Position Statement on Percutaneous Vertebral Augmentation: A Consensus Statement Developed by the Society of Interventional Radiology (SIR), American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS), American College of Radiology (ACR), American Society of Neuroradiology (ASNR), American Society of Spine Radiology (ASSR), Canadian Interventional Radiology Association (CIRA), and the Society of NeuroInterventional Surgery (SNIS)

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ABBREVIATIONS

ADR = adverse drug reaction, DVT = deep vein thrombosis, FREE = Fracture Reduction Evaluation trial, INVEST = Investigational Vertebroplasty Safety and Efficacy Trial, NRS = numeric rating scale, PVA = percutaneous vertebroplasty, RDO = Roland-Morris disability questionnaire, SF-36 = Short Form-36, VAS = visual analog scale, VCF = vertebral compression fracture

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It is the position of the Societies that percutaneous vertebral augmentation (PVA) with the use of vertebroplasty or kyphoplasty is a safe, efficacious, and durable procedure in appropriate patients with symptomatic osteoporotic and neoplastic fractures, when performed in a manner in accordance with published standards (1–4). These procedures are offered only when nonoperative medical therapy has not provided adequate pain relief or pain is significantly altering the patient’s quality of life. Regarding vertebroplasty, multiple case series (5–24) and retrospective (25–27) and prospective nonrandomized studies (28–40) and, more recently, randomized controlled trials (41–46) have shown statistically significant improvement in pain and function, particularly ambulation.

Kyphoplasty was subsequently introduced as an alternative approach for vertebral augmentation (47). It is quite similar to vertebroplasty, and has been referred to as “balloon-assisted vertebroplasty.” Kyphoplasty entails the inflation of a percutaneously delivered balloon in the vertebral body, followed by the injection of bone cement into the cavity created by the balloon. The balloon was originally intended to restore the vertebral body height in addition to creating the cavity (47).

Similar to the literature on vertebroplasty, most data about kyphoplasty represent nonrandomized case series (38). Features that might affect the choice of procedure include the degree of compression deformation (PVA) with the use of vertebroplasty or kyphoplasty is a safe, rapid return to ambulation. In addition to reducing the need for costly skilled care, drugs, or orthopedic devices, a return to ambulation is known to reduce adverse outcomes in elderly patients confined to bedrest (97).

RATIONALE

Vertebral Augmentation versus Nonoperative Medical Treatment

Nonoperative medical treatment of VCFs has often been described as “conservative” or “traditional” management. As we have stated previously, although “conservative” implies “safe,” such therapy is neither benign nor risk-free, and its complications are well documented (98–100). Nonoperative medical treatment of painful VCFs usually consists of bedrest, bracing, and narcotic analgesia. In a prospective study of 498 hospitalized patients age 70 years or older (97), low mobility (defined as bedrest or ability to transfer to chair) or intermediate mobility (defined as ambulation one to two times with total assistance) were independent predictors of the following poor hospital outcomes at discharge: (i) decline in activities of daily living, (ii) new institutionalization, and (iii) death compared with high mobility (defined as ambulation two or more times with partial or no assistance). The contribution of low mobility to these outcomes remained statistically significant in multivariate analyses even after controlling for multiple variables including age, sex, severity of illness, and comorbidities. In summary, prolonged nonoperative medical treatment leads to adverse outcomes associated with low mobility and bedrest, which may be viewed as iatrogenic events leading to complications such as functional decline.

As previously mentioned, nonoperative medical treatment often includes immobilization with bedrest. During bedrest, virtually every organ system is adversely affected, and these effects tend to be more pronounced in older patients who have less reserve than younger patients. Bone density declines approximately 2% per week, a serious concern in patients who already have osteoporosis, and these patients are unlikely to ever regain the lost bone mass (101). Bone loss tends to occur in stages, with the most dramatic changes occurring in the first 12 weeks of immobilization.

Muscle strength declines 1%–3% per day or 10%–15% per week (98). Nearly half of normal strength is lost within 3–5 weeks of immobilization, and the rate of recovery from disuse weakness is slower than the rate of loss. Complete rest results in decreased endurance, which leads to a sense of fatigue and reduced patient motivation, setting up a
vicious circle of greater inactivity. Ligament complexes are also affected by immobilization, leading to contractures, which are more prone to occur in frail, elderly individuals. Muscles that cross two joints, such as the back muscles, are particularly at risk of shortening during immobilization. There is abundant evidence that shows early active mobilization after initial stabilization—a benefit of vertebral augmentation—is the key to contracture prevention.

