Kyphoplasty and vertebroplasty in the management of osteoporosis with subsequent vertebral compression fractures

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Summary

Osteoporosis with subsequent vertebral compression fractures (VCFs) is an increasingly common problem in western countries. This systematic review tries to update the evidence base for Balloon Kyphoplasty (BKP) and Vertebroplasty (PV) in the management of VCFs. We have analyzed 16 reviews and 97 articles. The majority of studies compares conventional medical management of VCFs to patients undergoing BKP or VP. We discuss selection criteria, techniques, potential complications, advantages and disadvantages, and results of each technique, recognizing that prospective, randomized controlled studies are necessary to objectively compare these techniques.

KEY WORDS: Balloon Kyphoplasty, Vertebral Compression Fractures, Osteoporosis, Systematic review, Mobility Osteoporosis, Functional outcomes, Osteoporosis.

Osteoporosis

The Consensus Development Conference (1991) defined Osteoporosis as a disease that is characterized by a decrease in bone mass and by microarchitectural weakening of bone tissue, predisposing to enhanced bone fragility and risk of fracture. In 2000 the National Osteoporosis Foundation (NOF) added to this definition the bone mineral density (BMD) T-score to provide diagnostic criteria to classy the extent of the process. A T-score from -1 to -2.5 standard deviation (SD) defines decreased bone mass or osteopenia, a T-score >2.5 SD is indicative of low bone mass or osteoporosis (1-3). This criterion of bone density indicates conventionally a proxy for overall bone strength and is expressed as grams of mineral per square centimetre or grams per cubic centimetre (4). However, even if BMD is the standard test for the diagnosis of osteoporosis before treatment, a recent research indicates that BMD test alone is not sufficient for assessing fracture risk and therapy efficiency (4). It should be necessary to evaluate also the bone quality, which together with BMD contributes to the bone strength. Osteoporosis is a chronic and multifactoral skeletal disease, it is present in both sexes and is becoming a major public health problem in developed countries (5, 6).

This bone condition is characterized by an imbalance between bone production (by osteoblasts) and bone resorption (by osteoclasts) (5, 7). In normal condition there is a balance between bone resorption and formation; in osteoporotic bone there is an increase in osteoclastic bone resorption due to an overall decrease in osteoblastic bone production or a direct increase in bone resorption (5, 6). There are three categories of osteoporosis: primary, secondary and idiopathic. Primary osteoporosis is subdivided into postmenopausal (type I) and senile (type II) osteoporosis (2). Post menopausal osteoporosis is due to the loss of estrogens and its inhibiting effect on osteoclasts that determines a rapid bone loss after menopause (2, 3, 5). After menopause, the primary source for estrogens is in the adipose tissue, so this may account for the fact that it is uncommon for obese patients to develop osteoporosis (2). Senile osteoporosis is characterized by an excessive bone loss due to a decrease in osteoblastic formation that causes a gradual decrease in bone mass in all people during midadulthood and continues until death (2, 5). Secondary osteoporosis is the result of any age-independent factors that lead to bone loss, such as long-term glucocorticoid steroid use, moderate to heavy alcohol intake, and cigarette smoking (2, 3, 8). Other factors that induce osteoporosis include dietary factors (high protein, low calcium, high caffeine), diseases (hyperthyroidism, hyperparathyroidism), malabsorption states, amenorrhea, sedentary lifestyle, postbilateral oophorectomy, and low body weight (2, 3).

Vertebral compression fractures

The loss of bone mass places the individual at increased risk for vertebral body, hip, and wrist fractures. Osteoporosis with subsequent vertebral compression fractures (VCFs) constitute an increasingly important health care problem in western countries, not only because occur more frequently than hip and ankle fractures combined, but also due to its direct and indirect negative consequences for patient health-related quality of life, its significant economic impact and to the increasing age of our population (9-12). These fragility fractures frequently result in both acute and chronic pain, but most important they are a source of increased morbidity and possibly mortality (13). Osteoporotic VCs can be caused by a minor trauma and can result in an acute collapse or microfractures without a compressive component (2, 14). Microfractures decrease the stability of the vertebral body and generally the structural compression of the vertebral body can occur in the anterior portion, causing wedging of the vertebral body (15). The weakened anterior portion of the thoracic and lumbar vertebral body creates a kyphotic curvature of the spinal column (15, 16). Kayanja et al. describe that "kyphosis begets kyphosis" because the erect position determines a continual force or a compressive load on the anterior portion of the vertebral body causing further compression (17). Progressive kyphosis can cause pain, deformity, significant height loss, immobility, protrusion of the abdomen, and even the reduction of the pulmonary cavity limiting the ability to expand the lungs (15, 16, 18).VCFs can be divided into two different morphologic types. The first type is the acute crush fracture, characterized by sudden onset of pain and muscle spasm after minor or major trauma (7, 19). It is difficult to differentiate these kinds of fractures from the pathologic ones and sometimes it is necessary to perform a biopsy (20). The second type is a mini-

