 3.16 | 2.5900 | 30 | 0.7% | 3.8% | 3.16 [2.23; 4.09] |
| Senol 2022 | 4.20 | 2.3400 | 41 | 1.1% | 4.3% | 4.20 [3.48; 4.92] |
| Shawky Abdelgawaad 2021 | 4.20 | 2.2100 | 60 | 1.8% | 4.7% | 4.20 [3.64; 4.76] |
| Tomasian 2021 | 5.00 | 1.0500 | 166 | 22.4% | 5.3% | 5.00 [4.84; 5.16] |
| Wallace 2015 | 5.10 | 2.6200 | 72 | 1.6% | 4.6% | 5.10 [4.49; 5.71] |
| Wang 2022 | 6.60 | 0.8200 | 35 | 7.7% | 5.2% | 6.60 [6.33; 6.87] |
| Yildizhan 2021 | 5.13 | 1.2800 | 66 | 6.0% | 5.1% | 5.13 [4.82; 5.44] |
| Zheng 2014 | 4.73 | 1.0300 | 26 | 3.6% | 5.0% | 4.73 [4.33; 5.13] |
| Total (common effect, 95% CI) | | | 1113 | 100.0% | -- | 5.19 [5.11; 5.26] |
| Total (random effect, 95% CI) | | | | -- | 100.0% | 4.82 [4.48; 5.16] |

Heterogeneity: Tau$^2$ = 0.5600; Chi$^2$ = 343.90, df = 21 (P < 0.01); I$^2$ = 94%

**Fig. 1.** Pain: meta-analysis forest plot of the mean difference of pre-op and follow-up pain scores.

**Table 3**
Pain Relief

| Article author and year | Pain Scale used | Preop mean pain score (1–10) | Final follow up mean pain score (1–10) | Follow up (months) |
|---|---|---|---|---|
| Anchala et al 2014 | VAS | 7.35 +/- 2.9 | 1.75 +/- 2.6 | 6 |
| Bagla et al 2016 | NPRS | 5.9 | 2.1 | 3 |
| Cazzato et al 2018 | VAS | 7.8 (6.6-8.9) | 3.5 (1.5-5.5) | 2 |
| David et al 2017 | n/s | 8.4 | 4 | 3 |
| Hoffman et al 2008 | VAS | 8.5 | 3.5 | 0.5 |
| Jain et al 2020 | VAS | 6.5 | 3.5 | 6 |
| Levy et al 2020 | BPI | 8.2 (6.5-9.9) | 3.5 (0.3-6.7) | 6 |
| Lu et al 2019 | VAS | 8.16 (7.10-9.22) | 2.39 (1.5-3.28) | 6 |
| Lv et al 2020 | VAS | 7.52 (6.08-8.96) | 2.23 (1.77-2.69) | 6 |
| Madani et al 2022 | VAS | 7.3 +/- 2.4 (4.9-9.7) | 2 +/- 0 (0-2) | 1 |
| Maugeri et al 2017 | VAS | 8.05 | 3 | 6 |
| Mayer et al 2021 | VAS | n/s | n/s | n/s |
| Pusceddu et al 2021 | VAS | 5.7 (4.9-6.5) | 0.9 (0.4-1.3) | 12 |
| Ragheb et al 2022 | VAS | 6.9 (4.3-9.5) | 0.7 (-0.7-1.7) | 6 |
| Reyes et al 2018 | VAS | 7.9 (5.4-10.4) | 3.5 (0.9-6.1) | 1 |
| Sayed et al 2019 | NRS | 5.77 (2.96-8.58) | 2.61 (0.33-4.89) | 3 |
| Senol et al 2022 | VAS | 7.4 | 3.2 | 6 |
| Shawky Abdelgawaad et al 2021 | n/s | n/s | n/s | n/s |
| Tomasian et al 2018 | VAS | n/s | n/s | 1 |
| Tomasian et al 2021 | BPI | Median: 8.0 (7.0-9.0) | Median: 3 (2-4) | 6 |
| Wallace et al 2015 | NRS | 8.0 +/- 1.9 | 2.9 +/- 3.0 | 1 |
| Wallace et al 2016 | n/s | n/s | n/s | n/s |
| Wang et al 2022 | VAS | 8.46 (7.61-9.31) | 1.86 (1.08-2.64) | 6 |
| Yildizhan et al 2021 | VAS | 7.44 (6.38-8.50) | 2.31 (0.89-3.73) | 6 |
| Zheng et al 2014 | VAS | 7.69 (6.57-8.81) | 2.96 (2.04-3.88) | 6 |