Early mobilization also leads to the prevention of pressure sores, the prevalence of which tends to increase significantly with age (99). Patients older than 70 years have more than 70% of all pressure sores and usually acquire them within 2 weeks of admission to the hospital. When decubitus ulcers have occurred, nursing costs may increase by as much as 50%, with the total cost of treatment per ulcer estimated between $15,000 and $20,000. Complications often develop with pressure sores. Infection is the most common complication and may lead to septicemia, osteomyelitis, anemia, and protein loss through chronic discharge.

Cardiovascular effects include increased heart rate, shorter diastolic times, and reduced coronary blood flow. Cardiac output, stroke volume, and left ventricular function decline overall. In elderly patients, orthostatic hypotension occurs within the first 3 weeks of bedrest. This, along with the elevated heart rate, leads to diminished diastolic ventricular filling and a decline in cerebral perfusion. Depending on the duration of bedrest, it may take 20–72 days to restore prebedrest cardiac function (98).

In patients at bedrest, the incidence of deep vein thrombosis (DVT) is 61%, with proximal DVT occurring in 29%. Pulmonary embolism is seen in 2%–12% of patients and is fatal in 0.5%–10% (101). The importance of DVT and pulmonary embolism should not be minimized; symptomatic or fatal pulmonary embolus in patients at prolonged bedrest is more frequent than serious reported complications from PVA.

Pain and decreased mobility associated with VCFs produce a restrictive impairment, an overall decrease in muscle strength, deconditioning of respiratory muscles, and failure to fully expand the chest wall that results in a 25%–50% decrease in respiratory capacity (99). The lungs also suffer from decreased ciliary clearance, less effective coughing, atelectasis, and a predilection for pneumonia. Dong et al (102) and Tangawa et al (103) reported that vertebral augmentation improved pulmonary function in patients with VCF. Gastrointestinal effects include reduced appetite, constipation, and fecal impaction, all exacerbated by the concomitant use of narcotic agents. Glucose intolerance is a frequent but often overlooked complication of bedrest and can mimic brittle diabetes (99). Patients are at increased risk of genitourinary calculus formation, incontinence, urinary tract infections, and urosepsis. Even the central nervous system is not immune; patients at bedrest exhibit higher levels of anxiety, depression, insomnia, pain intolerance, sensory deprivation, and balance problems.

Narcotic analgesia is commonly used in conjunction with bedrest in the treatment of acute and chronic nonmalignant musculoskeletal pain (100,104). Adverse drug reactions (ADRs) have been seen in more than 70% of individuals treated with opioid drugs (100), and, although the majority of side effects are minor, elderly subjects are more likely to experience severe ADRs such as confusion. In one study (100), severe ADRs occurred in more than 10% of patients. A multivariate analysis of the findings showed that the only factor associated with severe ADRs was advancing age. Finally, the high societal cost of the theft and abuse associated with narcotic analgesic prescriptions cannot be ignored (105–109).

The aforementioned effects of prolonged inactivity are well known to have been the cause of the very high mortality rate following femoral neck fractures in the elderly population before the advent of surgical fixation and rapid mobilization. Although femoral fracture healing would occur in most cases without fixation, no rational argument can be made that nonoperative care would be preferable. The standard and accepted medical treatment for virtually all fractures remains reduction and fixation by external or internal means whenever feasible.

PVA has consistently shown immediate and considerable improvement in pain and patient mobility following treatment (3–42,43–58,65–67). It is, of course, well documented that the natural history of most healing compression fractures comprises gradual improvement in pain over a period of 2–12 weeks with variable return of function (110,111). What is not described as “natural history” is sudden improvement in pain and return in function—the hallmark picture of a positive therapeutic response following PVA. Most of the patients enrolled in the initial PVA studies did not undergo treatment until all noninvasive therapies had been exhausted. These patients acted as their own internal controls, as PVA was performed at a point in their clinical course at which, if improvement associated with healing were to occur, it should already have happened. It is therefore unlikely that the rapid, marked improvement in clinical findings following PVA was associated with the natural course of the disease.

More than 1,000 papers concerning vertebral augmentation have been published in the past 20 years. Among these papers, approximately 150 studies address the clinical outcomes of patients treated with PVA. Almost without exception, these reports describe PVA as a successful therapy for the relief of the pain associated with VCFs caused by osteoporosis or tumor involvement.

Clinical Evidence

Data from multiple case series, nonrandomized studies, and small pilot randomized studies were previously summarized (112). All these reports favored PVA versus medical therapy. Many additional such series have been reported in the interim, again, all of which support PVA (20–24,27,33,35–40,65,113). However, now that multiple randomized controlled studies have been reported, we will not again summarize the findings from the other interval studies, as they are of much lesser importance.

Results from six prospective randomized controlled trials of PVA versus nonoperative medical or sham therapy for osteoporotic VCFs have been reported (41–46,67). These trials included a total of 842 patients. The inclusion criteria, primary outcome measures, and results of each trial are briefly summarized as follows.

