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Current status of percutaneous vertebroplasty and percutaneous kyphoplasty – a review

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Percutaneous vertebroplasty (PV) and kyphoplasty (PK) are the 2vertebral augmentation procedures that have emerged as minimally invasive surgical options to treat painful vertebral compression fractures (VCF) during the last 2 decades. VCF may either be osteoporotic or tumor-associated. Two hundred million women are affected by osteoporosis globally. Vertebral fracture may result in acute pain around the fracture site, loss of vertebral height due to vertebral collapse, spinal instability, and kyphotic deformity. The main goal of the PV and PK procedures is to give immediate pain relief to patients and restore the vertebral height lost due to fracture. In percutaneous vertebroplasty, bone cement is injected through a minimal incision into the fractured site. Kyphoplasty involves insertion of a balloon into the fractured site, followed by inflation-deflation to create a cavity into which the filler material is injected, and the balloon is taken out prior to cement injection. This literature review presents a qualitative overview on the current status of vertebral augmentation procedures,especially PV and PK, and compares the efficacy and safety of these 2 procedures. The review consists of a brief history of the development of these 2 techniques, a discussion on the current research on the bone cement, clinical outcome of the 2 procedures, and it also sheds light on ongoing and future research to maximize the efficacy and safety of vertebral augmentation procedures.

Key words: vertebroplasty • kyphoplasty • bone cement

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Background

Vertebroplasty (PV) and kyphoplasty (PK) are 2well-known percutaneous procedures effective in relieving pain caused by acute and sub-acute vertebral compression fracture (VCF). Previously, the only surgical option to treat VCF involving decompression and fusion often failed in elderly patients due to osteopenia [1]. Although osteoporotic compression fractures are the most common indication for vertebro-/kyphoplasty, the application of these procedures has recently expanded to include the treatment of traumatic and metastatic compression fractures. The basic procedure involves percutaneous injection of bone cement into the cancellous or spongy bone of the vertebral body (VB) to alleviate pain associated with compression fractures, prevent further loss of vertebral height, and correct kyphotic deformity. Both PV and KP can provide pain relief and other benefits to patients, with acceptable safety when used by skilled physicians. Kyphoplasty is only a modification of vertebroplasty, and it involves the insertion of a balloon into the VB, followed by inflation/deflation to create a cavity before injecting the bone cement.

Vertebroplasty *vs.* Kyphoplasty

History

The first percutaneous vertebroplasty was performed in 1984 by Gakibert and Deramond, interventional neuroradiologists in Amiens, France. [2] These French physicians injected polymethylmethacrylate (PMMA) bone cement into C2 vertebra destroyed by painful vertebral hemangioma, and the patient'schronic pain was alleviated. Later on, PMMA, following a similar percutaneous technique, aided with fluoroscopic guidance, was injected into the vertebral body of vertebrae fractured by osteoporosis [3]. Interventional neuroradiologists in the US began using this technique in 1993 and the first case series was published in 1997 [4]. The technique became popular among radiologists and patients for rapid pain relief andover time was modified in terms of materials and methods to minimize the risk of extravasation, thereby increasing safety. It has been successful in relievingpain in 75–85% of patients, and also has been shown to effectively stabilize the vertebra [5–9]. However, vertebroplasty is not effective in restoring vertebral height. There are some other serious concerns associated with this particular technique: injecting bone-cement at high pressure into the vertebral body may lead to bolus embolization through the venous channel in the VB to the lungs, and bone cement extravasation through the spinal cord can lead to devastating neurological complications. As a solution to all these issues, kyphoplasty was introduced in the 1990s with the aim of stabilizing the vertebral fracture and restoring the vertebral height as close as possible to the pre-fracture level and minimizing the associated kyphotic deformity. Dr. Mark Reiley, an orthopedic surgeon, introduced the idea of inserting an inflatable balloon tamp into the VB to elevate or expand the vertebra to its original height. The extent of pain relief in KP is similar to PV. These 2procedures differ mainly in the surgical techniques used. PV involves the injection of liquid PMMA into the closed space of a fractured vertebra,but KP first creates a cavity inside the vertebral body, followed by the controlled filling of the cavity with partially cured PMMA [10–12].