mally symptomatic anterior wedge compression fracture that leads to a kyphosis and a loss of height (7 chronically several studies have shown that disturbance of the normal sagittal balance can lead to further back pain) (23, 24). Increased morbidity and mortality in this population is associated to compromised pulmonary function, pain, and complications associated to immobility, deep vein thrombosis, infection, muscle atrophy (1, 2, 16). Pain, physical limitations, and postural changes caused by osteoporotic fractures can have serious psychologic effects, including depression, loss of self-esteem, anxiety, fear, and strained interpersonal relationships (2, 25, 26). and it is often difficult to differentiate whether the fracture is acute, or chronic or pathologic. Magnetic resonance imaging (MRI) is an excellent imaging modality because not only it can determine if there is edema associated with acute compression fractures or the fractures are old (no inflammatory changes), but it can also detect any tumoral lesions that may have caused the fracture or may be present in other vertebral bodies (22, 27). The sagittal T2-weighted and fat-suppressed T2-weighted or the short tau inversion recovery images show increased signal intensity at the fracture site in patients who have acute and subacute fractures (28). Nuclear scintigraphy (bone scan) can be used to evaluate the acuity and physiologic activity at the fracture site for patients who have a contraindication to MRI. CT scan can also be used to evaluate the potential spinal canal compromise, foraminal stenosis, posterior vertebral wall involvement, and extent of bony involvement (22, 27).

Pain reduction and stabilization are of primary importance in osteoporotic VCFs. Osteoporotic VCFs were treated in the past with conservative treatment consisting of rest or activity modification, analgesics (nonsteroidal anti-inflammatory drugs, narcotis), muscle relaxants, and orthotic bracing (20, 29-31). Surgery to restore height and alignment meant subjecting the patient to the tremendous morbidity of thoracotomy or abdominal surgery; this could not be tolerated by elderly patients who often suffered from multiple medical comorbidities. Approximately one third of vertebral compression fractures becomes chronically painful (32). The percutaneous vertebral augmentation techniques, Vertebroplasty (VP) and Ballon Kyphoplasty (BKP), are minimally invasive surgical techniques and can stabilize these fractures maintaining a relatively safe risk profile. In the great majority of patients VP and BKP provide immediate pain relief (5). The findings of history, physical examination, and imaging studies are essential to identify patients who would benefit from VP and BKP procedures (33). Generally acute compression fractures cause a sudden onset of back pain that may or may not be associated with a traumatic event (15).

Epidemiology of osteoporosis and osteoporotic vertebral fractures

As a natural result of aging the risk of osteoporotic fractures grows more and more, thus becoming a social and an economic burden for society (34). The National Osteoporosis Foundation (NOF) estimates that 41 million (55%) Americans aged over 50 years have osteopenia-osteoporosis and more than 10 million people are only in the United States. Osteoporosis is projected to impact approximately 14 million adults over the age of 50 by the year 2020 in the United States (1, 35). Women account for 80% of the affected individuals, with 50% of women aged 80 having osteoporosis (20). The annual incidence of osteoporotic fractures exceeds 1.5 million in the United States (1). Worldwide, approximately 200 million women have osteoporosis (36). It is estimated that 20% of individuals over 50 and 45% of white women over 50 have osteoporotic VCFs (15, 22).

Economic burden

Direct and indirect cost of osteoporotic fractures for the US health care system is approximately $17 billion annually, with the pro-

jected cost for the year 2040 to approach $50 billion (37, 38). These medical costs represent a greater burden than the annual costs of stroke, breast cancer, diabetes, or chronic lung disease (38). In the world the economic burden for osteoporotic fractures rises faster than the general rate of inflation in almost every country (34). Moreover, the indirect costs of osteoporotic fractures associated with morbidity and mortality, are substantial (1, 2, 16).

Treatment: conservative medical management, percutaneous vertebral augmentation techniques and surgical intervention

Conservative medical management

General medical management of VCFs includes calcium supplements with vitamin D and bisphosphonates with annual bone density studies to evaluate progression of osteoporosis. This therapy prevents the risk of other fractures (2, 37). Nonsteroidal anti-inflammatory drugs (NSAIDs), narcotics, muscle relaxants, and orthic bracing are useful for pain control (15, 16, 18).
The pain generally subsides from some weeks to some months, when a fracture heals; instead if the pain increases in intensity or becomes chronic probably this means there is a progression of the fracture (39) (Table I).

Surgical intervention

Surgical intervention is generally not considered because the potential surgical risks are further exacerbated by the increased age of the individual and the likelihood of comorbidities (15).