The simultaneous publication of the two trials that reported no statistically significant advantage for PVA vs. sham therapy (43,44) was followed by months of controversial editorials and discussion about these unexpected results (114–130). Before the time when these two trials were published, only the results of the much larger Fracture Reduction Evaluation (FREE) study (67) had been reported, with relatively little note made at that time of yet another study supporting that PVA was beneficial. More recently, results of the large vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (VERTOS II) trial (45), positive for PVA, and of the smaller trials by Rousing et al (41,42) and Farrohki et al (46), also positive for PVA, have been published. Patient selection and the optimal timing of PVA remain controversial topics. We encourage readers to review each of these trials in detail for himself or herself, with regard to the implications of treatment for their own patients. Data from these trials are summarized in Table 1 (41–46,67).

Trial Summaries

The FREE trial (67) enrolled 300 patients over a 34-month period. A total of 1,279 patients were assessed; 614 of these met eligibility criteria, among whom 300 (49%) were enrolled. Inclusion criteria included one or three VCF(s), at least one of which had edema demonstrated by MR imaging and more than 15% height loss, and fracture age of less than 3 months. Although patients with multiple myeloma or metastases were included, only two such patients were enrolled in each treatment arm, so this was effectively a study of osteoporotic VCFs. Kyphoplasty procedures were performed in 149 patients; the remaining 151 patients were treated with medical therapy. Follow-up evaluation included clinical and radiographic evaluations as long as 1 year after treatment. The primary outcome measure was the change in the Short Form–36 (SF-36) physical component score from baseline to 1 month. The primary
outcome measure was significantly greater for those patients treated with vertebral augmentation \((P < .001)\). Secondary outcome measures of back pain and disability showed consistently superior and statistically significant results for the vertebral augmentation group as long as 1 year after treatment, with the exception of opiate agent use at 12 months, which was not significantly different between the two groups. This was an industry-sponsored study.

INVEST \((43)\) enrolled 131 patients over a 50-month period. The original enrollment target was 250 patients, which was revised downward \(\text{“after early difficulty in recruitment”} (43)\). A total of 1,813 patients were assessed; 431 of these met eligibility criteria, among whom 131 \((30\%)\) were enrolled. Inclusion criteria included one to three VCFs and fracture age no more than 12 months. Patients with known malignancy were excluded. Patients with VCFs of uncertain age could be enrolled if an MR image showed edema or a bone scan showed hyperactive uptake. Vertebroplasty procedures were performed in 68 patients and sham procedures in 63. The sham procedure included superficial and deep injection of local anesthetic agents and mixing of cement within the operating room to simulate a vertebral augmentation procedure, as this was to be a blinded trial. Follow-up consisted of interviews conducted in person at 1 and 12 months and by telephone at 3 and 14 days and 3 months, and radiographs at 12 months. Physical reevaluation was not performed as part of the follow-up protocol. The primary outcome measure was the change in the modified Roland–Morris Disability Questionnaire \((RDQ)\) and average pain intensity at 1 month. The primary outcome measures were not significantly different between the two patient groups at 1 month. A secondary outcome measure was clinically meaningful improvement in pain at 1 month; this was achieved in 64% of patients who received vertebral augmentation versus 48% of control subjects \((P = .06)\). This outcome is particularly notable because the \(P\) value is so close to reaching statistical significance. In fact, had the original enrollment target been met, and with the same distributions of patient outcomes, this study would have shown statistically significant positive results for clinically meaningful pain improvement at 1 month for the vertebral augmentation arm.

The randomized trial of vertebroplasty for painful osteoporotic fractures reported by Buchbinder et al \((44)\) enrolled 78 patients over a 54-month period. A total of 468 patients were assessed; 219 of these met eligibility criteria, among whom 78 \((36\%)\) were enrolled. Inclusion criteria included one or two VCF(s), fracture age of less than 12 months, and MR imaging showing edema and/or a fracture line within the target vertebrae. Patients with known malignancy were excluded. Vertebroplasties were performed in 38 patients and sham procedures in 40. The sham procedure was essentially the same as that used in INVEST \((43)\); this was also intended to be a blinded trial. Follow-up consisted of mailed questionnaires at 1 week and 1, 3, and 6 months. As with INVEST \((43)\), physical reevaluation was not performed as part of the follow-up protocol. The primary outcome measure was the score for overall pain over the course of the previous week at 3 months \((44)\). The investigators reported that overall pain was not significantly different between patients who had undergone vertebral augmentation and control subjects at any of the measured time points. This study was partially supported by industry.