According to the guidelines published by the Society of Interventional Radiology (SIR) in 2003, the common indications for PV include osteoporotic VCF older than 2 weeks and refractory by medical therapy, painful vertebra with extensive osteolysis or invasion secondary to benign or malignant tumor, and painful vertebral fractures associated with osteonecrosis [13]. The absolute contraindications include asymptomatic vertebral body compression fractures, active osteomyelitis of the target vertebra, uncorrectable coagulopathy, allergy to bone cement, patient condition improving upon medical therapy, prophylaxis in osteoporotic patients, and myelopathy originating at the fracture level. There also remain several other relative contraindications. In 2009, the American College of Radiology (ACR), the American Society of Neuroradiology (ASNR), the Society of Neurointerventional Surgery (SNIS), the American Society of Spine Radiology (ASSR), and the Society of Interventional Radiology (SIR) collaboratively prepared the official practice guidelines for vertebroplasty [14]. The indications and contraindications for KP aresimilar to those for PV.

Technical aspects

Imaging plays an important role in the process of vertebral augmentation, especially fluoroscopy. Both PV and PK should be performed by a clinician with in-depth knowledge of spinal anatomy and fluoroscopy imaging. The spinal level of the patient is verified by preoperative imaging and image intensifier before placing any cannula or syringe. Real-time fluoroscopic imaging is used to monitor the proper advancement of the trocar and injection of bone cement into the fractured site of the VB to avoid extravasation of cement into the neighboring tissues. Biplanar or C-arm fluoroscopy is generally used to provide maximal safety. General anesthesia or monitored anesthesia is used. General anesthesia is the optimal choice for lengthy cases of multiple levels of vertebral fracture. In case of monitored anesthesia, the anesthetist should generously inject local anesthesia, especially into the periosteum, as some patients feel discomfort during the advancement of the trocar through the posterior cortical margin with balloon inflation (in case of kyphoplasty) and with injection of bone cement. A small incision is made to insert the 11-inch cannulated trocar and biopsy needle. The cannula is advanced through the pedicle into the vertebral body being treated. Different approaches

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have been used for the advancement of the cannula followed by the injection of the bone cement. The cannula is inserted between the lateral margin of the thoracic vertebra and rib head in parapedicular approach, while the unipedicular approach involves insertion between the middle and anterior thirds of the vertebral body [15]. After the uni- or bipedicular access is obtained, the bone cement is injected. Some physicians prefer to perform venography before the injection of bone cement to minimize extravasation of bone cement. Venography provides the anatomical knowledge of the venous channel near the trocar [16–18]. However, there is some controversy regarding the efficacy of using venography prior to bone cement injection. The bone cement PMMA mixed with some contrast agent (typically barium sulfate) is injected into the fractured vertebra. It takes about 20 min to set and achieves 90% strength within 24 h. The patient is expected to feel pain relief within 4 to 24 h. The entire process is guided with real-time fluoroscopic imaging. Kyphoplasty involves the transpedicular or extrapedicular insertion of a pair of balloons (or tamp) under fluoroscopic guidance into the VB, followed by inflation/deflation to create a cavity inside the cancellous bone. After the realignment of the endplates of the vertebra (if possible), balloons are retrieved and PMMA is injected into the cavity.

Filler materials

Bone cements, used as the filler materials in vertebral augmentation procedures such as PV and PK are basically self-curing systems, generally supplied as powder and liquid phases packaged separately and mixed in the operation theater prior to use. These materials undergo subsequent *in situ* polymerization following injection into the VB and harden to provide adequate support to the vertebral column [19,20]. Previously, the main function of the bonecement was to fill the gap between the prosthesis and the bone and to transfer the load from the prosthesis to the bone. PMMA has long been used as bone cement due to its bio-inertness and biocompatibility for long-term use. Although PMMA was frequently used in dentistry and for joint replacements, it was rarely used for stabilization of fractured vertebra. In 1960 Charnely first reported the use of PMMA in total hip replacement (THR) [21]. Since this major breakthrough, PMMA has been used in various orthopedic applications [22]. Although PMMA had been regularly used for vertebral augmentation procedures, it was not approved by the US Food and Drug Administration (FDA) before 2004 [23]. In April 2004 certain brands of PMMA received approval by the FDA for treating vertebral fractures resulting from osteoporosis and tumors [24].