Percutaneous vertebral techniques and surgical intervention

Given the detrimental effects of nonoperative care and the morbidity associated to open reduction and internal fixation of vertebral compression fractures, there have been recent advances in minimally invasive modalities to treat these fractures. It is well-documented that 66% of patients who have vertebral compression fractures becomes asymptomatic after several months; it is important to remember that these fractures heal in a malaligned position, so it is important restore stability, anatomic alignment as soon as safely possible (27, 32). PV and BKP are minimally invasive techniques to stabilize the vertebral body and provide pain control. Both methods allow for the introduction of bone cement into the fracture site with clinical results indicating substantial pain relief in approximately 90% of patients (13). BKP also provides some restoration of the vertebral body height (15, 16, 18, 22, 27). Then, PV was introduced by Deramond, a French radiologist, in 1984, when he injected polymethylmethacrylate (PMMA) bone cement into a painful hemangioma (40). Then, vertebroplasty was developed as a way to stabilize vertebral compression fractures without inducing the morbidity and mortality associated to open surgery, injecting PMMA into the vertebral body (41). In 1997 it was introduced BKP, which has been developed to treat vertebral compression fractures (15). BKP is differentiated from PV because it involves the insertion of an inflatable balloon in the vertebral body, that creates a cavity to elevate the vertebral end plates; PMMA is then inserted in this cavity (33). The balloon used in BKP may allow for improved height restoration, cavity creation, and decreased cement leakage rates (5). The advantages of this procedure vs. PV include the height restoration of the vertebral body and a more controlled deposition of the PMMA in a cavity, thus decreasing the risk for cement leakage. PV and BKP have been shown to reduce the back pain resulting from vertebral compression fractures (15, 33, 41). The contraindications for PV and BKP are: neurological injury, a fracture with a cleft or vertebra plane fractures with a burst component,

Table I - Approved pharmacologic agents for treatment of osteoporosis.

Drug	Dose	Proven fracture reduction	Indication
Alendronate	70 mg weekly	Vertebral, hip, nonvertebral	Postmenopausal women, men; glucocorticoid-induced osteoporosis
Risedronate	35 mg weekly, 75 mg 2 days/month	Vertebral, hip, nonvertebral	Postmenopausal women, men; glucocorticoid-induced osteoporosis
Ibandronate	150 mg monthly, 3 mg IV every 3 months	Vertebral, nonvertebral	Postmenopausal women
Zoledronic acid	5 mg IV yearly	Vertebral, hip, nonvertebral	Postmenopausal women
Raloxifene	60 mg daily	Vertebral	Vertebral postmenopausal women
Teriparatide	20 mcg subcutaneously daily for 18 months	Vertebral, nonvertebral	Postmenopausal women

and healed, chronic compression fractures (33). Moreover, severe cardiac disease poses an additional risk that is cumulative because the PMMA contains a vasodilator agent that is rapidly absorbed systemically (33).

Selection criteria for vertebroplasty and balloon kyphoplasty

Indications for PV and BKP include acute, painful osteoporotic, osteolytic metastatic vertebral compression fractures, painful vertebral hemangioma and Kümmell's disease (33). They are not indicated if the bony destruction is greater than 90% or there is significant posterior wall destruction (15, 16, 42-44). Only the symptomatic fractures can be treated, as healed fractures are stable and do not cause pain (42, 43). Absolute contraindications are the presence of uncorrected coagulopathies and the presence of an active infectious process (15, 22, 42-44).

Technique of vertebroplasty

Galibert et al. introduced in France percutaneous PV in 1984 for the treatment of painful cervical hemangioma by the injection of polymethylmethacrylate (PMMA), bone cement (45). Subsequently VP was performed in United States in 1993 (30). VP is a minimally invasive procedure that in the last 10 years has been widely used to treat vertebral metastatic lesions and osteoporotic compression fracture (46, 47). This procedure has been recognized as an effective treatment for osteoporotic fractures refractory to conventional medical therapy (48, 49). In VP it is very important a good visualization of the needle placement and the cement application and this lowers the complication rate (50). Fluoroscopy is used to identify the pedicles and end plates of the vertebrae. The procedure was performed using single-plane fluoroscopy or biplane monitoring, CT fluoroscopy, a combination of CT and single-plane fluoroscopy decreases procedure time (51) and allows an accurate visualization of the needle position and cement distribution. The cement distribution is observed by direct fluoroscopic control (51).

VP can be performed under local anaesthesia in almost all patients (52), therefore, patients affected by cardiopulmonary diseases or suffering from other risk factors non-compatible with general anaesthesia can be treated. General anaesthesia is necessary only in patients undergoing multiple-level VP or unable to stay still during the treatment under local anaesthesia (52, 53). The antibiotic administration is indicated similar to open bone surgery that re-

quires PMMA implant (54, 55), particularly in patients with immune disease (54, 55).

VP is performed with the patient in a prone position with bolsters under the sternum and pelvis to reduce kyphosis at the fractured vertebra (56).

