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Percutaneous Vertebroplasty for Pathological Vertebral Compression Fractures Secondary to Multiple Myeloma – Medium-Term and Long-Term Assessment of Pain Relief and Quality of Life

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. In patients with multiple myeloma (MM) there is a high risk of compression fractures of the spine. In the majority of cases, the method of treatment is percutaneous vertebroplasty (PV) or kyphoplasty (PK). The number of studies verifying their efficacy in MM is still relatively small.
Objectives. The aim of this study has been to assess medium- and long-term pain relief as well as improvement in the quality of life (QL) after PV in MM cases.
Material and Methods. There was a prospective group of 34 MM cases in which a total of 131 vertebral bodies were augmented by means of PV. It was possible to follow up 22 patients who agreed to take part in the assessment. Their level of daily activity and the level of pain were assessed using the Oswestry Back Pain scale and a visual analogue scale (VAS) before PV and at a later date (medium-term follow up was a mean of 10 months after the last operation). Five out of eight cases in which 4.5–5 years had elapsed since the first PV were tested again (long-term follow-up).
Results. Relief of pain and improvement of QL, assessed a mean of 10 months after PV, proved to be statistically significant. On the average, pain decreased by 4.7 points as measured on the VAS scale and the average improvement in the QL measured on the Oswestry scale was 27.7%. There were no neurological or general complications. After 4.5–5 years, there has not been any significant change in the level of pain relief or the improvement in the QL in the 5 cases in which long-term assessment was possible.
Conclusions. In MM cases, PV is a simple, effective and safe method for the treatment of vertebral infiltration and compression fractures, giving permanent long-term pain relief and concomitant improvement in the QL (**Adv Clin Exp Med 2015, 24, 4, 651–656**).

Key words: myeloma, vertebroplasty, vertebral fractures.

Percutaneous vertebroplasty (PV) is a method of injecting polymethylmetacrylate cement (PMMA) into a collapsing vertebral body. PV was developed in the late 1980s and was first described in 1987 by Galibert and Deramond for the treatment of a hemangioma of the C2 vertebral body [1]. Percutaneous kyphoplasty (PK) is a modified augmentation technique in which a space for the cement is prepared beforehand, using an inflated balloon. The expected potential advantage of PK was that the restoration of vertebral height by means of a balloon would improve the axis of the vertebral column and therefore reduce the angle of kyphosis [2]. Regardless of the method used, PMMA augmentation of the vertebra seems to be a perfectly reasonable procedure when the aim is to prevent spinal disability in osteoporotic fractures, selected traumatic compression fractures, vertebral metastases and multiple myeloma (MM) infiltration.

Depending on their severity, vertebral lesions can produce various signs: kyphosis of the thoracic spine may manifest itself in local and/or radicular pain followed by hypoventilation, while kyphosis in the lumbar region may give rise to local pain or signs of compression. Pain radiating around the abdomen can cause increased abdominal pressure, and in advanced cases can lead to malnutrition. The aim of PV/PK treatment is to relieve pain and prevent any further deformation of the spine. It is the accompanying exothermic reaction that is responsible for the pain relief brought about by the use of this technique. In neoplastic cases, shrinkage of the tumor mass and potential prevention of proliferation are also significant treatment factors. Primary infiltration of the vertebra occurs quite often in MM, and in about 30% of cases can lead to compression fractures [2]. As improvements in the effectiveness of MM treatment are prolonging the lives of these patients, it is increasingly important to ensure pain relief and stability of the spine in order to achieve better quality of life (QL). Improved QL also contributes to the patient's ability to maintain a positive attitude in the fight against MM and a good tolerance of chemotherapy.

Although PV and PK are used quite frequently, the number of studies verifying their efficacy in MM is still relatively small. The post-procedure follow-up time is usually between 6 months and 1 year – rarely longer – but no more than 4 years.

The aim of the present study was to assess medium- and long-term pain relief as well as the improvement of the quality of life after PV in a series of MM cases involving vertebral fractures.

Material and Methods

There was a prospective group of 34 MM cases in which a total of 131 vertebral bodies were augmented by means of PV. Seven cases were excluded from the study, as death occurred before the completion of follow-up owing to the progression of the disease. Of the remaining 27 patients (81.5% of the original number), 22 responded to a request to take part in the assessment (medium--term follow-up between 6 and 18 months – a mean of 10 months after the last surgical procedure): 11 males and 11 females aged between 38 and 79, the average being 61. To date, another 7 patients have died. In 8 of the remaining 15 patients, 4.5 to 5 years have elapsed since the last PV. Five patients responded to a request to take part in further (i.e. long-term) assessment.