As mentioned above, the bone cement consists of 2parts: (1) a solid phase consisting of spherical particles (beads) of PMMA or acrylic polymers containing ethyl acrylate and methyl acrylate or even copolymer of methyl methacrylate-styrene at a concentration of 80 wt% and (2) a liquid phase consisting of methylmethacrylate (MMA) monomer at a concentration of 95 wt% [19]. The solid phase also contains benzoyl peroxide (BPO) as the initiator, physically mixed with the beads. Since the complete procedure of PV/PK is guided by the fluoroscope, the filler material should have radiopaque properties. For this purpose a radiopaque agent such as tantalum powder, tungsten, barium sulfate, or zirconium dioxide is incorporated into the solid phase. To initiate the polymerization at room temperature,*N, N*-dimethyl-4-toluidine (DMT) is generally incorporated into the liquid phase as an activator. A smallamount of inhibitor, typically hydroquinone, is also added to the liquid phase to avoid premature polymerization [19]. An important aspect of acrylic bone cement formulation is the ratio of solid to liquid phases, the cement's setting parameters are sensitive to this ratio. It is normally optimized as 2.18:1 (solid: liquid), although it can vary between 2:1 and 2.7:1 [19]. Care should be taken in manipulating this ratio because its failure can result in severe adverse effects due to excessive polymerization shrinkage or under-polymerization; both of these results can hamper the stabilization of the fractured vertebra. Moreover, the initiator-activator ratio has a substantial effect on the polymerization temperature, cement setting time, and mechanical strength [25]. The ideal material for use during vertebroplasty should have a longer liquid phase working time and shorter set time, whereas material with shorter liquid phase and longer partially cured doughy phase working time is preferred during kyphoplasty. To minimize the infection, antibiotics are sometimes added to the cement mixture before injection by clinicians [4,26]. A small amount (less than 2 gm of per standard cement packet) of antibiotics (gentamicin, oxacillin, cefazolin) does not affect the mechanical strength of the bone cement [27,28]. However, there are some conflicting reports that showed substantial decrease in the mechanical strength when using 250–500 mg of gentamicin inthe bone cement [29,30]. One alternative approach is administering antibiotics intravenously before vertebroplasty without compromising the mechanical strength of bone cement [31].

Bone cement is an implant biomaterial, which should be biocompatible. Once injected, its main function is the transfer of forces from bone-to-implant and implant-to-bone. Therefore, the materials used as bone cement should possess mechanical and physical properties such as stiffness (flexural or bending properties, dynamic elastic modulus, and dynamic storage modulus), toughness, radiopacity, and certain rheological properties (mixing-handling characteristics and viscoelastic properties). The bone cement is subjected to high stress and a challenging body environment. If the external stress factor is greater than the inherent strength, the bone-cement may break over time. To have long-term sustainability, the bone cement material should possess mechanical stability, with a substantial degree of strength and toughness.

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Several inherent advantages, including bio-inertness, ease of handling, good biomechanical strength, and cost-effectiveness, make PMMA an ideal choice for bone cement. However, important disadvantages ofPMMA are the toxicity of the residual monomer MMA and heat generated during exothermic polymerization. However, different studies showed that exothermic polymerization did not have any effect on bone generation and did not add to surgical trauma [32]. Leakage of monomer was also reduced after the curing phase [33]. The bone-cement interface temperature reached a maximum of 55°C, thus thermal necrosis was not an important factor [34].