An extrapedicular or a transpedicular approach can be used to enter the vertebral body (57). The access path depends on the level to be treated. For lumbar vertebrae and lower thoracic spine treatment is preferred transpedicular approach, while in the mid and upper thoracic spine an extrapedicular, intercostovertebral access is suggested (58, 59). VP can be performed by unipedicular or bipedicular approaches. There are evidences that a unipedicular access when the needle tip is positioned in the anterior third of the vertebra across the midline is sufficient for a homogeneous cement distribution within the central part of the vertebra (60-62). This has been also shown in cadaver studies comparing stiffness of osteoporotic vertebral bodies after both approaches of VP (63). An angiographic analysis of the vertebral venous system before cement introduction has been suggested to identify potential routes of venous cement extravasation. However, some authors recommend venography only for hypervascularized lesions (52, 64). The cement flow changes over the time and it should be used during its tooth-paste like phase to reduce the possible extravasation in the surrounding tissue. Effectively, viscosity of the cement seems to be the key factor for reducing the risk of PMMA cement leakage and it should be adapted to the degree of osteoporosis encountered in each patient (65). It is extremely important to inject the barium-impregnated cement under live fluoroscopy or while using multiple single-frame fluoroscopic views (65). If occurs the extravasation of the cement from the vertebral body, particularly in the posterior part of the vertebral body next to the spinal canal, the procedure must be immediately halted and the situation assessed (65). A certain degree of cement extrusion from the vertebra can be tolerated without any deleterious effects for the patient, but there have been reported cases in which cement extrusion has caused neurological damage (33). The cement injection can be stopped when the anterior two/third of the vertebral body are filled and the cement is homogenously distributed between both endplates (54, 57). No data are reported on the cement volume that is necessary for good results about stiffness and reduction of complaints. However, it has been shown that 2,5-4 ml of cement provides good filling of the vertebra and it is sufficient for consolidation and pain relief (32). The introduced cement reaches its definitive strength after about two hours from the in-

tervention. Neurological and pulmonary function should be monitored and an increase of pain or other acute changes should be immediately evaluated to prevent complications or extravasations of the cement into spinal canal (59). The administration of anti-inflammatory drugs for 2-4 days can be useful to reduce possible inflammatory status due to the heat during PMMA polymerization (54).

Technique of kyphoplasty

BKP is the other procedure first performed in 1998 that restores the vertebral body height and improves clinical symptoms in patients with vertebral compression fractures from primary or secondary osteoporosis, trauma and neoplastic disease (66, 67). This technique uses inflatable bone tamps to restore the vertebrae structure (66, 67). Similarly to VP, BKP begins with prone positioning on a radiolucent table with bolsters and by using biplanar fluoroscopy guide (anteroposterior and laterolateral projection) to execute a safe procedure and to introduce the cannula through a minimal skin incision into vertebral pedicle and body (66, 67). Entry into the vertebral body is performed similarly to BKP, using an extrapedicular or transpedicular approach as described previously (3). Unlike VP, however, after the cannula is appropriately placed in the vertebral body, a hand drill is placed through the cannula with the goal to create a channel through which the balloons can be inserted into medullary space (3). Always with fluoroscopic guide the manual drill is used to penetrate the vertebral body and the penetration is stopped at a distance of 2-5 mm from the anterior vertebral wall (68), the manual drill is then removed and the inflatable balloons are inserted into the cannula and then connected to the contrast prefilled syringe (68). The balloons are placed in the cavity and inflated using a manometer with a digital pressure gauge.The balloons contain saline solution with barium in order it may be visualized under fluoroscopy as it is inflated (68). It is recommended to inflate the balloons under live fluoroscopy to ensure that they correctly reduce the fracture and don't damage the vertebral end plate (68). After the tip of the balloons are fluoroscopically checked they are slowly inflated in 20-50 PSI steps under radiological guide until the normal height of the vertebral body is restored or the maximal inflation volume of the balloons is reached (68). After a correct inflations the balloon(s) are removed and PMMA pre-filled cannulas are inserted into the working cannulas (68). When two balloons are to be used, most surgeons first place them both and then inflate them at the same time or alternatively ("back-and-forth") to prevent "herniation" of the first balloon to the contralateral side, thus preventing ideal placement of the second balloon (68). The consistency of the cement used for BKP is different than that for VP. For VP, the cement must be in a more liquefied state to permeate and spread into the vertebral cancellous bone, whereas for BKP, it can be in a more viscous or "doughy" state because it is deposited in a cavity created by the balloon. The volume of liquid used to inflate the balloon provides a general idea about the quantity of cement that will be required for each level. A cement cannula is advanced to the anterior part of the vertebral body by passing it through the working cannula. Fluoroscopy is used to confirm the location of the cannula. When the cannula is in a satisfactory position, cement is slowly deposited by pushing it out of the cannula with a blunt probe. As more cement is deposited into the cavity, the cement cannula should be pulled back slightly to allow cement to be injected into the posterior part of the cavity. The cement generally does not jeak unless it is too thin or there has been a breach in the vertebral cortex. When a cement leak (out of the intended cavity) is detected, the deposition should be stopped immediately and the cement allowed to harden for 1 to 2 minutes before slowly depositing it again under live fluoroscopic guidance. When the cement is hardened, the cannula can be removed and final imaging views can be taken.

Results

Vertebroplasty

Some of the patients treated with VP can feel pain relief immediately after treatment and a recent study, in which eighty-four percent (562/673) of VP procedures were performed for compression fractures related to osteoporosis, shows that after 2 h from VP procedure it occurs a significant decrease of pain, evaluated by VAS score (69). Normally significant pain relief occurs within 24 h after treatment (70). Numerous prospective and retrospective studies on VP have been published and described a high clinical success rate in up to 78% to 97% of patients suffering from osteoporotic VCFs (64, 71-75). A recent systematic literature review demonstrated the effectiveness of VP in 87% of patients in terms of pain relief as well as a short- and long-term improvement of function (76). A meta-analysis of the literature for treatment of vertebral compression osteoporotic fractures with VP, performed until up 2006 including prospective and randomized studies, identified 60 reports that provided specific data for VAS pain scores after VP (77). These studies provided data on 3,321 patients and 5,060 fractures. The mean preoperative and postoperative VAS scores (standard deviations) were 8.36 (0.78) and 2.68 (1.09), respectively (p<.001). The mean improvement in VAS score was 5.68 (1.24) (77).