Using the Oswestry and visual analogue (VAS) scales, levels of life activity and pain were assessed by means of relevant questionnaires before surgery and in the medium- and long-term periods [3]. The results were subjected to statistical analysis. Normal distribution of variables was checked using the Shapiro-Wilk test. The *t* test was used to compare 2 dependent groups with a normal distribution of dependent variables. The Wilcoxon test was used to compare 2 dependent groups if normality was not observed. The Friedman test was used to compare 3 dependent groups without a normal distribution of variables. Results with a p-value of less than 0.05 were considered statistically significant.

All the calculations were performed using STATISTICA 10 PL software (StatSoft, Inc., USA), licensed to Jagiellonian University, Kraków.

In all cases, the PV procedures were performed under local anesthesia and neuroleptic analgesia (NLA). Under biplanar fluoroscopic control, a one- or two-portal approach was used, *via* the extrapedicular or transpedicular route, respectively. In most cases, a unilateral approach was sufficient. It was of paramount importance to reach the anterior third of the vertebra with the tip of the needle — close to the midline, using the unilateral approach (in the A-P view), and symmetrically, using the bilateral approach. The injection volume of PMMA ranged from 4 to 7 mL, depending on the size of the vertebra and the level of the vertebral column: a lesser volume is needed for the thoracic spine and a greater volume for the lumbar spine. The procedures were carried out using Synicem® (Biomet), Confidence® (Johnson) and Autoplex® (Stryker) sets. The procedure was halted when leakage was observed outside the vertebra, and was restarted 1 or 2 min later. It was possible to carry out an augmentation of between 1 and 4 vertebral bodies during one session. The patients were able to stand up on the day of the surgery. Standard antibiotics and anticoagulants were administered intravenously in prophylactic doses. The number of sessions varied from 1 to 5, and the augmented levels from 1 to 11.

Results

At the beginning of the assessment, most of the 22 patients reported intense pain which greatly impaired the quality of their lives, preventing them from performing basic daily activities. The reported values varied from 12% to 98% (a mean of 56.6%) on the Oswestry scale and from 3.4 to 10 points (a mean of 7.8) on the VAS scale. Three patients were unable to get out of bed without assistance.

At the medium-term follow-up (a mean of 10 months after surgery) in 19 out of 22 cases, significant pain relief according to the Oswestry scale was observed, accompanied by an improvement in

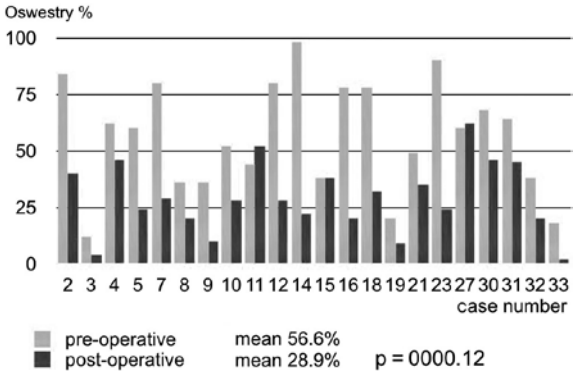

Fig. 1. Medium-term follow-up according to the Oswestry Scale

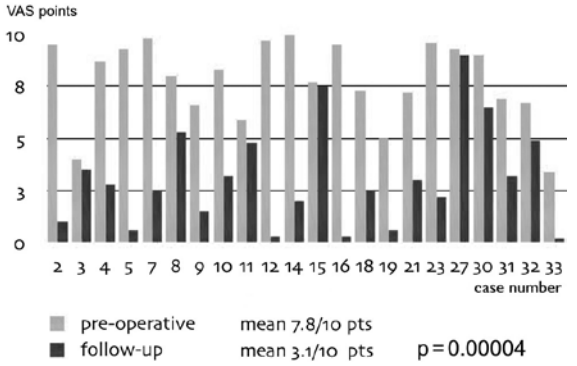

Fig. 2. Medium-term follow-up according to VAS

daily activity. Two patients deteriorated and one remained unchanged. The average pre-surgery value of 56.6% on the Oswestry scale decreased significantly during the course of the study to a level of 28.9% (p = 0.000012), giving an average improvement of 27.7%. There was also a significant decrease in pain perception. As measured on the VAS scale, pain decreased by 4.7 points after a mean period of 10 months: the average pain was 7.8 points prior to surgery, dropping to 3.1 in the follow-up (p = 0.00004). There were no neurological or general complications, with the exception of a transient increase in body temperature (> 38°C) in one patient (Fig. 1 and 2).

For the group of 5 patients who were assessed between 4.5 and 5 years after PV treatment, the level of pain relief remained practically unchanged since the first follow-up (p = 0.24198 for VAS). In 3 out of 5 cases, daily activity assessed by means of the Oswestry scale worsened, though not significantly (p = 0.10881) (Fig. 3 and 4).