Types of bone cement

Acrylate based bone cements are primarily used for vertebral augmentation. PMMA is the most frequently used bone cement. Acrylate-based filler materials also include acrylic polymers containing ethyl acrylate and methyl acrylate, or even copolymer of methyl methacrylate-styrene. They are sold under different brand names differing slightly in composition: PMMA bone cement Simplex P contains 75% w/w methylmethacrylate-styrene-copolymer, 10% w/w barium sulfate, 15% w/w polymethyl methacrylate in solid phase, and 97.4% v/v methylmethacrylate(monomer), 2.6% v/v *N*, *N*-dimethyl-p-toluidine, 75±15 ppm hydroquinone in liquid phase, while Osteobond is composed of 88.75% w/w polymethyl methylmethacrylate-styrene, 10% w/w barium sulfate, 0.0125% w/w benzoyl peroxide in solid phase, and 97.3% v/v methylmethacrylate (monomer),2.7% v/v *N*, *N*-dimethyl-p-toluidine, 80 ppm hydroquinone in liquid phase [23,35,36] There are some other PMMA bone cement products available on the market, such as HV-R, Palacose R, and DePuy 1 (CPW). Apart from PMMA-based bone cement, there are few published reports containing histological data oncalcium phosphate-based bone cement (Bone source, SRS, Alpha-BSM, Biopex) in a vertebroplasty model. However, calcium phosphate-based bone cements are still in the development stage *in vitro* and there are few animal studies [37–40]. BonePlust is a calcium sulfate-based bone cement designed and developed as a substitute for PMMA. However, studies revealed that it would be inappropriate for use for vertebral augmentation procedures due to its inability to provide adequate spinal alignment [41–43]. Research has already shown that PMMA cannot adhere to bone or induce new bone formation [44,45]. Few new generation bioactive bone cements have been found to induce new bone formation and also have good mechanical stability. Bioactive composite materials prepared from acrylic cements in conjunction with ceramics showed good radiopacity and robust mechanical properties. Bioactive glass beads or glass ceramic powder when added to the organic matrix containing bisphenolA-glycidyl methacrylate (Bis GMA) and PMMA resulted into new bone formation around the beads [46,47]. Cortoss, a composed material-based bone cement currently undergoing clinical trials for vertebroplasty and kyphoplasty is composed of terpolymer resin with combeite glass-ceramics [48,49]. Strontium is radiopaque and it has also been shown to induce new bone formation and to inhibit bone resorption *in vitro* and *in vivo* [50–53]. Cheung et al. [54] reported on a new bioactive bone cement composed of strontium containing hydroxyl apatite (Sr-HA) with Bis-GMA,showing promising results and currently undergoing extensive clinical trials to examine its effectiveness and safety. A novel bone cement containing bone morphogenic protein (BMP) is under investigation [55]. This protein, found in bone matrix, belongs to the transforming growth factor-β (TGF-β) superfamily. BMP-containing cement injected into bone showed formation of new bone, although no work specific to PV is reported [56,57].

Mechanism of pain relief

Chemotoxicity of MMA, thermal necrosis during exothermic polymerization, and mechanical stability provided by the cured bone cement are the probable mechanisms for pain relief in vertebroplasty [58]. The component monomer (MMA) of the most commonly used bone cement, PMMA, was known for its toxicity on cells as well as neurotoxicity, and hence a chemical effect was postulated for the pain relief [59,60]. However, this hypothesis was invalidated by a matched control clinical study in which calcium phosphate was used as the bone cement (without any toxic monomer) and similar pain relief was observed [61]. It has already been shown in animal studies that thermal necrosis of bone tissues occurs when the temperature exceeds 50°C for over 1 min [62], while injury to sensory nerves occurs if temperature is maintained at 45°C for over 30 min [63]. These results suggested the thermal necrosis of the vertebral nerve endings during PMMA polymerization exothermy as the mechanism for the pain relief in the past [64]. Some *ex vivo* studies on cadaveric specimens (placed in a saline bath at 37°C) have been done to show the effect of PMMA polymerization on the bone [64]. However, this experimental condition can only create a partial in an *in vivo* environment without taking into account the lowering of temperature due to the convective effect of blood-flow and cerebrospinal fluid surrounding the vertebral body. Even with the limitations associated with mimicking the exact *in vivo* conditions in these experiments, the temperature in the spinal canal did not exceed 41°C during polymerization, and the authors hypothesized that the pain relief in vertebroplasty is unlikely due to the thermal necrosis of the vertebral nerve endings [64,65]. Later, Verlaan et al., in an *in vivo* animal study physiologically demonstrated that the local temperature never rose to the value known to cause bone tissue necrosis [66]. The first human *in vivo* study for measuring the polymerization temperature of different bone cements was performed by Anselmetti et al. [67], who found that none of the bone cements maintained the temperature at 45°C for more than the 30 min necessary for thermal

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necrosis of the sensory nerves [63]. Additional studies investigated the effect of polymerization temperature. However, all these studies ruled out the thermal necrosis of the sensory nerves as the cause of pain relief in vertebroplasty [68,69].

After ruling out the "chemical effect" and "thermal effect" as probable causes of pain relief in vertebroplasty, "mechanical stabilization" can be regarded as the most probable mechanism for pain relief. Vertebral cancellous bone can also be a source of pain. During fluoroscopy of the vertebral fracture, it is quite common to see end plate motion if a cleft is present due to osteonecrosis. Typically, the patients with mobile fractures experience pain during coughing, breathing, sneezing, or bending. The pain is mainly related to the motion of the end plate and the micromotion of the trabecular fractures – both these conditions are the most common histologic findings in osteoporotic fractures[70,71]. Thus the immediate pain relief after PV or PK can easily be related to the cessation of the cleft motion after curing of the bone cement. Variousvolumes of bone cement were required to beinjected, depending on the extent of the fracture, in order to restore the original mechanical stability of the vertebra. This provided immediate pain relief after curing of bone cement, suggesting the restoration of mechanical stability in a clinical outcome study [72].