VAS = visual analog scale, NPRS = numeric pain rating scale, NRS = numerical rating scale, BPI = brief pain inventory.

with spinal metastases underwent combined RFA and balloon kyphoplasty as a palliative treatment for painful spinal osteolytic metastasis. In their study, the mean pre-procedure and post-procedure VAS scores for back pain were significantly reduced, emphasizing its role as an effective analgesic option in the palliative population. This study underscores the idea that RFA and VCA are oftentimes reserved for palliative patients with widely metastatic disease or complex comorbidities precluding surgical operations. Thus, to further elucidate the analgesic effects of RFA and VCA in managing spinal metastases and its potential

as a first-line treatment option, longitudinal studies with larger patient samples and standardized follow-up intervals should be conducted.

Local tumor control was also evaluated, revealing a low pooled LTP rate of 5% at long-term follow-up, with the majority of lesions successfully managed through intralesional resection and/or repeat RFA. It should be noted that although one would expect tumor progression rate to increase as follow-up length increases, our meta-analysis showed a drop-off in tumor progression rate from 22% in the mid-term follow-up to 5% in the long-term follow-up. This could be explained by a multi-
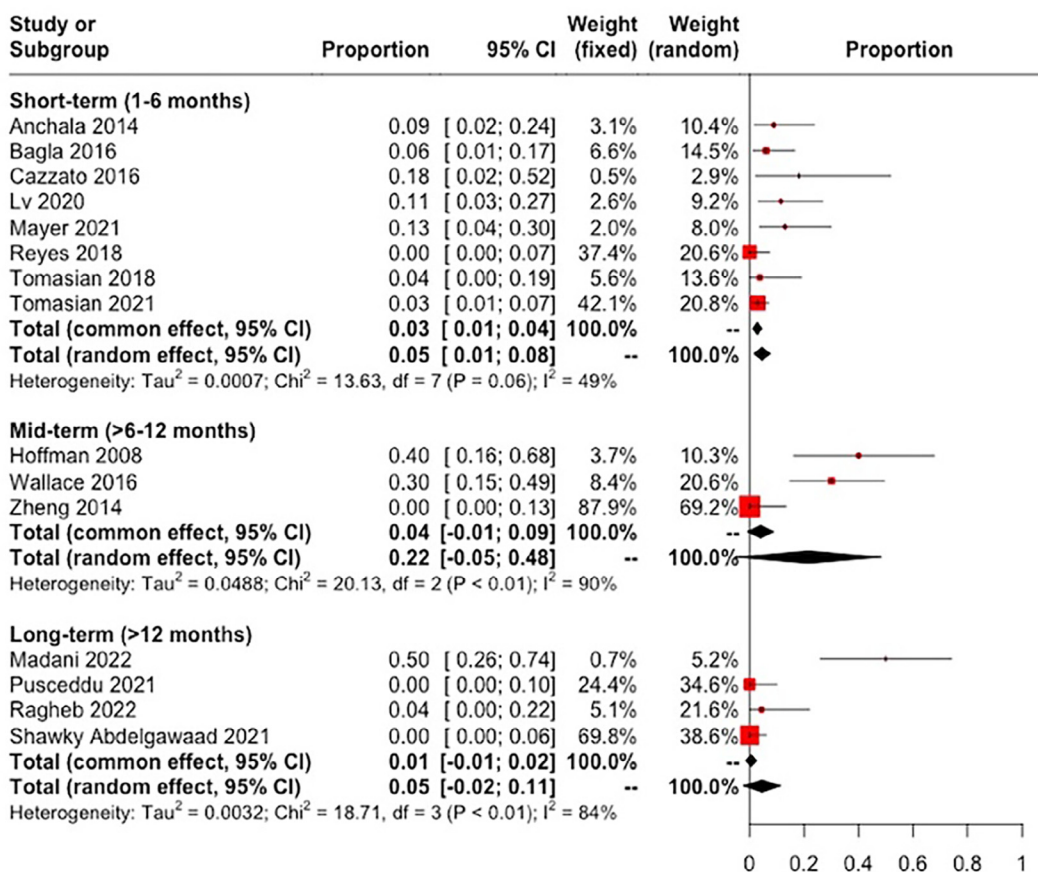
## Meta-Analysis Forest Plot of Tumor Progression Rate

