VERTEBRAL AUGMENTATION VERSUS CONSERVATIVE TREATMENT IN OSTEOPOROTIC SPINAL COMPRESSION FRACTURES: A LITERATURE REVIEW

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ABSTRACT

Background: With greater life expectancies the incidence of osteoporosis is increasing across the African continent. Post-menopausal females are especially at risk and an increasingly common presentation to the orthopaedic surgeon are elderly female patients presenting with symptomatic osteoporotic vertebral compression fractures. Traditional management has for decades been a variable period of bed rest followed by progressive mobilization according to pain. Newer minimally invasive spine procedures, under the umbrella term vertebral augmentation, include vertebroplasty and balloon kyphoplasty and are claimed to shorten the period of bed rest allowing earlier mobilization and earlier functional recovery. We aimed to assess the effectiveness and benefit of these procedures by comparing the results of recently published randomized clinical control trials that compared them to the conservative approach more commonly employed.

Data source: We conducted a Pubmed and Medline search using the words "Postmenopausal women vertebral augmentation"; "Postmenopausal women kyphoplasty"; "Postmenopausal women vertebroplasty" and "Postmenopausal vertebral compression fractures". We limited the articles chosen to include only large randomized clinical control trials published in the last 5 years. In total only four suitable articles that met the criteria for this stringent review were chosen.

Results: Comparing percutaneous vertebroplasty versus the conservative approach the studies unanimously report a significant reduction in immediate and early post-operative pain allowing earlier mobilization. This benefit is however inconsistently significant at as early as 6 weeks follow-up and largely insignificant at 1-year follow-up. Comparing percutaneous vertebroplasty versus percutaneous kyphoplasty there is no significant difference in outcome.

Conclusion: While vertebral augmentation procedures have added immediate and short-term benefit to patients with symptomatic osteoporotic vertebral compression fractures they have, in practice, failed to add significant intermediate and no long-term benefit. Medical management aimed at prevention, combined with the conservative approach in patients that incur these fractures, remain fundamentally entrenched as the cornerstones of modern-day treatment.

Key words: Osteoporotic vertebral compression fractures, Vertebral augmentation, Kyphoplasty, Vertebroplasty

INTRODUCTION

Osteoporosis is a chronic condition in which overall bone density decreases resulting in thin, brittle, fragile bones (1). The disease is especially prevalent in postmenopausal women where reduced estrogen levels result in progressive cortical bone loss. Following menopause there is an alarming 25-30% decline in bone mass over the immediate 5-10 years (2). The disease has a high incidence affecting 1 in 4 women over the age of 50 years (1). Taking a global perspective, the highest incidence of osteoporotic vertebral compression fractures is noted in Scandinavia where up to 26% of women are diagnosed with this problem at some point in their lives. In North America the incidence is only marginally less with 20-24% of the Caucasian population over 50 years of age being affected. The incidence in South America is considerably less with an incidence of only 11-19% in women over 50 years of age (3). In Australia, approximately 111 per 100 000 women are affected with osteoporotic vertebral compression fractures per year which translates into an estimated 2078 symptomatic vertebral compression fractures occurring each year (4). In Southern Africa the exact incidence is unknown however this is regarded as lower than the rates recorded from countries in the Northern hemisphere.

Vertebral compression fractures are two times more prevalent than hip fractures (4). These fractures cause constant back pain, kyphosis, and are a major cause of morbidity (Figure 1). Historically, and still widely utilized to date, the traditional treatment of stable vertebral compression fractures is conservative with a period of bed rest followed by progressive mobilization. Measures employed in the conservative regimen include analgesics such as NSAIDS, calcitonin and acetaminophen. Other types of non-surgery treatments include physical therapy, bracing,

and caudal and nerve root blocks. A significant proportion of patients managed conservatively still however continue to experienceconsistent axial pain at 6 - 8 weeks (3,4).

Vertebral augmentation procedures, which include kyphoplasty and vertebroplasty, were developed to help improve pain caused by vertebral compression fractures and thereby allow earlier mobilization. Vertebroplasty is the process of injecting bone cement percutaneously into the cancellous bone of the vertebral body. This allows for relief of pain and causes a reduction in further vertebral body collapse (5). Kyphoplasty was developed primarily to avoid the morbidity of vertebroplasty and has the additional benefit of restoring vertebral fracture height. Kyphoplasty uses an inflatable balloon which is placed into the vertebral body and causes compression of cancellous bone thereby producing a cavity for the bone cement (5) (Figures 2-7). Kyphoplasty and vertebroplasty have both been demonstrated to be effective minimally invasive techniques effectively reducing pain in vertebral compression fractures (6). Kyphoplasty in particular provides not only pain relief but is also safer than vertebroplasty and additionally more effectively reduces the degree of kyphosis (5).