Clinical outcome

PV and KP are the most routinely used minimally invasive procedures to treat osteoporotic or tumor-associated VCFs with the primary aim of relieving pain. There are several literature review articles that assess the efficacy and safety of these procedures in comparison to medical management alone in VCFs patients. The superiority of these procedures still remains a subject of debate. McGirt et al. [73] published a systematic literature review covering a large number of articles published between 1980 and 2008. The studies were classified in different categories based on the level of evidence and grades of recommendation in support of using PV or PK according to the clinical guidelines of North America Spine Society (NASS) – (i) Level I studies with consistent findings (*Good Evidence*); (ii) Level II or III studies with consistent findings (*Fair Evidence*); (iii) Level IV or V with consistent findings (*Poor Quality Evidence*); and (iv) studies with inconsistent findings or lack of evidence (*Insufficient Evidence*) [74]. According to the level of evidence rated by NASS, among 74 published articles on PV until 2008, only 1article classifies as Level I (randomized control trial) [75], 3articles qualify for Level II (nonrandomized control trials) [76–78], while the remaining 70 classify as Level IV [79–86] (only a few representative references are cited here; for a comprehensive list please refer to the review by McGirt et al. 2009). No other randomized control trials have been performed for PV, with the exception of the study by Voormoloen et al. [75], until 2008. They carried out a randomized study on 34 patients with painful osteoporotic VCFs. Patients were randomly divided into 2groups: one treated with PV and the other with optimum pain medication (OPM). The PV group showed immediate pain relief when compared to the OPM group. There was substantial improvement in mobility, function, and stature in the PV group; 88% of patients in the OPM group requested the PV treatment two weeks after initiation with OPM treatment. However, 2randomized trials [87,88] published in 2009 showed results thatare not in agreement with the outcomes of the randomized trial by Voormoloen et al. [75]. Two different groups of researchers, Buchbinder et al. [87] and Kallmes et al. [88], each separately reported 1 randomized trial of PV in which the control group underwent a sham procedure. The patients in the control group went through the preprocedural steps similar to the steps for the PV group (e.g., a needle was inserted but only to rest on the lamina, the sharp stylet was replaced by a blunt stylet, applying a lighttap on the vertebral body, opening the methacrylate bottle so that they could associate with the odor of the bone cement) to simulate the PV procedure without injecting any bone cement. Their observations are quite interesting. Both of these randomized trials found similar improvements in terms of pain and associated discomfort in control and PV groups. The Kallem et al study included follow-up results from 1–3 months, whereas Buchbinder et al reported upto 6 months follow-up.

In the Level II studies mentioned above [76–78], there was immediate pain relief and greater improvement in physical functioning in the PV group. However, there were no differences in PV and OPM groups in terms of VAS (visual analog score for back pain) or Barthel functional Index at 1, 5, 6, 12, or 24 months. Incidence of adjacent VCFs didnot increase for 2 years in the PV cohort. The remaining 70 nonrandomized studies in the Level IV category showed substantial and rapid pain relief, although there was no control OPM group.

McGirt also referred to 35 articles (1980–2008) reporting the status of patients receiving KP for the treatment of osteoporotic VCFs. Among these 35, there was no study that qualified for Level I ranking, and a single Level II study was published in 2separate manuscripts [89,90]. In the first study, greater pain relief and faster return to daily activity was reported within 3–6 months of treatment in the KP cohort relative to OPM. There were fewer backpain-related doctor visits in the KP cohort. The second manuscript compared the outcomes of the patients treated with KP and OPM after 1 year, reporting greater reduction in pain at 12months, improvement in physical functioning at 6 months, and reduction in backpain within 12-month related doctor visits, and fewer incidences of new adjacent VCFs in KP compared to the OPM cohort. The remaining 33 articles qualified as Level IV evidence, showing substantial, consistent,and rapid pain relief [91–95] (a few representative references are cited here; for a comprehensive list, please refer to the review by McGirt et al. 2009).

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According to McGirt et al., there are 18 articles (1980–2008), reporting on a total of 698 patients receiving PV or PK for the treatment of tumor-associated VCFs. None of the studies provide level I, II, or III evidence that PV or PK is superior to OPM in managing tumor-associated VCFs. All of them belong to Level IV, and meta-analysis of these 698 patients showed a substantial decrease in acute pain after PV or PK procedures [96–100] (a few representative references are cited here, for a comprehensive list please refer to the review by McGirt et al. 2009).