The randomized controlled trial of vertebroplasty versus nonoperative medical therapy for osteoporotic VCF reported by Farrokhi et al \((46)\) prospectively enrolled 82 patients over a 15-month period. A total of 105 patients were assessed, and all patients who met inclusion criteria were enrolled. The inclusion criteria included one to four VCF(s), edema demonstrated by MR imaging, pain persisting for at least 4 weeks but not greater than 1 year, and documented osteoporosis by bone densitometry. Crossover to the vertebroplasty group was permitted after 1 month; 10 patients crossed over before 1 year. Follow-up evaluation included clinical and radiographic assessments as long as 3 years after treatment. The primary outcome measures were pain relief at 1 month and 1 year as measured by VAS. Statistically significant improvement in pain relief was reported for patients treated with vertebral augmentation versus controls at all measured time points from 1 day through 1 year. Secondary analyses included positive proof of cost-effectiveness for vertebral augmentation. This study was partially supported by industry.

The randomized controlled trial of vertebroplasty versus nonoperative medical therapy for osteoporotic VCF reported by Barr et al \((41)\) – 46, 67) reported on 49 patients treated with vertebroplasty or conservative therapy for osteoporotic VCFs over a period of 84 months. The numbers of patients screened and assessed were not reported, so the percentage of eligible patients enrolled remains unknown. Inclusion criteria included one to three VCF(s) and fracture age less than eight weeks. If more than one fracture was present, edema on MR imaging or hyperactive uptake on a bone scan was used to determine which fractures were subacute. Forty patients were enrolled with pain for less than 2 weeks duration. Patients with known malignancy were excluded. Vertebralplasties were performed in 25 patients; the remaining 24 patients were treated with medical therapy. Clinical and radiographic follow-up evaluations were performed as long as 1 year after treatment. The primary outcome measures were pain relief at 3 and 12 months as measured by visual analog scale \((VAS)\). The investigators reported no statistically significant differences between the vertebral augmentation recipients and controls for pain or various functional measurements at 3 or 12 months. Supplementary analysis of pain at 1 month after treatment, however, showed a significant difference between the two groups. The mean VAS score for the vertebral augmentation group \((score 3.5)\) was significantly less than that for the control subjects \((score 6.4; P < .01)\).

The VERTOS II \((45,131)\) trial enrolled 202 patients over a 31-month period. A total of 934 were screened; 431 of these met eligibility criteria, among whom 202 \((47\%)\) were enrolled. Inclusion criteria included one to three VCF(s), more than 15% vertebral height loss, bone edema on MR imaging, and fracture age of less than 6 weeks. Patients with known malignancy were excluded. Vertebralplasties were performed in 101 patients, and the other 101 patients were treated with medical therapy. Follow-up evaluation included clinical and radiographic evaluations and patient questionnaires as long as 1 year after treatment. The primary outcome measures were pain relief at 1 month and 1 year as measured by VAS. Statistically significant improvement in pain relief was reported for patients treated with vertebral augmentation versus controls at all measured time points from 1 day through 1 year. Secondary analyses included positive proof of cost-effectiveness for vertebral augmentation. This study was partially supported by industry.

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up to 3 years. The 10 patients who crossed over to the vertebroplasty group also had significantly improved VAS scores. Significant improvements in vertebral body height and kyphosis reduction were reported at all times for the vertebroplasty group. One patient (1%) required surgical decompression for a symptomatic epidural cement leak. This study was partially supported by industry.

In conclusion, the two largest trials with the highest rates of patient enrollment (45,67) and inclusion criteria generally viewed as being similar to typical patients have demonstrated benefits for vertebral augmentation persisting through 1 year after intervention. The trial reported by Farrokhi et al (46) reported significant benefits for vertebral augmentation persisting as long as 3 years after treatment. The trial reported by Rousing et al (41,42) also demonstrated benefit from vertebral augmentation as long as 1 month after intervention, but not beyond this point. Interestingly, the vast majority of the patients in this trial were enrolled within 2 weeks of pain onset, which is dissimilar to the other trial populations. INVEST (43) reported a very strong trend toward clinically meaningful improvement in pain for the vertebral augmentation group at 1 month. This finding narrowly missed achieving clinical significance despite the reduced number of patients enrolled versus the original goal. Only the trial by Buchbinder et al (44) failed to show that vertebral augmentation was beneficial at 1 month after intervention. A long-term (ie, 1 y) benefit for vertebral augmentation was proven in the two largest trials (45,67) and the trial of Farrokhi et al (46), with total patient enrollment more than twice that of the remaining three trials. Therefore, after carefully weighing all the available evidence from these randomized trials, we conclude that vertebral augmentation of osteoporotic VCFs is clearly beneficial in the short term and likely also in the long term.

