

# How to Avoid Complications in Kyphoplasty - the Rule of Four

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## ABSTRACT

**Purpose.** There is no consensus on the number of levels that may be treated in a single kyphoplasty session; some authorities suggest up to four vertebrae while others have augmented more levels in one session. The purpose of this study is to define the optimal number of vertebrae that may be treated on a single operative session in a safe manner.

**Methods.** We retrospectively studied the patients that underwent kyphoplasty during a 7-year period (2010-2016) from a single surgeon. 70 consecutive patients were identified (mean 65 years). Overall 224 vertebrae were cemented in 82 operative sessions. Perioperative complications, 10-day morbidity, pain and kyphotic angle were analyzed. We used Stata version 9.1 for statistical analysis.

**Results.** Three serious (life threatening or lethal) adverse events were encountered during the 10-day perioperative period, related with multilevel prolonged operations (more than 4 levels) ( $p < 0.001$ ). The only other factor that was marginally correlated was the presence of vertebrae plana ( $p: 0.06$ ). Cement leak was observed in 44% (leakage per session not per vertebrae), correlating with the number of augmented levels (23.3% in 1-2 levels, 51.5% in 3 and 64.7% with more levels, odds ratio 2.53,  $p = 0.005$ ). Pain improved from 8.2 points to 4.4 points postoperatively ( $p < 0.001$ ) and kyphotic angle from 22.9 degrees to 20.8 degrees ( $p < 0.001$ ).

**Conclusion.** Up to 4 levels may be safely treated with kyphoplasty in one session. Augmentation of more vertebrae especially in debilitating patients suffering from pathologic fractures leads to more cement leakage and may predispose to major complications.

**KEY WORDS:** Rule of Four; Kyphoplasty; Osteoporosis; Vertebral Fractures; Complications

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## Introduction

Balloon Kyphoplasty (BKP) and Vertebroplasty (VP) are vertebral augmentation procedures successfully employed in the treatment of osteoporotic or malignant fractures [1-6]. In osteoporotic fractures usually a single level procedure suffices for the reduction and stabilization of the fracture; however in corticosteroid-induced fractures, and in vertebral compression fractures secondary to malignant and metastatic disease, multiple vertebral augmentation may be necessary to address the clinical condition of multilevel involvement [7-11]. Yet, there is no consensus on the number of levels that may be treated in a single session; while some authorities recommend a plateau of 4 levels per session [7, 12], there have been many reports of more than 4 levels being successfully treated in a single session [9, 10, 13-15]. The benefits both to the patient and the treating surgeon are obvious: one trip to the operating theater, less operative time overall and reduced cost (recycling of the same balloon device). However, it has been demonstrated that with increasing levels of augmentation the risk for cardiopulmonary complications rises, as well [16].

The aim of this study is to define the optimal number of vertebrae that may be treated in a single operative session in a safe manner. For this reason perioperative morbidity/ mortality were studied and correlated with the levels treated. Additional factors predisposing to complications were further analyzed.

## Materials & methods

We retrospectively studied the patients that underwent kyphoplasty during a 7-year period (2010-2016) from a single surgeon (IP). 70 patients (49 women, 21 men) were identified aged between 22 and 85 years old (mean 65 years). The majority of them were diagnosed with metastatic cancer (40%), followed by osteoporosis (24%), multiple myeloma (23%) and hematologic malignancies (13%). Sixty patients were treated in a single operative session. In nine patients a second session was necessary, and one patient underwent a total of four kyphoplasty sessions. Overall 224 vertebrae were cemented in 82 operative sessions. Single-level BKP was