| Study or Subgroup | Proportion | 95% CI | Weight (fixed) | Weight (random) | Proportion |
|---|---|---|---|---|---|
| **Short-term (1-6 months)** | | | | | |
| Anchala 2014 | 0.09 | [0.02; 0.24] | 3.1% | 10.4% | |
| Bagla 2016 | 0.06 | [0.01; 0.17] | 6.6% | 14.5% | |
| Cazzato 2016 | 0.18 | [0.02; 0.52] | 0.5% | 2.9% | |
| Lv 2020 | 0.11 | [0.03; 0.27] | 2.6% | 9.2% | |
| Mayer 2021 | 0.13 | [0.04; 0.30] | 2.0% | 8.0% | |
| Reyes 2018 | 0.00 | [0.00; 0.07] | 37.4% | 20.6% | |
| Tomasian 2018 | 0.04 | [0.00; 0.19] | 5.6% | 13.6% | |
| Tomasian 2021 | 0.03 | [0.01; 0.07] | 42.1% | 20.8% | |
| Total (common effect, 95% CI) | 0.03 | [0.01; 0.04] | 100.0% | -- | |
| Total (random effect, 95% CI) | 0.05 | [0.01; 0.08] | -- | 100.0% | |
| Heterogeneity: Tau$^2$ = 0.0007; Chi$^2$ = 13.63, df = 7 (P = 0.06); I$^2$ = 49% | | | | | |
| **Mid-term (>6-12 months)** | | | | | |
| Hoffman 2008 | 0.40 | [0.16; 0.68] | 3.7% | 10.3% | |
| Wallace 2016 | 0.30 | [0.15; 0.49] | 8.4% | 20.6% | |
| Zheng 2014 | 0.00 | [0.00; 0.13] | 87.9% | 69.2% | |
| Total (common effect, 95% CI) | 0.04 | [-0.01; 0.09] | 100.0% | -- | |
| Total (random effect, 95% CI) | 0.22 | [-0.05; 0.48] | -- | 100.0% | |
| Heterogeneity: Tau$^2$ = 0.0488; Chi$^2$ = 20.13, df = 2 (P < 0.01); I$^2$ = 90% | | | | | |
| **Long-term (>12 months)** | | | | | |
| Madani 2022 | 0.50 | [0.26; 0.74] | 0.7% | 5.2% | |
| Pusceddu 2021 | 0.00 | [0.00; 0.10] | 24.4% | 34.6% | |
| Ragheb 2022 | 0.04 | [0.00; 0.22] | 5.1% | 21.6% | |
| Shawky Abdelgawaad 2021 | 0.00 | [0.00; 0.06] | 69.8% | 38.6% | |
| Total (common effect, 95% CI) | 0.01 | [-0.01; 0.02] | 100.0% | -- | |
| Total (random effect, 95% CI) | 0.05 | [-0.02; 0.11] | -- | 100.0% | |
| Heterogeneity: Tau$^2$ = 0.0032; Chi$^2$ = 18.71, df = 3 (P < 0.01); I$^2$ = 84% | | | | | |

Scale: 0   0.2   0.4   0.6   0.8   1

**Fig. 2.** Tumor control: meta-analysis forest plot of tumor progression rates at short-term (1–6 months), mid-term (6–12 months), and long-term (>12 months) follow-up.