In addition to the data from the six randomized trials, Eddin et al (87) have reported a retrospective data analysis of 858,978 Medicare patients treated for newly diagnosed VCFs over a 4-year period beginning in January 2005. The outcome measure was mortality after a diagnosis of VCF. The increased mortality associated with VCF has been well documented (132–136). Analgesia and disability could not be assessed from the database. A 1-year “look-back” period was used to exclude patients diagnosed with a VCF or undergoing vertebral augmentation in the year before “to minimize a history of VCFs in the study population.” Patients of age less than 65 years, those enrolled in a health maintenance organization, and those not enrolled in both Part A and Part B of Medicare were also excluded (87).

The 1-year look-back period was also used to identify specific comorbidities so that the general health status of each patient before their VCF could be calculated by using the composite Charlson comorbidity index (137,138). Patients were then placed into one of four comorbidity groups based on their comorbidity index score. Survival rates during the study period were then normalized based on the identified comorbidities and additional covariates such as age and sex (87).

Among the 858,978 patients identified, 119,253 (13.9%) were treated with kyphoplasty and 63,693 (7.4%) with vertebroplasty. These 182,946 patients were designated as the operated cohort. The remaining 676,032 patients (78.7%) were designated as the nonoperated cohort. The demographics of the groups were very similar in most respects. The nonoperated cohort had significantly lower rates of arterial disease, chronic obstructive pulmonary disease, cancer, diabetes, hypertension, ischemic heart disease, and pulmonary heart disease, but higher rates of hip or wrist fracture, pneumonia, and stroke (87). The operated cohort had an adjusted survival rate of 60.8% at up to 4 years after VCF diagnosis, compared with 50.0% for the nonoperated cohort ($P < .001$). Patients treated with kyphoplasty had an adjusted survival rate of 62.8%, compared with 57.3% for those treated with vertebroplasty ($P < .001$). The magnitude of this study population far exceeds that of any of the reported prospective studies of vertebral augmentation. The survival advantage associated with vertebral augmentation for VCF was shown to be not merely statistically significant, but large as well (87).

Given the currently available scientific data, the Societies believe PVA has been shown to be more effective than prolonged nonoperative medical treatment in patients with painful VCFs in whom adequate analgesia and improved functional status has not been achieved by nonoperative therapy. To deny a patient PVA in favor of prolonged nonoperative medical therapy increases the chance of an adverse outcome associated with impaired mobility and complications associated with narcotic analgesia.

The definition of “failure of nonoperative medical therapy” has not been previously clarified to a sufficient degree. This has been previously defined as “minimal or no pain relief with the administration of prescribed analgesics or adequate pain relief with narcotic dosages that produce undesirable side effects (excessive and intolerable sedation, confusion, or constipation)” (1.3,4). It was not the intent of the authors of those documents to imply that a mandatory time period of days to weeks of medical management was necessitated by this definition. The concept of a mandatory period of medical management before PVA did not originate within the medical literature. The first published reference regarding this appears to be within a Food and Drug Administration guidance document published in 2004, “Clinical Trial Considerations: Vertebral Augmentation Devices to Treat Spinal Insufficiency Fractures” (139). The document states that trials should include “patients that have failed various, currently available conservative treatments after a sufficient time period when fractures would be expected to heal, generally eight weeks, or more.” This document does not identify the author(s). The document has an expiration date of May 31, 2007, but has never been updated. Among the 19 references, including the original American College of Radiology practice guidelines (1), none describes a mandatory 8-week, or other, time period for medical management. To our knowledge, there is no published recommendation from any medical society to support this concept.

Defining what constitutes “failure of nonoperative medical therapy” for patients with VCFs must integrate the patient’s pain level, their response to analgesic drugs, and their functional status, including the impact of the medical therapies employed. Pain is, of course, subjective and individual, so that a certain level on a scale such as the VAS would be inadequate. However, pain that prevents ambulation or physical therapy represents a rather simple and dependable measure of “severe” pain and “significant” disability. In addition, prompt restoration of ambulatory status or return to best previous subambulatory status is clinically important. Even in the absence of other pathologic conditions, prolonged bedrest of greater than 48 hours of duration clearly represents a significant hazard to the patient. For patients who were nonambulatory before their incident VCF, a significant reduction in previous physical functional status should be considered the equivalent of being rendered nonambulatory. Guided by these principles, we propose the following definitions for failed nonoperative medical therapy, as used in the most recently updated version of the American College of Radiology guidelines (4):

1. For a patient rendered nonambulatory as a result of pain from a VCF, pain persisting at a level that prevents ambulation despite 24 hours of analgesic therapy; or
2. For a patient with sufficient pain from a VCF such that physical therapy is intolerable, pain persisting at that level despite 24 hours of analgesic therapy; or
3. For a patient with pain from a VCF, unacceptable side effects such as excessive sedation, confusion, or constipation as a result of the analgesic therapy necessary to reduce pain to a tolerable level.