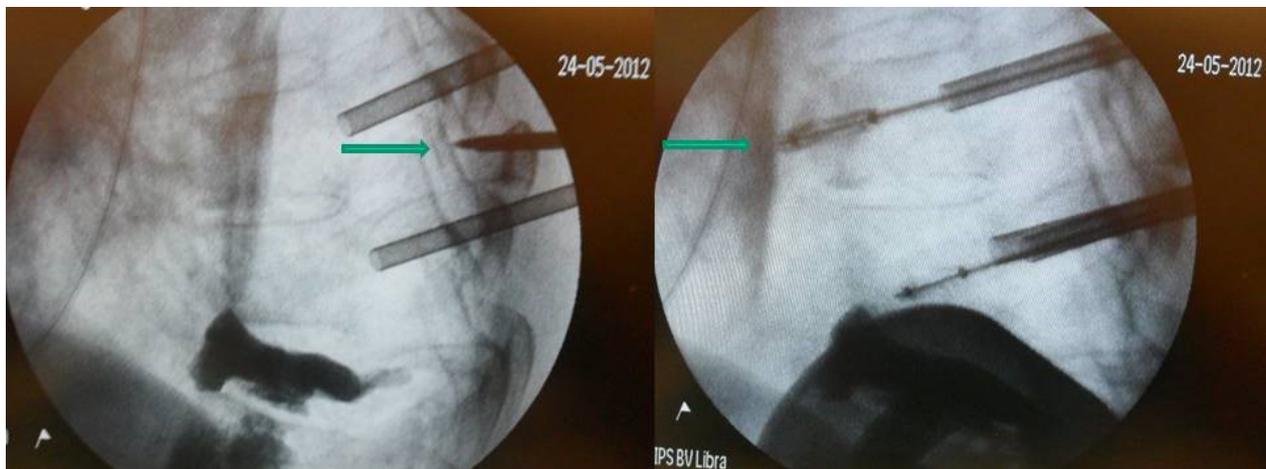
performed in 11 sessions (13.4%); 2-level BKP in 20 (24.4%); 3-level BKP in 33 (40.2%); and 4-level BKP in 15 sessions (18.3%). More levels were augmented in three cases; two patients underwent a 5-level and one patient a 6-level BKP (3.7%). Vertebra plana and intravacuum cleft were observed in 15% and 7% of patients, respectively. In addition epidural spinal cord compression/ spinal stenosis was noted in 22% of patients (without clinical myelopathy which was considered a contraindication for the procedure [17]). Nine of these patients (13%) underwent simultaneous laminectomy (open BKP without fusion (patients with either open or percutaneous fusion were excluded from analysis). Inclusion criteria for the procedure were pain intensity at least 4/10, recent fracture or edema as seen in the Magnetic Resonance Imaging (MRI) and clinical exam corresponding to the fracture seen on the MRI (pain at percussion at the fractured level) [17]. In cases where the patient was not suitable for MRI a bone scan was performed instead to differentiate between acute and chronic fractures [18].

The perioperative complications and 10-day morbidity were studied, and a correlational analysis was performed for adverse events and independent variables, including age, number of treated vertebrae, diagnosis, spinal cord compression, vertebra plana, intravacuum cleft, concomitant laminectomy (open kyphoplasty), and cement leakage. Cement leakage was also correlated to the number of levels treated. Pain, was evaluated with a numerical rating scale from 0-10, and the pain scores before surgery, as well as 10 days after surgery were analyzed. In thoracic or thoracolumbar fractures kyphotic angle was compared pre and postoperatively. We used Stata version 9.1 for statistical analysis and the level of significance was set to 0.05.

Results. Two life threatening adverse events (hemothorax- figures 1-3 and cardiac tamponade-figure 4) and one death (figure 5) were encountered during the 10-day postoperative period. All major complications were related to multilevel prolonged operations (more than 4 levels). Univariate analysis showed that the occurrence of major complications was correlated with the number of augmented levels (>4 levels,  $p < 0.001$ , Fisher's exact test). The pres-



**Figure 1.** A 48year old female presented with T9 metastasis from breast cancer and fracture leading to significant kyphosis (1a- sagittal T1 sequence on Magnetic Resonance Imaging- MRI) that was aggravated after radiation therapy (1b- sagittal T2 sequence on MRI). The patient was treated with multilevel open kyphoplasty (1c- lateral xray).