Figure 1

Pre-operative X-ray of a typical osteoporotic vertebral wedge compression fracture

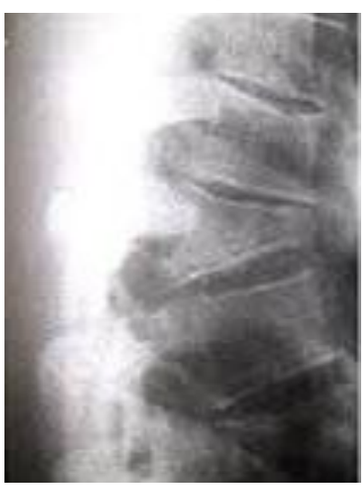


Figure 2

Intra-operative patient positioning for vertebral augmentation- biplanar fluoroscopy is necessary

Figure 3

Intra-operative patient photograph of a vertebral augmentation procedure which is a percutaneous procedure performed under fluoroscopic guidance

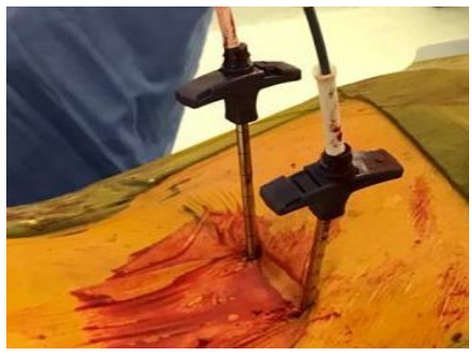


Figure 4

Intra-operative postero-anterior X-ray showing kyphoplasty procedure where 2 balloons are inflated within the collapsed vertebral body to correct segmental kyphosis and create a cavity for the introduction of the bone cement

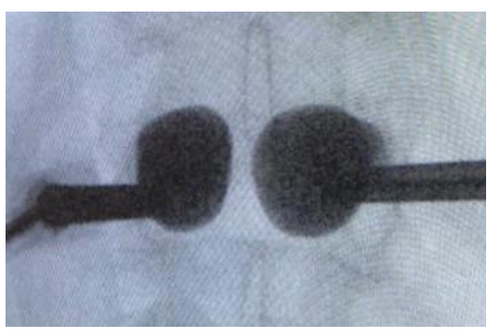


Figure 5

Intra-operative lateral fluoroscopic X-ray showing kyphoplasty procedure with balloons inflated

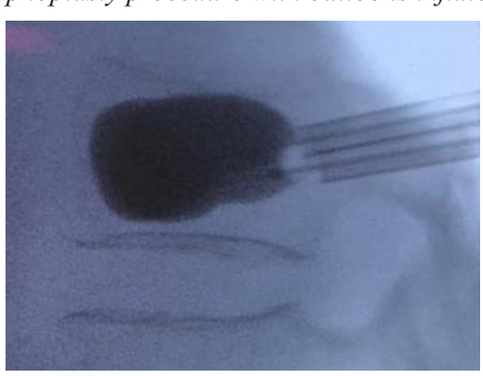


Figure 6

Intra-operative lateral fluoroscopic X-ray post kyphoplasty showing vertebral body height restored and bone cement filling cavity created by the balloons

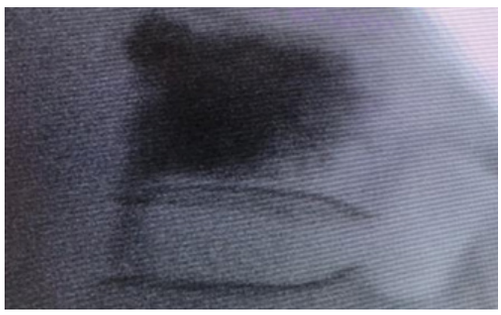
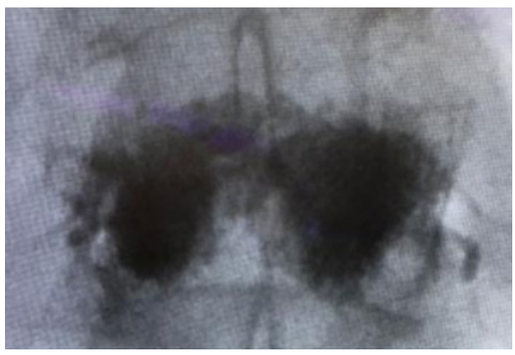