Discussion

PV is performed when it can reduce pain and/ /or inhibit the progression of pathological fractures of vertebrae. The method is also useful if an

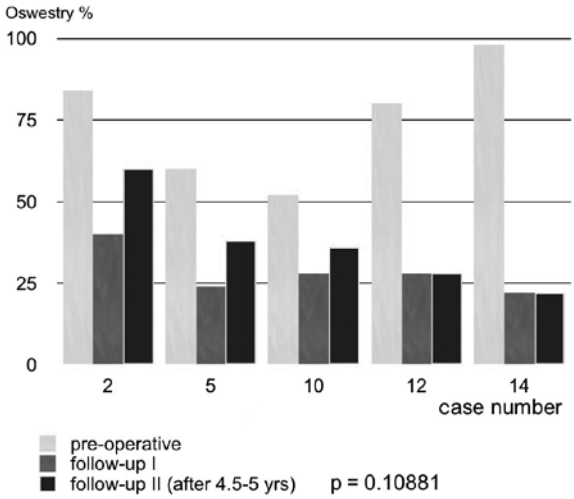

Fig. 3. Long-term follow-up according to the Oswestry Scale

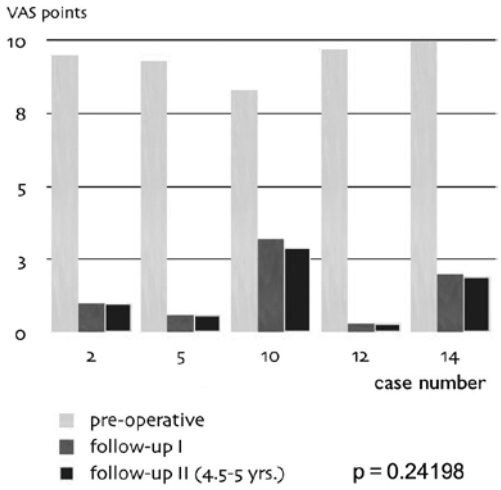

Fig. 4. Long-term follow-up according to VAS

infiltrating mass is found in a vertebra that does not decrease its height, as prophylaxis against expected fracture and instability. It is important to exclude the presence of tumor masses in the spinal canal or in the vertebral foramen, especially in patients with neurological deficits. In such cases, vertebroplasty may be of limited use and decompressive surgery should be considered, with or without appropriate instrumentation to stabilize the spine.

According to the guidelines of the International Myeloma Working Group [2], the indications for PV are as follows:

– when severe pain is present (exceeding 7/10 on the VAS scale) and there is collapse of one or more vertebrae, or bone destruction with a high risk of fracture (one or more vertebrae);

– when pain is absent (not exceeding 7/10 on the VAS scale) and there is significant loss of vertebral height and/or violation of the structural integrity or stability of the spine.

It is important to start treatment as soon as possible, i.e., before the onset of spinal deformity. Apart from rapid pain control, early vertebroplasty significantly improves the quality of the patient's life and precludes the need for the implementation of complementary treatments such as radiotherapy [4] and analgesic drugs. Additionally, it does not interfere with systemic bone marrow suppressive drug therapy [2]. The results of the procedure also have a significant impact on the implementation of adequate physiotherapy.

Between 1 and 4 levels of the spine are usually treated during a single PV procedure. However, multilevel augmentation requires that the patients lie in a prone position for a considerable length of time. And this is not always possible on account of the ensuing discomfort and pain. Absolute contraindications for VP include clotting disorders, pregnancy, infection at the planned injection site, allergy and contraindications for general or local anesthesia [2, 5]. Although most authors believe that destruction of the posterior wall of the vertebra and penetration of a tumor into the epidural space is a contraindication for PV, successful vertebroplasty in such situations has been reported [6]. However, extensive infiltration into the spinal canal or excessive destruction of the vertebral body – especially if it is accompanied by a resulting neurological deficit – would disqualify a patient for VP. Severe collapse of the vertebrae hinders the procedure, but does not preclude it [5].

Vertebroplasty can be performed under general or local anesthesia – or sedoanaglesia using intravenous anesthesia and 1% lidocaine at the injection site. Although general anesthesia affords the patient more comfort, local anesthesia allows him or her to maintain verbal contact with the surgeon. This is particularly important during the insertion of the needle. If the positioning is incorrect, the patient may report radicular pain, which allows immediate correction. In practice, sedoanalgesia is sufficient in almost all patients.

Radiofluoroscopic control is necessary in order to carry out PV. The anterioposterior and lateral positions are commonly used. However, the procedure can also be performed using computed tomography guidance.

The most common injection technique is basal placement of the needles either on one or on both sides – whichever is possible at the levels of Th3-L5. Because of their anatomical structure, higher levels of the spine (above Th2) make the use of the percutaneous technique much more difficult. Procedures involving the cervical and upper thoracic spine have been described: C2 using the anterolateral puncture method [7], and Th1 using the open method with anterior access [8].