There are 3 outcomes in PV and PK interventions: (i) rapid pain relief, (ii) improved body functioning, and (iii) vertebral height gain or improved spinal alignment. Direct comparison in terms of efficacy of PV and PK is not possible as there is no randomized control trial. In a comparative systematic review, Taylor et al. [101] included 1prospective study and 70 case series comparing the 2 procedures (PV and PK) for the treatment of VCFs due to osteoporosis or tumors. Similar findings of substantial reduction in pain were achieved for vertebroplasty at 5-year follow-up, and for kyphoplasty at 2-year follow-up. Physiological function was evaluated by the Oswestry Disability Score and Back Function Index. Kyphoplasty showed a substantial improvement in the patient's functional capacity. However, due to lack of a validated measurement of the patient's functional capacity, the outcomes are missing for vertebroplasty. Kyphoplasty also substantially improved the quality of life, but here again, due to different outcome measurements for vertebroplasty, the data cannot be compared. Vertebroplasty did show an improvement in quality of life. The single study comparing PV directly with KP found that level of pain relief measured by VAS was similar in both procedures [102]. However, the selection of application of procedures was notably biased, with more severe VCFs receiving kyphoplasty. Eighty-four percent of patients had substantial or complete pain relief with a short mean follow-up of 4.5 months [102]. Both procedures resulted in improved vertebral height gain and kyphotic deformity [89,102]. Hulme et al. [103] published a systematic review comparing vertebroplasty and kyphoplasty, including 69 clinical studies. In this analysis, more than 80% of cases were osteoporotic VCF. The review examines the outcomes of 4456 vertebroplasty and 1624 kyphoplasty procedures. Pain relief was observed in both groups (vertebroplasty, 87%; kyphoplasty, 92%). Inmost of the studies included in this systematic review, the follow-up observation was ofshort duration (less than 1 year); however, the pain-relief was persistent. Physical function and disability score improved in both procedures, despite the fact thatthe data could not be pooled because different scales were used by the research groups in evaluating those scores. Similar vertebral height gain (or kyphotic angle restoration) was achieved by both procedures, with a mean kyphotic restoration angle of 6.6°. However, there was no vertebral height gain or correction in kyphotic deformity in 39% of vertebroplasty and 34% of kyphoplasty cases. Restoration of vertebral height depends on the age of the fracture, as suggested by a few authors [104,105], although not validated globally [106]. Due to the wide variation in measurement scales and lack of prospective data comparing the 2 approaches, it is not possible to makedirect comparisons between vertebroplasty and kyphoplasty. Therefore, debate still exists regarding the superiority of one procedure over the other. Extent of pain relief and vertebral height gain were found to be similar with both procedures [107]. However, the controversy lies in the vertebral height gain, cost efficiency, safety, and efficacy of these 2 procedures.

Mathis et al. [108] critically compared PV and PK by analyzing pooled data from various studies. The main idea behind developing the kyphoplasty procedure was to restore vertebral body height and minimize the associated kyphotic deformity by inserting an inflatable balloon inside the vertebral body before injecting the bone cement. Mathis et al. [109] found that the height gain in PV was estimated at 3–4 mm with a 9° reduction in kyphotic angle, while Lieberman et al. [104] reported an average height restoration of approximately 3 mm per vertebra after kyphoplasty. This raises the issue of reliability of kyphoplasty in superior restoration of vertebral height compared to vertebroplasty, and there are no clinical trials available that show the maximum height gain after kyphoplasty. In some PK studies, vertebral height gain has been linked with the correction of kyphotic deformity of the spine [110,111]. PV also showed a similar effect on kyphotic deformity. Improved pulmonary function is reported as a secondary benefit of the kyphotic correction, although no clinical data is available [108]. Mathis et al. [108] also mentioned that the manufacturer claimed that reduced cement leakage is associated with KP when compared to PV. Cement leakage is linked to the pressure at the time of bone cement injection. The cement injection in PV is under high intravertebral pressure, while in KP it is under low pressure since in the latter the cement is filled inside the void created by the balloon. There is 1study [112] in which investigators quantitatively demonstrated that under regular operating conditions high pressure injections were not observed with any of these vertebral augmentation procedures. The higher intravertebral pressure is associated with higher injection rate and size of the cannula. Most of the PK studies showed lower incidences of cement leakage compared to PV. However, most of the cement leakage associated with PV was asymptomatic [108]. Symptomatic cement leakage occurred with both the procedures [109], and for patient safety the FDA issued a warning regarding the use of PMMA for both procedures in April 2003. There is a substantial price difference between these 2procedures. The PK kit costs USD $3400 without bone cement, while the PV kit costs USD $400 and includes bone cement. Moreover, PK involves the use of general anesthesia and an overnight stay at the hospital. Intravenous sedation is usually used for PV, along with a few hours stay at the hospital after the procedure for