Figure 7

Intra-operative postero-anterior X-ray fluoroscopic image post kyphoplasty showing bone cement filling cavities created by the balloons



MATERIALS AND METHODS

We conducted a PubMed and Medline search using the words "Postmenopausal women vertebral augmentation"; "Postmenopausal women kyphoplasty"; "Postmenopausal women vertebroplasty" and "Postmenopausal vertebral compression fractures". The articles chosen were all large randomized clinical control trials and we limited these to studies conducted in the last 5 years. Our focus population comprised trials that enrolled postmenopausal women (>55 years old) with vertebral compression fractures due to primary osteoporosis. All participants included in the study had vertebral compression fractures secondary to primary osteoporosis. The participants were all 60 years and older and therefore almost exclusively comprised postmenopausal females. The intervention group underwent vertebral augmentation, either balloon kyphoplasty or percutaneous vertebroplasty, whereas the control group were restricted to have undergone conservative treatment.

Studies that involved vertebral compression fractures due to a malignancy were excluded from the study. Studies with large sample sizes were chosen. The bigger the sample size the greater the chances of determining whether the intervention was effective or ineffective i.e. more reliable results obtained, reducing any uncertainty. Qualitative studies, publication dates greater than 5 years, studies with small sample sizes, letters and comments to the editor, non-English academic journals and editorials were all excluded from the study. Postmenopausal women who had experienced secondary osteoporosis, females with any current or past malignancies, and females with previous spinal surgeries were all excluded from the study. In total four articles were chosen for inclusion in this review and below is a table of the study design and the level of evidence for each.

Levels of evidence

(i) Large randomized clinical control trials with clear cut results or systematic review of these articles

(ii) Small randomized clinical control trials with unclear results or systematic reviews of these articles

(iii) Prospective cohort and case-control studies or systematic reviews of these articles

(iv) Historical cohort or case-control studies of systematic reviews of these articles

(v) Case series, studies with no controls or expert opinion

Author (year)	Study design	Level of evidence
Yang E *et al*. (2016)	Large RCT	I
Balkarli H *et al.* (2016)	Large RCT	I
Leali P *et al*. (2016)	Large RCT	I
Dohm *et al*. (2014)	Large RCT	I

(Adapted from: Sackett DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1989; 95:2S–4S).

RESULTS

A prospective randomized clinical control trial from China compared percutaneous vertebroplasty versus conservative treatment noted the complications of vertebroplasty, such as cement extravasation and pulmonary embolism, however the study reported that these complications did not significantly influence clinical outcome (7). This study reports that though percutaneous vertebroplasty was unable to completely cure kyphosisit it did prevent further progression, whereas conservative treatment did not. One day after percutaneous vertebroplasty treatment the interventional group had a highly statistically significant reduction in pain compared to the conservative group ($p<0.0001$). This furthermore translated into a day one post the procedure benefit in mobilization with all 66 (100%) subjects who had undergone vertebroplasty being able to stand up and walk (with a brace and assistance) compared to 12/69 (23.5%) at 2 weeks in the conservative group (7).

A similar prospective randomized clinical control trial from Turkey also compared percutaneous vertebroplasty versus conservative treatment in the treatment of acute osteoporotic compression fractures and challenges the long-term benefit of the procedure. In this study 83 subjects were enrolled and 37 were assigned to conservative treatment and 46 were assigned to percutaneous vertebroplasty. Immediate post-operative pain as well as pain at follow-up utilizing the visual analogue scale and the Owestry disability index were the outcome measures employed. Similar to the results of the study above all 46 (100%) in the interventional group reported a significant immediate reduction in pain post the procedure. This benefit in pain relief as well as the benefit in functional outcome in the interventional group persisted at the 1-month and 3-month follow-up appointments. At the 6-month follow-up appointment there was no statistically

significant difference between the two groups and hence the study concludes percutaneous vertebroplasty to offer improved immediate and short-term benefit, but that this benefit does not persist at 6 months (8).

Another multi-center prospective randomized clinical control trial from Italy that enrolled 400 subjects further challenges the benefit of percutaneous vertebroplasty at an even shorter follow-up period. In this study 200 patients with osteoporotic compression fractures were assigned to percutaneous vertebroplasty and 200 similar patients were assigned to conservative treatment. The visual analogue scale and the Owestry disability index were again used as outcome measures. The results of this multi-center study echo the two previous trials by confirming the significance of the immediate reduction in pain ($p<0.023$), as well as the significance of the immediate improved functional outcome ($p<0.012$), in the interventional group. At the 6-week, 3-month and the 6-month follow-up appointments there was however no statistically significant difference in benefit between the two groups (9).