Prolonged arbitrary time periods of medical management do not have a role in the current treatment of patients with VCFs. It is clear from the available clinical data that early intervention for patients severely affected by VCF produces better clinical outcomes and that this is also cost-effective.

**Complications**
The types of complications that may occur with PVA were well summarized in a previous publication (112). Previous reports have described that serious complications occur in approximately 1.1%–1.3% of
Table 2. Significant Adverse Events Reported from Six Randomized Controlled Trials of PVA versus Nonoperative Medical Therapy or Sham Therapy (41–46,67)

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<tr>
<th>Trial</th>
<th>Complication</th>
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<tr>
<td>Vertos II (45)</td>
<td>Asthma attack</td>
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<tr>
<td>Vertos II (45)</td>
<td>Asymptomatic cement PE</td>
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<tr>
<td>FREE (67)</td>
<td>Hematoma</td>
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<tr>
<td>FREE (67)</td>
<td>Urinary tract infection</td>
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<tr>
<td>INVEST (43)</td>
<td>Thecal injury</td>
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<td>Buchbinder et al (44)</td>
<td>Osteomyelitis</td>
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<tr>
<td>Farrokhi et al (46)</td>
<td>Epidural cement leak requiring decompression</td>
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These six trials included a total of 455 patients with seven (1.5%) significant adverse events reported.

FREE = Fracture Reduction Evaluation trial, INVEST = Investigational Vertebral Augmentation Safety and Efficacy Trial, PE = pulmonary embolus, PVA = percutaneous vertebroplasty.

cases. Data now available from the six randomized controlled trials (41–46,67) provide the best assessment of the likely complications that may be encountered, and reaffirm that significant complications are indeed infrequent. Procedure-related significant adverse events occurred in seven (1.5%) of the 455 patients treated with PVA in these six trials (41–46,67). This incidence is not significantly greater than that derived from previous reports. The procedure related adverse events are summarized in Table 2 (41–46,67). No stroke, permanent spinal cord injury, myocardial infarction, or death was reported in association with treatment. Only a single adverse event was life-threatening: osteomyelitis occurred in one patient in the Buchbinder et al trial (44) who underwent treatment without antibiotic prophylaxis because the patient had multiple drug allergies. It is the authors’ opinion that most physicians would not attempt to perform PVA on a patient who could not be administered an appropriate antibiotic agent.

The Buchbinder et al (44) and INVEST (43) did not comment about cement leakage. Rousling et al (41,42) described only that asymptomatic cement leaks occurred. Farrokhi et al (46) reported that cement leakage occurred into the epidural (n = 1), disc (n = 5), and paravertebral (n = 8) compartments after treatment of 100 vertebrae. Such leakage appears to have been assessed by plain radiographs in most or all cases, as no routine postoperative computed tomography (CT) scans were reported. Their overall cement leakage rate may therefore be as high as 14% or as low as 8% depending on patients having multicompartmental versus unicompartmental leakage. The single patient with leakage into the epidural space had transient lower-extremity motor and sensory dysfunction that resolved after surgical decompression; all other cement leaks were asymptomatic. The FREE study (67) reported a 27% rate of cement leakage as detected by plain radiographs; all leaks were asymptomatic. The VERTOS II trial (45,131) reported a 72% rate of cement leakage as detected by CT; all leaks were asymptomatic, and no leakage into the spinal canal was detected. These three studies reaffirm results from earlier reports that cement leakage is very common, is more frequent when the more sensitive method (ie, CT) is used to detect this, and that cement leakage is rarely symptomatic.

In summary, clinically significant complications for PVA remain very infrequent and are most significant in the treatment of malignant disease. Most cases show a response to short-term medical therapy, and surgery is usually not required. The Societies recommend that all practitioners incorporate indicator thresholds into one’s quality improvement program to identify potential problems. As serious complications of PVA are infrequent, a review is recommended for all instances of death, paralysis, infection, and symptomatic pulmonary embolus. Recommended thresholds for complications can be found in the American College of Radiology’s Standards for the Performance of Percutaneous Vertebroplasty document (4) and SIR’s Quality Improvement Guidelines for Percutaneous Vertebroplasty document (2).

New Vertebral Fractures following PVA

The debate about whether PVA has any effect on subsequent fractures began shortly after the development of PVA. The development of kyphoplasty further complicated the debate with regard to any potential differences in new fractures associated with vertebroplasty versus kyphoplasty. As has been previously reported, new VCFs in patients with preexisting fractures are common.