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observation. All these make PK 10–20 times more expensive than PV [108]. However, the extent of the benefits with PK is not onpar with its cost. Systematic reviews published recently also concluded that both PV and PK are safe and efficacious percutaneous interventions in treating VCFs [113,114]. Higher procedural cost decreases PK utilization, despite the fact that there are less severe complications with PK (as documented in various studies described in the next section). PK showed superiority for intermediate-term (close to three months) only, but there is no substantial difference between these two interventions in long-term pain relief and physical functionality.

Complications

There are some perioperative and postoperative adverse events associated with both PV and PK, such as symptomatic cement leakage, cement embolism, pulmonary embolism, hematoma, neurodecline, spinal cord compression, radiculopathy, infection, and adjacent vertebral fracture [84,103,115,116]. The overall rate of complications with both procedures ranges from <2%(when treating osteoporotic fractures) to 10% (when treating malignant tumors) [5,117,118]. Hulme et al reported the rates of neurological complications with PV and PK were 0.6% and 0.03%, respectively [103]. Extravasation of bone cement into epidural spaces leads to more serious complications. As a result of bone cement leakage into the venous channel, lethal conditions such as pulmonary embolisms occur, with rates ranging from 0.6% (for PV) to 0.01% (for KP) [103]. The extent of cement leakage depends on the causeof the VCFs. The incidence of cement leakage was higher in the treatment of osteoporotic VCFs than in tumor-associated VCFs [119]. Phillips et al reported significantly less contrast extravasation-related complications in PK when compared to PV [OR (95% CI): .04 (.00–.68) P=0.03] [120]. The periprocedural complications involve fractures for transverse process, pedicle, sternum, ribs, [4,7,73,104,121,122], respiratory distress due to anesthetic complications [31,123], and infections [8,122,124]. Other complications include epidural hematoma, partial motor loss [111], and digestive tract bleeding [105]. Walker et al. reported osteomyelitis a rare complication, which requires corpectomy [125].

Adjacent level vertebral fracture is a major postoperative complication of vertebral augmentation procedures (PV and PK). However, there is a debate over the cause of the new compression fracture. Whether the new compression fracture is a result of a natural progression of osteoporosis or is caused because of stiffness by augmentation with bone cement is still a subject of controversy [126–130]. The risk of having a second osteoporotic fracture increases 12.6-fold in the presence of an old fractured vertebra [131]. In a comparative study on adjacent level vertebral fractures after vertebral augmentation procedures, Movrin et al found that the rate of adjacent level fractures widely varied for both PV (8–52%) and PK (3–29%) [132]. Due to inconsistencies in the current data, it still remains inconclusive whether vertebral augmentation procedures increase the risk of adjacent level vertebral fractures.

Future Developments

Vertebroplasty and kyphoplasty are both excellent percutaneous interventions in providing short-term painrelief and improved physical functionality. Several complications are associated with these 2 procedures. These procedures are mainly limited to the treatment of VCF. There are few reports in which these procedures have been performed to treat conditions such as severe vertebral body collapse, burst fracture, or cervical spine disease [133–137]. Therefore, research should focus on the design and development of materials and techniques to minimize the associated complications, maximize efficacy and safety, and broaden the area of implementation. Research has been focused on developing bioactive bone cement materials (discussed above under the section “Type of bone cement”), which not only minimize the toxicity, but also initiate new bone formation which can give long term benefit. The other area needing attention is the development of new stent materials that can provide extra reinforcement to the fractured vertebral body. In this connection, Rotter et al. [138] reported an alternative procedure called “vertebral body stenting” (VBS) to overcome the procedural disadvantages and loss in vertebral height with PV and PK. They compared the efficacy of this new procedure with kyphoplasty in cadaveric samples, and found substantially less height reduction when compared to kyphoplasty [total anterior height gain – kyphoplasty: 8.0±9.4; VBS: 13.3±7.6]. Therefore, VBS can be considered as a promising candidate for vertebral augmentation.