Another large randomized clinical control trial from the United States of America enrolled 381 subjects with osteoporotic compression fractures and compared 191 subjects randomized to percutaneous vertebroplasty and 190 subjects randomized to percutaneous kyphoplasty. The primary outcome end points were at 12 and 24 months post the procedure and the outcome measures utilized were the amount of pain and the incidence of additional osteoporotic vertebral compression fractures. The results of this study showed no significant difference in the amount of pain between the groups at either of the follow-up end points and although there was a trend to less osteoporotic compression fractures in the percutaneous kyphoplasty group this difference did not reach statistical significance ($p=0.06$) (10).

DISCUSSION

Considering the medical management of patients with osteoporotic vertebral compression fractures medical measures should be considered in all patients to maintain bone quantity and prevent the recurrence of multiple fractures. Regarding the benefit of percutaneous vertebroplasty versus conservative treatment the large randomized clinical control trials conducted in the last 5-years provide support for percutaneous vertebroplasty as offering only an immediate and short-term benefit in outcome. Comparing vertebroplasty and kyphoplasty there is still insufficient evidence if these treatments are equally effective or one is more beneficial than the other (7-10).

Besides the paucity of any long-term symptomatic benefit of vertebral augmentation versus conservative management, additional outcome measures have been measured in other studies. One study by McCullough *et al* (11) considered major medical outcomes and specifically assessed mortality, the incidence of major complications, and healthcare utilization. In this retrospective cohort study from the United States of America 10,541 patients who had undergone a vertebral augmentation procedure were compared to 115,851 patients who had been managed conservatively. The results of this very large study were firstly that no significant difference in one-year mortality was demonstrated. There was furthermore no significant difference in major medical complications at one-year. What this study found significant was that the augmented group had higher rates of health-care utilization which included intensive care admissions. Being in the augmented group also demonstrated significance in predicting admission to a specialized nursing facility .

Another large study Ong *et al* (12) analyzed the North American national database considered the cost effectiveness of vertebral augmentation and reported a significant reduction in length of hospital stay from an average of 10 days for patients managed conservatively versus an average of 3-6 days in patients who underwent vertebral augmentation. A similar finding is reported by a Taiwanese cohort study that considered 9,238 subjects and reported an average reduction in in-patient stay of 2 days in those that underwent vertebral augmentation (13). A cost analysis study from the United States of America Medicare database conducted between 2005 and 2008 considered 858,978 patients admitted with osteoporotic vertebral compression fractures of which 182,946 underwent vertebral augmentation. This study reported a 61% four-year survival rate in the vertebral augmentation group versus a 50% survival rate in the conservatively managed group ($p<0.001$) (14). Another study published in 2017 by Laratta *et al* (15) utilizing the same Medicare database reported the average cost of a vertebroplasty to be US$10,897 – US$ 14,404 and the average cost of a kyphoplasty to be US$12,187 - US$17,174. The same cost-analysis study mentioned above further analyzed both groups in terms of their modelled cost effectiveness and reported a modest cost gain of between US$1,863 – US$13,534 per year of life in the augmented group (14). Another Swedish study by Fritzell *et al* (16) does not support the cost effectiveness of vertebral augmentation and in the 63 subjects, who had undergone vertebral augmentation and were enrolled in the study, reported a cost gain of US$ 134,000 per year of life.

CONCLUSION

The large randomized clinical control trials published in the last five years demonstrate that vertebral augmentation offers only an immediate and short term benefit in pain relief and that at between 6 weeks and 1-year there was no significant difference in symptomatology between the augmented group and the conservatively managed group (7-10). While several studies report a modest reduction in length of hospital stay (12,13), other studies report the massive and increasing cost of the procedure itself (15).

The modest increase in years added to life are furthermore expensive in terms of ongoing increased utilization of medical care (14,16).

The Southern African situation is that of increasingly financially strained medical resources that battle to meet the basic health care needs of the population. The current HIV/AIDS pandemic centered in Southern Africa adds additional strain to already strained resources. The short-term improved symptomatology in those who undergo vertebral augmentation is outweighed by a paucity of any long-term benefit, the cost of the procedure itself, and the additional cost per year of life added by the procedure. As such vertebral augmentation remains unaffordable for most of the population in Southern Africa and the conservative management of these patients remains the standard of care in the Southern African region.

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DECLARATION OF INTEREST

None of the authors listed below have any financial nor personal relationships with other people, or organizations, that could inappropriately influence (bias) their work, all within 3 years of the beginning the work submitted.

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