**Table 4**

Complications

| Article author and year | Postop complications (CTCAE Classification) |
|---|---|
| Anchala et al 2014 | None |
| Bagla et al 2016 | None |
| Cazzato et al 2018 | Grade I - bone cement in paravertebral tissues safely removed (1 patient) Grade V - sepsis resulting in death (1 patient) |
| David et al 2017 | Grade 1 - asymptomatic cement leaks (amount unspecified) |
| Hoffman et al 2008 | Grade I- asymptomatic cement leaks (8 patients), asymptomatic hematoma at needle insertion (2 patients) |
| Jain et al 2020 | n/s |
| Levy et al 2020 | Grade III - pneumonia (1 patient), respiratory failure requiring hospitalization (1 patient) (Two unspecified adverse events) |
| Lu et al 2019 | Grade I - bone cement extravasation (8 patients) |
| Lv et al 2020 | Grade I - bone cement leakage (3 patients) |
| Madani et al 2022 | Grade I - cement leakages in epidural space (2 patients) |
| Maugeri et al 2017 | Grade I - minimal cement leakages (2 patients) |
| Mayer et al 2021 | Grade V - lethal sepsis (1 patient) |
| Pusceddu et al 2021 | Grade I - asymptomatic cement leakage (3 patients) |
| Ragheb et al 2022 | Grade I - minor cement extravasation (3 patients) |
| Reyes et al 2018 | None |
| Sayed et al 2019 | None |
| Senol et al 2022 | Grade I - transient neurological motor deficits without cement leakage (2 patients) Grade II - pulmonary embolism with transient mild symptoms (1 patient) |
| Shawky Abdelgawaad et al 2021 | Grade I - asymptomatic cement leakage (4 patients) |
| Tomasian et al 2018 | None |
| Tomasian et al 2021 | Grade I - asymptomatic spinal cord edema (2 patients) Grade II - delayed secondary vertebral body fracture (1 patient) Grade II - periprocedural transient radicular pain in the adjacent nerve distribution (4 patients) Grade III - spinal cord thermal injury resulting in bilateral lower extremity weakness, difficulty in urination, and inability to have an erection 3 d after procedure (1 patient) |
| Wallace et al 2015 | None |
| Wallace et al 2016 | None |
| Wang et al 2022 | None |
| Yildizhan et al 2021 | Grade I - bone cement leakage (4 patients) |
| Zheng et al 2014 | None |

CTCAE = Common Terminology Criteria for Adverse Events
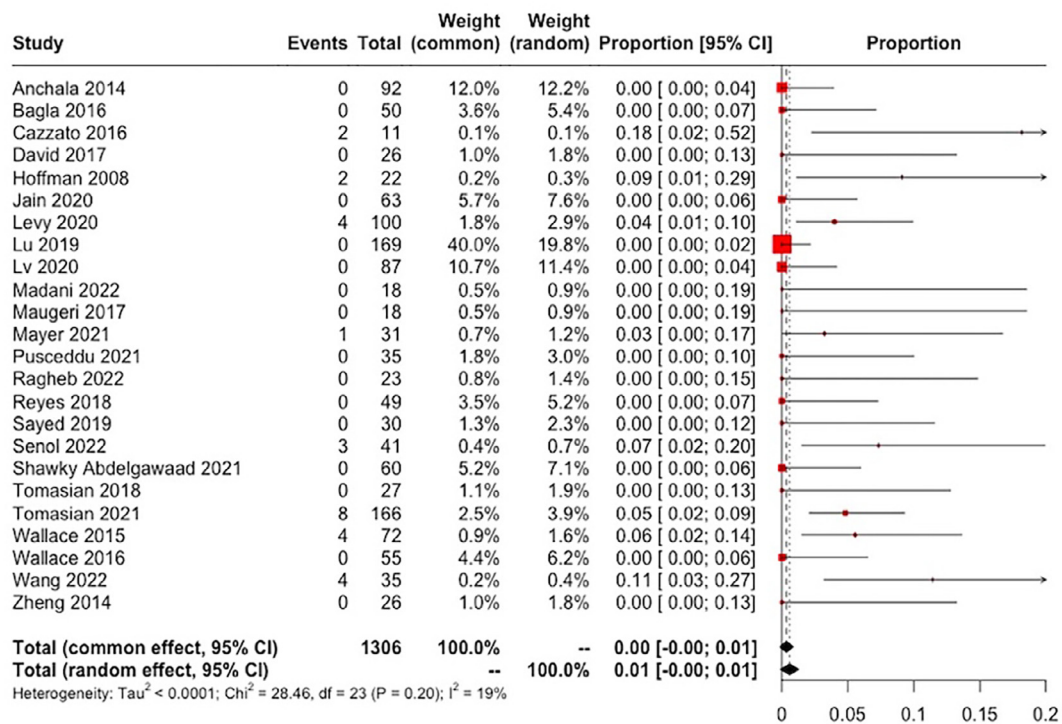
## Meta-Analysis Forest Plot of Complication Rate