Another alternative procedure forvertebral augmentation involves the use of Nitinol, a shape memory alloy, which showed promising results. Shape memory alloys are known for their shape memory and super-elastic properties, and have been very effective in treating scoliosis[139]. Nitinol endoprosthesis (“Nitinol cage”)(VerteLift™, SpineAlign, Inc., San Jose, CA) has been used to treat VCF. Antonio Manca, in his doctoral thesis, [140] reported the use of “Nitinol cage” to treat VCF, and a 1-year follow-up of 40 patients has also been documented. The method is somewhat similar to PV and PK and involves the injection of bone cement PMMA. In kyphoplasty, a bone tamp is inserted to create a cavity before injecting the bone cement, while this Nitinol implant-based method involves the placement of the implant inside the vertebral body (after making the pathway for the implant by using a coaxial manual drill). The implant is then opened when it reaches the exact fracture position. Thereafter, the PMMA is injected to fill the open nitinol cage. The nitinol implant is chosen according to the shape of the fracture and vertebral body size. In PK the balloon is

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taken out before injecting the bone cement,while the Nitinol implant remains inside to further reinforce the VB. Theoretically, the Nitinol VerteLift implant can prevent the loss of vertebral height intra-operatively and postoperatively, as these implants are designed to flex around the end plates, thereby broadening the pressure distribution and preventing end plate damage. Unlike the kyphoplasty, where loss of vertebral height could be possible after balloon deflation, the Nitinol VerteLift implant restored the vertebral height during the bone cement injection and after polymerization. The cemented nitinol implant restored the vertebral height even after 1 year, but substantial height loss was observed with PV and PK.No cement leak was observed with this implant. Therefore, the Nitinol implant is safe and effective for vertebral augmentation,and it provides long-lasting pain relief and persistent vertebral height gain [140]. However, more research has to be done to establish the Nitinol implant as superior to PV or PK.

Recently, researchers have developed an innovative procedure of vertebral augmentation to improve the safety and efficacy of the existing vertebral augmentation procedures (PV and PK). The new procedure is known as Radiofrequency kyphoplasty or Radiofrequency-Targeted Vertebral Augmentation(R-TVA) [141,142]. This novel procedure involves targeted delivery of radiofrequency (RF)-activated, warm, highly viscous bone cement PMMA using an articulating osteotome. No balloons are required – after creating an incision on the skin, a 10-g introducer is inserted into the middle third of the vertebral body. With the help of osteotomes, site-specific cavities are created inside the fractured vertebra. The cavities are then filled slowly with radiofrequency-activated warm bone cement (PMMA) in controlled way using a hydraulic delivery system. RF energy increases working time for the physician by allowing the consistent flow of ultra-high viscous bone cement without premature hardening. Controlled targeted delivery of RF-activated highly viscous bone cement through the middle third of the vertebral body not only addresses the cement leakage problem, but also shows improvement in height restoration [143,144]. This comparatively new procedure requires more randomized trials to establish its efficacy over the existing vertebral augmentation procedures.

Conclusions

Percutaneous vertebroplasty and percutaneous kyphoplasty both are effective in vertebral augmentation and pain-relief in patients with osteoporotic or tumor-associated VCFs. Both procedures have been proven to be superior to oral pain management. However, due to lack randomized trials, there are no data available for direct comparison between these 2 procedures. On the basis of systematic reviews of available literature, indirect comparisons have been found that showed very little difference in terms of clinical outcomes of these 2 procedures. Both procedures give immediate pain relief and improvement in physical functioning, although the effect is not long-term. The overall rate of complications associated with these 2 procedures is low, but the rate of cement extravasation is higher in PV. Controversy exists about symptomatic and asymptomatic cement leakage, as most of the cement leakage in PV is asymptomatic. Improved vertebral height restoration with PK is also controversial, because initial height gain is higher in kyphoplasty but this effect is lost subsequently during balloon deflation and repetitive loading. Clinical studies consistent with these findings found little difference in vertebral height gain between PV and PK. Postoperative adjacent level vertebral fracture is another subject of debate. Recently-developed radiofrequency kyphoplasty showed promising results in terms of height restoration and other procedure-associated complications like trabecular destruction, which frequently occurs in balloon kyphoplasty. To establish the relative strengths and weaknesses of all these procedures, well-designed randomized clinical trials are required. Further research should concentrate on the development of new material and methods that can overcome the drawbacks of these existing procedures, and come up with a new promising alternative technique with long-term efficacy and improved safety.

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