Other authors report a mean reduction of pain evaluated by VAS from 8.9 to 3.4 for up to 10 years after VP, and improvement in walking of 65% (245 patients) (78), and others a 97 % decrease of pain from 8.9 to 2 (VAS) and 93 % of patients improve in walking (100 cases) (75). Recent data indicate a significant decrease in the mean pain scores from 8.36±1.21 (range 6 to 10) to 0.55±0.52 (P<0.05) (79). M.H.J. Voormolen et al. evaluated both pain decrease by VAS score and a comprehensive tool for spine related disability by Roland-Morris Disability Questionnaire (69). In this study the pain response was obtained after 2-hours from the procedure and showed a decrease of average rest pain from 4.5 to 1.7 and further lowering up to 1.2 after 2 years. A similarly average activity pain decreased from 8.4 to 3.6 and 3.2 was obtained after 2 hours and 24 years respectively (69). Significant improvement in the Roland-Morris score was also measured at the 1-week follow-up, and this was sustained throughout the 2-year follow-up period (69). The decrease in VAS score and Roland-Morris score was highly statistically significant at every follow-up time point, with a *P* value of <0.001 (69). This study reports also a relatively high rate of follow-up with assessments in 89%, 84%, 75%, 67%, and 62% of patients at 1 week and 1, 6, 12, and 24 months, respectively (69). Most patients also reported an improvement in their mobility, a decrease in pain medication usage, and a qualitative decrease or complete resolution of their pain throughout the 2 years of follow-up (69). Although VP is considered to be the treatment of choice for painful vertebral compression fractures, it should still be validated by a prospective randomized study. There are randomized prospective studies currently underway in the United States and internationally, such as the Investigational Efficacy and Safety Trial (INVEST) for the treatment of fractures due to osteoporosis (80) that will address this shortfall in the current VP research. It is only after the results of these studies are available that we can unequivocally state that VP has been validated as a treatment option for patients with painful compression fractures (80). However, the most performed studies did not have a control group to compare with. Only two non randomised controlled trials have been published comparing VP with conservative therapy (81,82). Both studies demonstrated a significant better improvement in pain scores after VP compared to conservative therapy on the short-term (81, 82). However, after 6 months no differences could be demonstrated (81, 82). Thus, the question on the balance between costs and effects becomes all the more pregnant (81, 82). No large randomized controlled trial (RCT) with mid-

term follow-up after VP procedure has been published (83). Now there is in progress a study of a multicenter randomized controlled trial to estimate cost-effectiveness in terms of: pain reduction, quality of life, complications, secondary fractures and mortality in VP versus conservative therapy in patients with osteoporotic vertebral compression fractures (12, 84).

It should be necessary to have other studies to evaluate the effects of VP versus open surgery or best supportive care (60, 85). Another question is on the persistence or the return of pain after PV; in fact, in some cases, from 5% to 22% of patients treated with VP for osteoporotic VCFs, no improvement of pain occurs, thereafter these patients underwent a repeated percutaneous VP. Very few data are reported in the literature on those patients who do not respond to the initial VP. Back pain in VCFs is likely to be associated with intraosseous or periosteal nerves worsened by motion at the fracture site (86-88). Up to date, the mechanisms involved in the pain relief after VP are not clear. Because fractured VB lose both strength and stiffness, pain relief can be due to factors such as: the fracture mechanical stabilization and restoration of vertebral strength and stiffness (3), the heat necrosis of the surrounding tissues and the nerve endings and the possible toxicity due to the cement (89, 90).

Continuous pain after an initial VP in the cases of osteoporotic VCFs may have other causes. For example, it is often possible that a new fractures occurs in the adjacent treated vertebrae (91,92). Spondylitis is another uncommon cause for unrelieved pain after an initial VP. This is a rare and serious complication related to VP, causing progressive pain, high fever, and positive radiologic findings after the procedure (93, 94). Surgical debridement to remove the infected tissue and the use of acrylic cement to stabilize the spine is usually necessary if a conservative treatment of antibiotic administration fails to work in the infected VP (93, 94).

Recently a retrospective study was performed in patients submitted to another percutaneous VP at the same levels previously treated with VP (73). In this study, it were performed 334 procedures of VP in 242 patients and 15 vertebrae in 15 patients with unrelieved pain were treated again with VP (73). Authors report that in these patients no new fractures after previous VP, but inadequate filling of cement in the unstable fractured areas of the vertebral body as responsible for the unrelieved pain after the initial VP (73). VP was performed in unilateral transpedicular access by a single injection of cement (73). The most important point is to position the needle in the responsible area for the pain within the previously treated vertebra and to fill it with a sufficient amount of cement (73). Complete and partial pain relief were reached in 11 (73%) and 4 patients (27%) respectively in a mean follow-up of 15 months (73). Authors conclude that it is technically feasible to perform again a VP a vertebra that was already treated with this procedure and it results effective in those patients who didn't have any pain relief from the previous operation (73).