| Study | Events | Total | Weight (common) | Weight (random) | Proportion [95% CI] | Proportion |
|---|---|---|---|---|---|---|
| Anchala 2014 | 0 | 92 | 12.0% | 12.2% | 0.00 [0.00; 0.04] | |
| Bagla 2016 | 0 | 50 | 3.6% | 5.4% | 0.00 [0.00; 0.07] | |
| Cazzato 2016 | 2 | 11 | 0.1% | 0.1% | 0.18 [0.02; 0.52] | |
| David 2017 | 0 | 26 | 1.0% | 1.8% | 0.00 [0.00; 0.13] | |
| Hoffman 2008 | 2 | 22 | 0.2% | 0.3% | 0.09 [0.01; 0.29] | |
| Jain 2020 | 0 | 63 | 5.7% | 7.6% | 0.00 [0.00; 0.06] | |
| Levy 2020 | 4 | 100 | 1.8% | 2.9% | 0.04 [0.01; 0.10] | |
| Lu 2019 | 0 | 169 | 40.0% | 19.8% | 0.00 [0.00; 0.02] | |
| Lv 2020 | 0 | 87 | 10.7% | 11.4% | 0.00 [0.00; 0.04] | |
| Madani 2022 | 0 | 18 | 0.5% | 0.9% | 0.00 [0.00; 0.19] | |
| Maugeri 2017 | 0 | 18 | 0.5% | 0.9% | 0.00 [0.00; 0.19] | |
| Mayer 2021 | 1 | 31 | 0.7% | 1.2% | 0.03 [0.00; 0.17] | |
| Pusceddu 2021 | 0 | 35 | 1.8% | 3.0% | 0.00 [0.00; 0.10] | |
| Ragheb 2022 | 0 | 23 | 0.8% | 1.4% | 0.00 [0.00; 0.15] | |
| Reyes 2018 | 0 | 49 | 3.5% | 5.2% | 0.00 [0.00; 0.07] | |
| Sayed 2019 | 0 | 30 | 1.3% | 2.3% | 0.00 [0.00; 0.12] | |
| Senol 2022 | 3 | 41 | 0.4% | 0.7% | 0.07 [0.02; 0.20] | |
| Shawky Abdelgawaad 2021 | 0 | 60 | 5.2% | 7.1% | 0.00 [0.00; 0.06] | |
| Tomasian 2018 | 0 | 27 | 1.1% | 1.9% | 0.00 [0.00; 0.13] | |
| Tomasian 2021 | 8 | 166 | 2.5% | 3.9% | 0.05 [0.02; 0.09] | |
| Wallace 2015 | 4 | 72 | 0.9% | 1.6% | 0.06 [0.02; 0.14] | |
| Wallace 2016 | 0 | 55 | 4.4% | 6.2% | 0.00 [0.00; 0.06] | |
| Wang 2022 | 4 | 35 | 0.2% | 0.4% | 0.11 [0.03; 0.27] | |
| Zheng 2014 | 0 | 26 | 1.0% | 1.8% | 0.00 [0.00; 0.13] | |
| **Total (common effect, 95% CI)** | | 1306 | 100.0% | -- | 0.00 [-0.00; 0.01] | |
| **Total (random effect, 95% CI)** | | | -- | 100.0% | 0.01 [-0.00; 0.01] | |