Large trials have repeatedly shown the high incidence of new vertebral fractures in patients with osteoporosis. In 1999, Lindsay et al (140) reported that the incidence of a new vertebral fracture in the 1 year following identification of the first fracture was 19.2% in a pooled analysis of data from four large observational trials that included 2,725 postmenopausal female subjects. Also in 1999, Harris et al (141) reported 1- and 3-year incidences of 6.4% and 16.3% for new vertebral fractures in the placebo group of a randomized trial of 2,458 postmenopausal female subjects treated with risedronate or placebo. All subjects enrolled in this trial had at least one previous vertebral fracture. In 2000, Reginster et al (142) reported cumulative incidences of new vertebral fractures at 1 and 2 years of 13% and 29%, respectively, among the placebo group from a randomized trial of risedronate versus placebo in 1,226 women with osteoporosis who had at least two previous VCFs. In 2003, Kanis et al (143) reported a 22.3% cumulative incidence of new VCFs at 3 years among the placebo group from two combined randomized trials of risedronate versus placebo in 1,802 women with osteoporosis who had at least one previous VCF.

The results from the six randomized controlled trials (41–46,67) of vertebral augmentation provide further insight regarding new vertebral fractures after PVA. It must be understood, however, that none of these trials was designed or powered to detect a difference in the rates of new fractures between the treatment groups. The FREE trial (67) reported that 21(14%) of patients treated with PVA had new fractures at 1 year. This incidence was reported as being not significantly different from that of the control group, but the incidence of new fractures in the control group was not reported. “New or worsening” fractures were reported for 33% of the PVA group and 25% of the control group. The difference was reportedly not statistically significant. Buchbinder et al (44) reported that three of 38 patients (7.9%) in the PVA group and four of 40 control subjects (10%) had new fractures at 6 months; the difference was not statistically significant. No data regarding new fractures were reported from INVEST (43). Rousing et al (41,42) reported three of 25 patients (12%) in the PVA group versus four of 24 control subjects (16.7%) experienced new fractures within 1 year, without a statistically significant difference. The VERTOS II trial (45) reported that 15 of 91 patients (16.5%) in the PVA group and 21 of 85 control subjects (24.7%) had new fractures at 1 year; the difference was not statistically significant. Farrokhi et al (46) reported that one of 40 patients (2.5%) in the PVA group and six of 42 medically treated patients (14.3%) had new fractures at 3 years; the difference was statistically significant (P < .01).

Multiple nonrandomized case series also report similar incidences of new vertebral fractures following PVA and in patients treated with medical therapy. Mudano et al (144) reported that 18.8% of patients treated with PVA versus 6.7% of patients who received conservative therapy experienced new fractures at 1 year. This was a retrospective study of medical records from 48 PVA recipients and 164 control patients. Al-Ali et al (145) reported an 18% incidence of new fractures at 1 year from a prospective study of 357 patients undergoing vertebroplasty. Hierholzer et al (146) retrospectively analyzed 316 patients treated with vertebroplasty and reported that new fractures developed in 16.4% at a mean follow-up interval of 8 months. With regard to the incidence of new fractures following vertebroplasty versus kyphoplasty, Frankel et al (147) reported that three of 17 patients (17.6%) treated with kyphoplasty developed new adjacent-level fractures versus none of 19 who were treated with vertebroplasty at 3
months after treatment. A 2008 metaanalysis of the PVA literature by Eck et al (79) described a statistically significant 17.9% incidence of new fractures following vertebroplasty versus a 14.1% incidence following kyphoplasty (P < .01). They did not, however, state the time interval at which these incidences were calculated from pooled data with different follow-up periods. Chang et al (148) reported a 48% incidence of new fractures within 1 year after PVA in 60 patients. This high incidence of new fractures may be partially explained by the fact that these 60 patients had 159 VCFs at presentation; the presence of multiple VCFs in a patient is well recognized to markedly increase the incidence of additional VCFs. Kasperk et al (149) reported that the 3-year incidence of new fractures after kyphoplasty were 14 of 34 (41.2%) versus 10 of 14 (71.4%) for medically managed patients in a prospective, but nonrandomized, study; this difference was reportedly statistically significant (P = .0341).

In summary, multiple series, including the results of five prospective randomized controlled trials (41,42,44-46,67), report that the incidences of new vertebral fractures approximate the reported natural history risk of additional VCFs. There are conflicting and inconclusive data regarding any possible difference in new fracture incidence following kyphoplasty versus vertebroplasty. The best available evidence suggests that there is minimal, if any, impact on the incidence of new fractures following PVA by any method.