Significant pain relief in 5 of 6 patients (83%) after the re-operation with VP is also reported by Gaughen et al. (49). These results indicate that the repeat VP might offer therapeutic benefits, not only for pain relief but also for improved mobility and elimination of analgesics within 24 hours after the repeat VP. No symptomatic complications were observed in these patients (49).

In conclusion, the data reported in literature suggest that VP not only decreases the pain and then the amount of necessary analgesics but improves the physical mobility and the quality of life (42). It has been shown that this treatment is useful also in the elderly (95) and in patients with severe osteoporotic fractures (96). Other studies demonstrate that for these patients the benefits of VP remain for a long period of time (97).

Then Pitton MB et al. investigated geometrical stability and preservation of height restoration of vertebral bodies after percutaneous VP during 2 years' follow-up and showed the geometric remodelling process of the vertebral body disk unit (VDU) of the affected segment (98). They enrolled patients with osteoporotic vertebral compression fractures with pain resistant to analgesic drugs. A total of 83 vertebral bodies of 30 patients (7 men, 23 women, age 70.7±9.7 years, range 40-82 years) were treated with VP (98). In the moderate compression group the vertebral heights were stabilized over time at the preinterventional level (52). Thus, posterior height loss of vertebrae and adjacent intervertebral disk spaces contributed to a remodeling of the VDU, resulting in some compensation of the kyphotic deformity of the affected vertebral segment (98). VP with PMMA cement improved vertebral geometry during midterm follow-up and has the potential for a sustainable anterior height restoration in cases with substantial compression fractures (98). In severe vertebral compression, significant height gain and improvement of end plate angles were achieved (98). The remodeling of the VDUs contributes to reduction of kyphosis and an overall improvement of the statics of the spine (98). Recently, Shin JJ et al. have investigated clinical outcomes, kyphosis correction, wedge angle, and restoration of thoraco-lumbar osteoporotic burst fractures treated with percutaneous VP (99). They successfully used the procedure as a safe treatment, and this method could avoid the need for and risks of major spinal surgery (99). Others performed a multicenter, randomized, double-blind, placebo-controlled trial in patients with one or two painful osteoporotic vertebral fractures (less than 12 months' duration and unhealed) were randomly assigned to undergo VP or a sham procedure (100). They found no beneficial effect of VP as compared with a sham procedure at one week or at 1,3 or 6 months after treatment.

Ballon kyphoplasty

A randomized, controlled study compared 149 patients that received Balloon Kyphoplasty treatment vs 151 patients with non surgical treatment, providing a I level of clinical evidence. The goal of this study was to outline the safety and the efficacy of BKP in reducing pain and improving quality of life. The results showed an improvement on SF-36 score, EQ-5D, Roland Morris, Back Pain (VAS) and Reduced Activity (Days) for both treatments but those who received BKP had statistically significant better outcomes. The follow-up was obtained at discharge from hospital and at 1, 3, 6, 12 months after the treatment. Only 2 serious adverse events related to the BKP procedure are reported. Balloon Kyphoplasty procedure didn't lead to a significant increase in new radiographic vertebral fractures (147).

Another prospective, controlled study examined the reduction of the incidence of new fractures in a group of patients that underwent a BKP procedure. This study outlines that there were significantly fewer patients with new vertebral fractures after 12 months in the BKP group (17,5%) than in the control group (50%).

A retrospective, single-centre study examined patients who underwent BKP for long-lasting clinical and radiological effects, including changes in vertebral body shape with 2-year follow-up (101). This study shows that BKP markedly improves pain, patient ability to walk with no support and without difficulty and need for pain medications; results remained unchanged or improved at 2 years postoperatively. Complete pain relief (VAS=1) was reported by 68% (n=51) of patients after 1 week and by 86% after 3-6 months postoperatively, and was maintained for 2 years (90%) (101). This study also provides radiographic evidence of a statistically significant improvement in vertebral height restoration, with >/= 10% height increases in 90% fractures and normalization of morphologic shape indexes that remain stable for at least 2 years following surgical treatment (101).

Subsequently a long-term prospective multicenter study of BKP examined elderly patients with back pain caused by osteoporotic VCFs. The study showed that BKP provided rapid, marked, and sustained (for at least 2 years) improvements in back pain, back function, and quality of life (102). The mean number of days spent in bed decreased markedly after BKP, this outcome is very im-

portant because are well documented the negative consequences of bed rest on elderly patients, including rapid reconditioning and further bone loss (103). The mean number of "limited activity days"(days when daily activities were limited because of back pain) decreased after BKP (101), and the satisfaction following BKP was high and persistent. The results of this multicenter study were very similar to those of numerous single-center studies (104-106). Quality of life was assessed using the SF-36 instrument from the Medical outcomes study (107). This study reported a rapid and marked improvement in SF-36. Several investigators have reported a clear improvement in overall SF-36 function scores in a large group of patients treated with BKP (108, 109). A recent study analysed elderly patients, an average mean of 72 years (range 65-82) with recent vertebral fractures (thoracic and lumbar fractures) (110).The patients had not neurological deficits and were followed up for an average of 13 months after surgery (110). The results were: the improvement of the kyphosis angle and of back pain. In conclusion elderly patients showed good early results (110).