Heterogeneity: Tau$^2$ < 0.0001; Chi$^2$ = 28.46, df = 23 (P = 0.20); I$^2$ = 19%

**Fig. 3.** Complications: meta-analysis forest plot of postop complication rates.

**Table 5**
Other Information

| Article author and year | VCA access same as RFA (Y/N) | Adjuvant chemotherapy (Y/N) | Adjuvant radiation therapy (Y/N) | Clinical symptom improvement (Y/N) | Vertebral stability achieved (Y/N) |
|---|---|---|---|---|---|
| Anchala et al 2014 | Y | Y (24/34 patients) | Y (17/34 patients) | Y (54% of patients decreased pain meds) | n/s |
| Bagla et al 2016 | Y | N | Y (18/50 patients) | Y | n/s |
| Cazzato et al 2018 | Y | N | Y (3/11 patients) | Y | n/s |
| David et al 2017 | Y | n/s | n/s | Y | n/s |
| Hoffman et al 2008 | Y | Y (15/15 patients) | n/s | Y (68% of patients decreased pain meds) | n/s |
| Jain et al 2020 | Y | Y (29/34 patients) | Y (15/34 patients) | Y | n/s |
| Levy et al 2020 | Y | Y (33/100 patients) | Y (5/100 patients) | Y | n/s |
| Lu et al 2019 | Y | N | N | Y | n/s |
| Lv et al 2020 | Y | n/s | n/s | Y | Y |
| Madani et al 2022 | Y | n/s | Y (24/24 lesions) | Y | n/s |
| Maugeri et al 2017 | Y | n/s | n/s | Y | n/s |
| Mayer et al 2021 | Y | n/s | Y (13/37 lesions) | Y (16/20 patients) | n/s |
| Pusceddu et al 2021 | Y | n/s | Y (15/35 patients) | Y | n/s |
| Ragheb et al 2022 | n/s | n/s | Y | Y | n/s |
| Reyes et al 2018 | Y | Y (14/49 patients) | Y (16/49 patients) | Y | n/s |
| Sayed et al 2019 | Y | n/s | n/s | Y | n/s |
| Senol et al 2022 | N | n/s | n/s | Y | n/s |
| Shawky Abdelgawaad et al 2021 | n/s | n/s | n/s | n/s | n/s |
| Tomasian et al 2018 | Y | n/s | Y (7/27 patients, 8/33 lesions) | n/s | n/s |
| Tomasian et al 2021 | Y | n/s | Y (69/166 patients, 108/242 lesions) | Y | n/s |
| Wallace et al 2015 | Y | n/s | Y (22/72 lesions) | Y | n/s |
| Wallace et al 2016 | Y | n/s | N | n/s | Y (after 3 mo: 41 lesions; after 6 mo: 26 lesions; after 1 y: 21 lesions) |
| Wang et al 2022 | Y | Y (9/15 patients) | N | Y | n/s |
| Yildizhan et al 2021 | Y | n/s | n/s | Y | n/s |
| Zheng et al 2014 | Y | n/s | n/s | Y | Y |

RFA = radiofrequency ablation, VCA = vertberal cement augmentation.