Pre- and Postaugmentation Spinal Imaging

Significant debate regarding the type(s) and necessity of pre- and postoperative imaging of patients with VCF continues. Although radiographs and physical examination may suffice in some patients as a preoperative evaluation, most patients will require MR imaging or radiographs and physical examination may suffice in some patients as a preoperative evaluation, most patients will require MR imaging or nuclear medicine bone scans to reliably confirm or refute the presence and location of subacute, nonhealed VCFs that may be amenable to treatment. MR imaging, CT, or CT/mammography may also be useful to evaluate for other pathologic conditions such as disk herniation, spinal stenosis, or unknown malignancy that may complicate the clinical presentation. MR imaging and bone scans are well recognized as being more sensitive than plain radiographs for the detection of subtle vertebral fractures. However, it has also been shown that a significant analgesic response following PVA does occur in some patients who did not exhibit bone edema on MR imaging (150). Finally, the cost-effectiveness of evaluating all patients with advanced imaging before PVA remains unproven (151,152). In general, the physical examination should be correlated with the minimum necessary imaging to select appropriate candidates for PVA. For patients who do not show a response to PVA with significantly decreased pain, or experience early relapse of similar pain, additional or repeat imaging evaluation should be performed to attempt to determine the cause of treatment failure. This is particularly important for patients enrolled in clinical trials.

PVA for Neoplastic Disease

The majority of the PVA literature and the majority of PVA procedures performed relate to the treatment of benign osteoporotic compression fractures. The primary focus of the present document appropriately reflects this. However, from its inception, PVA has been used to treat neoplastic lesions of the spine as well (1,5–8,10–12,14–18,53,58,153,154). Vertebral weakened by primary and metastatic neoplastic diseases are effectively treated by PVA to provide analgesia and structural reinforcement. There are numerous reported case series that document the safety and efficacy of PVA for treatment of neoplastic disease.

The Cancer Patient Fracture Evaluation study (155) prospectively enrolled patients randomized to treatment by kyphoplasty or nonsurgical management. A total of 477 patients were assessed, of whom 229 satisfied all eligibility criteria. A total of 134 patients were enrolled, with 70 assigned to treatment with kyphoplasty and 64 to nonsurgical management. The inclusion criteria included known cancer diagnosis, one to three VCFs, pain numeric rating scale (NRS) score greater than 4, and RDQ score greater than 10. Patients with a primary bone tumor, plasmacytoma, or a lesion deemed unsuitable for treatment with kyphoplasty were excluded. A total of 117 patients (kyphoplasty, n = 65; nonsurgical treatment, n = 52) actually completed the assigned treatment and had at least 1 month follow-up. Thirty seven patients (71%) crossed over to the kyphoplasty group after 1 month.

Follow-up evaluation included clinical assessments at 1, 3, 6, and 12 months and radiographs at 1 and 12 months. The primary outcome measure was the change in RDQ score at 1 month. Secondary outcome measures included Karnofsky performance status, SF-36 score, NRS score, and RDQ score at 1, 3, 6, and 12 months. As would be expected, mortality in this patient group was high; only 74 patients completed 12-month follow-up (155).

The primary outcome measure, the RDQ score at 1 month, was significantly improved by 8.4 points for the kyphoplasty group, versus 0.1 points for the nonsurgical management group (P < .0001). Improvements in the RDQ and SF-36 scores were significantly better in the kyphoplasty group through 6 months, but not at 12 months. Improvement in the NRS score was significantly better for the kyphoplasty group through 1 month, but not beyond that time. All outcome measures favored the kyphoplasty and crossover groups at all time points, but statistical significance vanished with time, perhaps because of the relatively few remaining patients in the nonsurgical management group. Two serious procedure-related complications were reported, both within the kyphoplasty group. One patient had an intraoperative myocardial infarction and one other patient had an adjacent-level fracture 1 day after treatment (155). This was an industry-sponsored trial.

Especially following the publication of the Cancer Patient Fracture Evaluation trial (155) results, the evidence to date continues to support that PVA represents an important, safe, and effective treatment for vertebral weakened by neoplasia.

PVA in Conjunction with Spinal Instrumentation

Although prophylactic vertebral augmentation for patients with osteoporosis is generally considered to be a relative contraindication to treatment (1,3,4), vertebral augmentation performed in conjunction with spinal instrumentation is described as being effective in allowing for successful and durable placement of pedicle screws and other devices in patients with severe osteoporosis and malignancies (156–160). Fenestrated pedicle screws to allow polymethylmethacrylate or other cement to be injected through the screws themselves have been developed (161). PVA performed under such circumstances is appropriate when the risk of hardware failure without such augmentation is considered to be high by the involved physicians.

CONCLUSIONS

It is the position of the Societies that PVA remains a proven medically appropriate therapy for treatment of painful VCFs refractory to nonoperative medical therapy and for vertebral weakened by neoplasia when performed for the medical indications outlined in the published standards (1–4).

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