BKP reduces spinal compression fractures and restores the sagittal alignment of the column. It has been proved to correct up to 97% of the deformity (compared with 30% with VP) in an ex vivo model (111). Then a recent prospective study evaluated the reduction of pain (evaluated by visual analogue scale VAS), improvement of sagittal alignment (Cobb and kyphosis angles, anterior, middle and posterior height, determined by CT scans), complications and intermediate term results of BKP, in the treatment of osteoporotic VCFs (112). The study group consisted of 87 patients with 145 VCFs, which were not responsive to non-operative treatment (112). These results indicate that BKP reduces pain and improves sagittal alignment in patients with VCF (56).

A study compared efficacy of BKP in restoring vertebral height and correcting Kyphosis in patients having vertebra plan with or without osteonecrosis (113). This study identified that patients with vertebra plan with osteonecrosis have the mean corrections of kyphosis and vertebral height higher than patients without osteonecrosis (113). Therefore the presence of osteonecrosis can be considered among the indications for BKP to restore vertebral height and correct kyphosis (113). A comparative study analysed the two techniques of unilateral and bilateral BKP in osteoporotic vertebral compression fractures (114). The authors found that the bilateral approach had a greater advantage in the reduction of kyphosis and loss of reduction was minor than the unilateral approach for the treatment of osteoporotic vertebral compression fractures (114).

Potential complications

Vertebroplasty

The complications can occur in both procedures, even if they are very rare, in fact the overall complications are 1%-6% for VP and about 1.2% for BKP (115). Recently the risk of major complications after VP seems to be less than 1% (116). Cement leakage and neurological injuries are reported with in both procedures and extravertebral cement leakage represents the major risk of VP (40%-65%) (5, 52), generally this is clinically asymptomatic (18, 60, 64, 117-119), cases of spinal cord and nerve root injuries due to cement leakage have been reported (2, 25-27, 32, 120-122). Recent results show that cement viscosity is the key factor for reducing this risk and suggest adapting the viscosity to the degree of osteoporosis encountered in each patient (73). Cement leakage in some cases 1% of the patients, can induce neurological compromise and radiculopathy and surgical decompression may be indicated (64, 123, 124). Complications due to dislocated cement into the vena cava, lungs, heart and also in the kidneys have been described (125). Pulmonary embolism has been reported only in VP and it seems related to the high-pressure injection that is required for this procedure (15).

Another important question after VP and BKP procedures in patients with osteoporosis is the development of fractures in adjacent level vertebrae, it should be related to the hardening of the vertebral body due to the cement placing the levels above and below at risk for further fractures (15). The NOF Prevalence Report (2002) stated that the risk of additional fractures after the first osteoporotic VCF is fivefold and both VP and BKP does not prevent additional VCFs (126). It remains unclear whether VP is associated with a higher risk of secondary VCFs in adjacent vertebral bodies. Some authors believe in an increased risk of new VCFs after PV compared to the natural fracture incidence in osteoporosis, probably caused by the increased stiffness of the cemented vertebral body (125, 127-130). The non-randomized study by Diamond reported no significant difference in the risk of new VCFs between VP and conservative therapy (81). Other authors have evaluated the incidence of secondary symptomatic VCFs after VP and their anatomical distribution in previous fractures (131). In this study a large cohort of patients is considered, 52 of 316 (16.4 %) patients (45 female, 7 male) returned to treat 69 secondary VCFs adjacent to (35/69; 51%) or distant from (34/69; 49%) previously treated levels. Adjacent secondary VCF occurred significantly more often compared to distant secondary VCFs. These data might suggest a higher susceptibility to future fractures induced by VP. This issue has been subject to debate in the literature (19, 8). This study reports 75% incidental fractures within the first 6 months after VP, and only 25% the years thereafter. Authors state that the rate found in secondary VCFs remains below the level expected from epidemiologic studies (13) and adjacent fractures occur more often and follow the cluster distribution of VCF as expected from the natural history of the underlying osteoporosis. In accordance to the pertinent literature, short-term and also midterm clinical results show a low complication rate of this procedure indicating that VP is a valid procedure in patients with severe midline back pain due to osteoporotic spine fractures (131). Main risk factors for new VCFs after VP have been prevalently associated to the proximity to the treated vertebra, greater kyphosis correction, and low patient body mass index; these factors suggest osteoporosis is mechanism for new fractures (132, 133).

Some authors showed that thoracolumbar vertebrae adjacent to a Vertebroplasty treated site have a higher incidence of new compression fracture than do other vertebrae (134). Other complications after VP include bleeding at the puncture site, pedicle fracture, local infection, nerve root injury (59, 126, 135).

Balloon kyphoplasty

Several different studies have reported 10% extravertebral cement leakage in BKP without any clinical consequences or leakage into the spinal canal (33, 136-138). In an interesting study it was discovered that only 34% of intraoperative cement leaks are discovered using lateral fluoroscopy the detection rate increases to 48% (139).