The rate of symptomatic complications ranges from 2% to 6.8% [9, 10]. Complications can arise from leakage of the cement outside the vertebrae. Although this occurs quite often, it does not usually result in clinically significant symptoms of compression [11, 12]. Penetration of the cement into the paravertebral veins can be dangerous, however, as it may lead to the rare complication of pulmonary embolism (in 1.7% of cases). Hematoma at the injection site and puncturing of the pleura are very rare.

In cases of infiltration of the spinal canal, which often results in neurological deficits, decompressive surgery should be considered, as well as stabilization of the spine with the use of implants. The results of such treatment are not good, however: in patients who cannot move prior to surgery, only 38% report a significant improvement in their neurological status, while 62% of all patients report diminished mobility, notwithstanding decompression of the spinal cord [13].

The proportion of patients with good analgesic results after VP is high, ranging from 67% to 100%, while up to 70% report an improvement in active locomotion [4, 9, 12, 14–16]. The percentage of patients in the present study who reported a significant reduction of pain was as high as 92.3%. All 28 articles published to date have reported rapid, substantial and consistent pain relief and concomitant improvement in the quality of life [16–23]. In the current study group, pain – as measured on the VAS scale – decreased by 4.7 points after a mean period of 10 months. In 23 published studies that provided acceptable statistics, the decrease in pain was 4.6 VAS points over one year of observation [19].

Long-term assessment – i.e., more than 4 years after surgery – is difficult, owing to the course of multiple myeloma and the mortality associated with the disease. In all 28 of the available studies involving thoracic and lumbar augmentation in MM, late follow-up has not exceeded 4 years after the first surgical procedure. The present authors have been able to assess 5 patients between 4.5 and 5 years after PV treatment. In these cases, the reduction in pain has been maintained, while the quality of life as measured on the Oswestry scale has slightly deteriorated, though to a statistically insignificant degree. At this stage, these findings cannot be definitive owing to the small number of patients who have been observed.

Percutaneous kyphoplasty (PK) is also commonly used for the treatment of myelomatous vertebral compression fractures. However, the effects are comparable with PV and no conclusive data exists to suggest the superiority of PK as far as pain relief is concerned [19, 24, 25]. PK would seem to be

beneficial from a mechanical point of view in order to reduce the angle of kyphosis. However, there is a lack of evidence to suggest that the quality of life of patients who have been treated using this procedure is any greater than that of those who have been treated using percutaneous vertebroplasty.

Another way to treat MM infiltration of vertebral bodies is radiotherapy. Using this method, one can limit the infiltration of the cancer, but recent studies have shown that in patients who have had PV, radiotherapy does not improve their condition as far as the vertebral column is concerned, either in terms of analgesia or in terms of treating the underlying disease [26].

The overall results of PV are better in myeloma and metastatic cases than in patients with osteoporotic fractures. Recently, two double-blind randomized studies have been reported, both focusing on osteoporotic cases – one comparing PV with a sham intervention involving no injection of cement and the other comparing PV with conservative treatment [27, 28]. Surprisingly, these reports suggest that PV is no better than a sham procedure as far as relieving pain or improving function for patients with vertebral fractures is concerned. This positive placebo response is certainly difficult to explain. In all probability, the response to the placebo was encouraged by the same ritual in both procedures, a positive attitude towards the surgeon on the part of the patients and also their high expectations concerning the anticipated benefits of PV. On the basis of the placebo response hypothesis, therefore, the risk-benefit ratio of PV would not appear to be very favorable. However, these findings cannot be extrapolated to include myeloma cases, where the pathology of the disease is quite different: In MM, progressive bone destruction is associated with the failure of new bone formation [29].

In two other randomized and controlled studies that compared the efficacy of PK and PV with traditional conservative non-surgical management (the FREE 2009 and VERTOS 2010 trials [30, 31]), the authors concluded that improvement in the quality of life in the kyphoplasty group was greater than in the non-surgical group, and also that the pain relief afforded by vertebroplasty was significantly greater.

On the basis of data from the literature concerning the results of PV in MM [4, 12, 14–16, 18, 20–24, 26, 29–31] and also on the basis of the present authors' own clinical observations, which show that there is a huge number of patients who are very satisfied with the results of this treatment, it can be concluded that for the time being, at least, it need not be abandoned.

The author concluded that PV is a minimally invasive and relatively safe vertebral augmentation procedure for symptomatic vertebral body lesions in cases of myeloma. In the majority of cases presenting myeloma infiltration and a collapsing vertebral body, vertebroplasty is an excellent method of achieving pain relief and improving the quality of life. Long-term assessment has shown consistently good results, though a greater number of patients must be observed in order to determine whether this is really the case. The current authors' own results, along with data from the literature, have shown that this treatment should be continued, as – unlike the case of PV in patients with osteoporosis – its effectiveness has yet to be called into question.

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