tude of reasons. Firstly, the study population is not consistent across all follow-up intervals. As shown by Fig. 2, each study article was sorted into either short-term, mid-term, or long-term follow-ups based on the average follow-up length reported in each study making each follow-up interval's population unique from one another. Additionally, it is important to consider the heterogeneity identified in the mid-term follow-up interval ($I^2$=90%) and long-term follow-up interval ($I^2$=84%), which may be attributed to variations in the included studies, such as differences in patient populations, tumor characteristics, or treatment protocols. Lastly, some individual studies do demonstrate the expected long-term tumor progression rate. For example, the retrospective study by Wallace et al. [24], which investigated radiographic local control of spinal metastases treated with a combination of radiofrequency ablation and vertebral augmentation, reported radiographic local tumor control rates of 89% at 3 months, 74% at 6 months, and 70% at 1-year post-treatment. Despite this heterogeneity, the consistently low tumor progression rates reported in the literature support the notion that combining RFA and VCA is a promising treatment strategy for patients with spine metastases. Notably, most spinal lesions in this analysis were located within the vertebral body rather than the posterior elements, with only a few tumors exhibiting epidural spread. Whenever there is postero-lateral involvement of the spinal elements, it renders the spine unstable and necessitates fixation [43]. However, many of the studies indicated that involvement of the posterior elements resulting in an unstable spine or spinal cord compression fell under their exclusion criteria. As a result, the local control rates for patients with posterior element lesions with or without epidural tumor spread remain uncertain, underscoring the need for further research to evaluate the effectiveness of these treatments in managing tumors with epidural spread and spinal cord compression.

With regard to complications, patients generally tolerated RFA and VCA well, with meta-analyzed studies demonstrating a pooled incidence of total complications at 1%. In comparison, complications following RFA of spinal metastases have been reported in up to 16% of the cases in the current literature [20]. In Nakatsuka et al. [21], 10% of patients reported transient neural damage secondary to the high temperature raise during RFA. In another study by Yang et al. [23], 16% of patients reported side effects related to the procedure that included transient contralateral lower limb pain and numbness. The lower rate of pooled complications in our analysis could be attributed to the majority of tumors treated exclusively in the vertebral body leading to lower neurovascular compromise. Additionally, thermal protective measures were implemented in conjunction with RFA in the some of the studies in our review. These measures included thermal insulation with cooled dextrose 5% or $CO_2$ and somatosensory and motor-evoked potential monitoring. These ancillary protective procedures are particularly important in lesions with close proximity to the spinal canal. Future studies can be conducted to further analyze the vertebral fracture rates of RFA procedures on the spine with and without VCA [6].

This study encounters several significant limitations, primarily attributable to the substantial heterogeneity in study design and data collection among the included studies, coupled with the predominantly short-term follow-ups reported. Consequently, conducting a sub-group analysis based on tumor location and the number of metastases proved challenging. The majority of the studies were nonrandomized, retrospective in nature, and reported outcomes such as pain relief, complication rates, and tumor control in aggregate forms, rather than distinguishing these outcomes by tumor location or the number of metastases. Furthermore, detailed individual patient data, essential for a more detailed and nuanced analysis, was often unavailable. The absence of detailed individual patient data underscores the critical need for standardized reporting of follow-up data. Standardization would enable meaningful comparisons between different treatment modalities in the literature, facilitating a deeper understanding of treatment outcomes. Additionally, many patients who underwent RFA and VCA presented with advanced systemic diseases and comorbidities, factors that could potentially confound the outcomes of these treatments. The scarcity of detailed assess-

ment data, the limited durations of follow-up, and the heterogeneity of the studies at each follow-up interval render definitive conclusions about tumor progression rates and local tumor control challenging. Accordingly, there is a pressing need for multi-center randomized controlled trials that compare open surgery, radiation therapy, and other ablative and stabilizing techniques against RFA and VCA. Such trials would elucidate the relative efficacy of RFA and VCA in reducing tumor burden and providing effective pain relief, thereby guiding the development of standardized treatment approaches.

## Conclusions

In conclusion, this systematic review and meta-analysis demonstrates the potential clinical efficacy and safety of the combined use of RFA and VCA as a minimally invasive treatment for spinal metastatic tumors. The significant improvement in pain scores, low local tumor progression rates, and relatively low incidence of complications observed in the present analysis suggest that the combination of RFA and VCA may be a promising therapeutic option for managing spine metastases. However, further high-quality prospective studies are needed to confirm these findings, determine the optimal treatment protocol for the integration of RFA and VCA in the management of spinal metastases, and compare the effectiveness of this approach with other treatment modalities. Ultimately, these efforts will contribute to the development of more effective, safe, and personalized treatment strategies for patients with spinal metastases, improving their quality of life and overall outcomes.

## Funding

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2024.100317.

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