In the retrospective single-center study, Lidlie et al. showed that there were no Ballon Kyphoplasty related adverse events observed (101). Cement extravasion occurred in 11,3% (151 fractures) but did not result in any clinical consequences (101). Other studies report the incidence of cement leaks between 0% and 33%, with only rare complications (105, 140-143). There have been no reported cases of pulmonary embolism as a result of cement extravasation with BKP (118).

In the long-term prospective multicenter study of BKP, Garfin et al. showed that the extravasion of polymethylmethacrylate outside the vertebral body occurred in 21/214 VCFs (10%) of treated levels (102). The polymethylmethacrylate extravasations were asymptomatic, the cement remained in the immediate area of the treated vertebrae, and no medical or surgical intervention was required to remove the leaked polymethylmethacrylate (102). A subject with pre-existing heart disease had a myocardial infarction 28

days after the procedure (102). No one of them was deemed to be procedure related (102). There was one subject who had three rib fractures while being moved intraoperatively (102).Subsequent fractures occurred in 20% vertebrae at one year and in 23% at two years (119). The majority (61%) were adjacent-level fractures (119). No deviced-related or procedure-related complications occurred during the 24-month follow up period (119). Voggernreiter et al. observed in their prospective study of 87 patients with 145 VCFs asymptomatic leakage of cement in 28 out of 145 vertebrae (19,3%) (112). There were 4 new symptomatic fractures and 5 clinically asymptomatic (only seen on CT) fractures, 7 fractures were adjacent to and 2 fractures were remote from the initially treated level (112).

In a prospective multicenter study, a major complication rate of 1.1% has been reported; of these complications, 0.75% were neurologic complications (33, 108). A study of 360 procedures of BKP in 222 patients reported 38 cement leaks (11% of procedures), with one resulting in an episode of radicolupathy.

Balloon kyphoplasty and vertebroplasty

Pasquale De Negri et al. enrolled in a prospective twenty-one patients, who underwent BKP and VP, in a prospective nonrandomized study with painful compression fractures resistant to common therapies, such as analgesic use, bed rest, and bracing (144). No significant differences could be found between both groups for the mean VAS and ODI (Oswestry disability index) scores pre-procedure and post procedure (144). Cement leakage outside the vertebral body was observed only during VP, in 37,6% of the treated patients (144).

Zhou J L et al. observed 98 patients with VCFs treated treated with VP (n=42) or BKP (n=56) (145). Their results suggest no significant difference in VAS, operation time and blood loos between two groups (P<0.05), but a statistical difference between two groups in the recovery of vertebral height after operation (P<0.01), BKP resulted superior in the recovery of vertebral height (145). An other study observed in VP group5 cases of bone cement leakage into anterior border of vertebral body, and leakage into the spinal canal in one case; in BKP group, 3 cases of bone cement leakage into anterior border of vertebral body, but no leakage into the spinal canal (145).

Hiwatashi et al. compared restoration of vertebral body height, wedge angle and cement leakage in BKP and VP in osteoporotic compression fractures (146). Forty patients (51 vertebrae) were treated with BKP, and 66 patients (124 vertebrae) were treated with VP (146). Cement leakage into the disk space and paravertebral soft tissues or veins was analyzed on immediate postoperative CT scans (146). The height and wedge angle were measured before and after treatment and analyzed with the Mann-Whitney *U* test and χ^2 test (146).

Both BKP and VP improved vertebral body height and the wedge angles (146). There was no statistically significant difference between the 2 techniques, and no complications related to cement leakage were observed (146). BKP resulted in less cement leakage into the disk space and paravertebral soft tissues or veins compared to VP (146).

Summary

The procedure of VP and BKP can stabilize osteoporotic vertebral compression fractures that in the past were treated nonoperatively due to the morbidity of open surgery. These minimally invasive techniques are both useful in the treatment of painful progressive osteoporotic compression fractures (using VAS and ODI), improving the quality of life. Numerous studies have shown that there aren't significant differences between BKP and VP in functional outcomes, ability to walk, operation time and blood loos. Some authors stated that BKP resulted superior in the recovery of ver-

tebral height; others don't show statistically significant differences between the two techniques in the improvement of vertebral height and the wedge angles. Some authors found that the bilateral approach had a greater advantage in the reduction of kyphosis and loss of reduction was minorthan the unilateral approach for the treatment of osteoporotic vertebral compression fractures. The complications can occur in both procedures, even if they are very rare, in fact the overall complications are 1%-6% for VP and about 1.2% for BKP. Cement leakage and neurological injuries are reported in both procedures and extravertebral cement extrusion constitutes the major risk, but BKP resulted in less cement leakage into the disk space and paravertebral soft tissues or veins compared to VP. Recent results show that cement viscosity is the key factor for reducing this risk and suggest adapting the viscosity to the degree of osteoporosis encountered in each patient. Pulmonary embolism has been reported only in VP and it seems related to the high-pressure injection that is required in the procedure. In conclusion we can say that both procedures, VP or BKP, are clearly effective treatments for painful progressive osteoporotic compression fractures. Future studies will clarify if the choice of procedure could be made based on the fracture configuration or on other clinical or radiographic parameters.

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