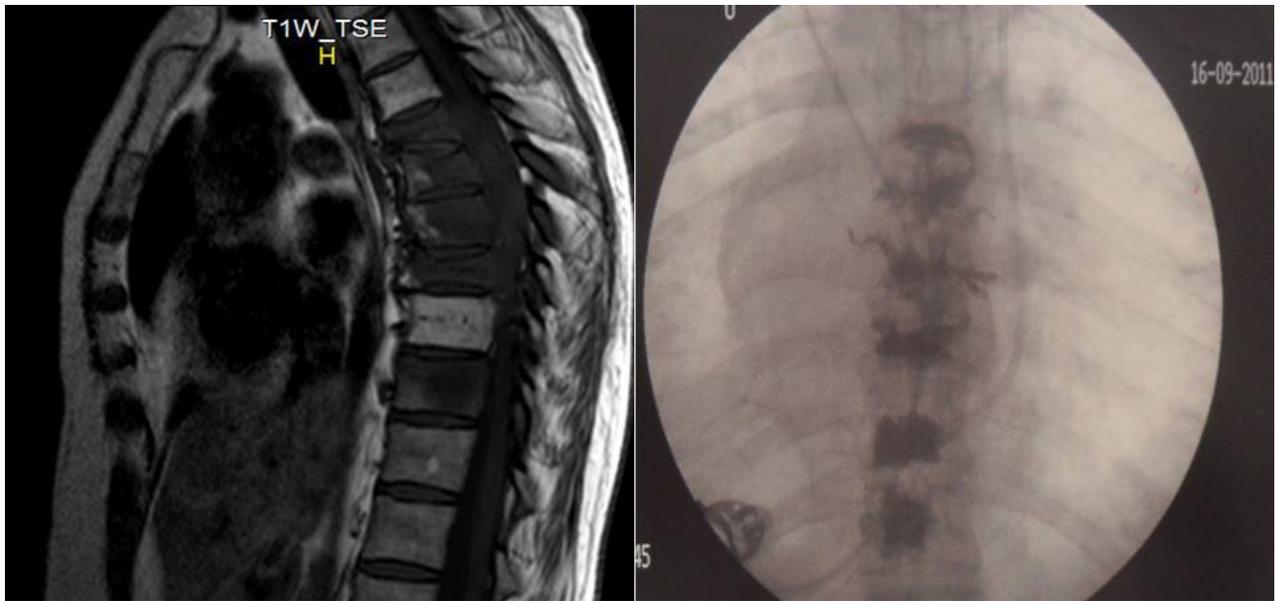


**Figure 2.** A 5-level kyphoplasty was attempted instead of fusion due to severe tumor encroachment of the adjacent vertebral bodies. Since decompression was needed, we chose to augment 2 levels above and below the fracture in order to strengthen the kyphotic area and avoid catastrophic collapse. On the left image possible injury of a segmental thoracic vessel is depicted (left C-arm image, green arrow). On the right image, the balloon introducer is placed outside the vertebral body (green arrow) due to significant cancerous destruction of the vertebral body which was left uncemented.

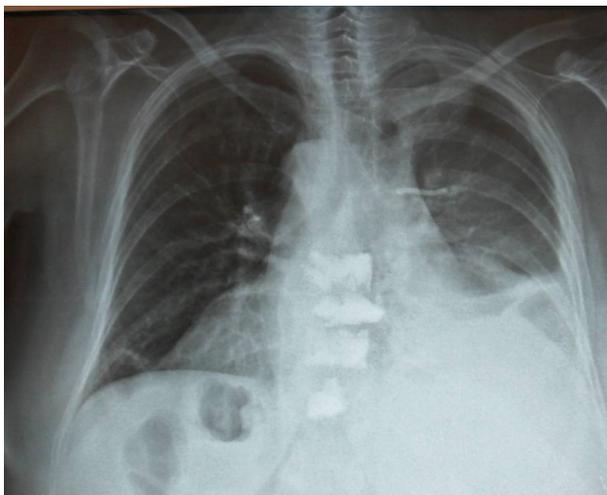
ence of vertebra plana was marginally correlated with complications, yet did not reach the level of significance ( $p=0.06$ , Fisher's exact test). None of the rest factors studied, including age, diagnosis, spinal cord compression, intravacuum cleft, concomitant laminectomy (open kyphoplasty), and cement leakage, were found to predispose to major complica-

tions. Logistic regression or multivariate analysis could not be performed in the present patient series, due to the limited number of major complications noted.

Cement leak was observed in 44% of operative sessions. In logistic regression analysis the presence of cement leakage was related to the number of aug-



**Figure 4.** A 48year old paraplegic female patient with metastasis in multiple thoracic vertebrae (left image- sagittal T1 sequence MRI) treated with 6-level kyphoplasty (right image). She developed atraumatic cardiac tamponade attributed to the prolonged prone position and osmotic exsanguination of pericardiac fluid; she was treated with pericardiocentesis that yielded xanthochromatic fluid.



**Figure 3.** Postoperative left hemothorax (same patient) that resolved conservatively. The patient is doing well four years postoperatively.

mented levels (odds ratio 2.53,  $p=0.005$ ). More precisely, the incidence of cement leakage was 23.3% in single and 2-level procedures, 51.5% in 3-level procedures, and 64.7% in 4-,5- and 6-level procedures. Nevertheless, cement extravasation caused clinical sequela only in two cases; a cement leak into the S1 foramina that caused postoperative sciatica and was

surgically treated; and another T5 foramina leak that caused pain and was sufficiently managed with intraforaminal injections and oral analgesics.

Regarding pain relief, the mean score for pain significantly decreased from 8.1 (range, 7-10) before surgery to 4.4 (range, 1-5) after surgery ( $p<0.001$ , paired t-test). This difference should be considered not only statistically but also clinically important (a minimum difference of 2 points is considered by some authorities the minimal clinically important difference [19]. The mean kyphotic angle also changed significantly, and was decreased from 22.9 degrees (range, 18.4 - 27.4 degrees) before surgery to 20.8 degrees (range, 16.2 - 25.5 degrees) after surgery ( $p<0.001$ , paired t-test).

### Discussion

Multilevel kyphoplasty/ vertebroplasty may be indicated in the context of multiple fractures in cancer/ myeloma patients or corticosteroid induced fractures [7-10]. The maximum number of vertebrae that may be augmented in a single session still remains an issue of controversy; societies like the Myeloma Working Group or the Cardiovascular and Interventional Radiological Society recommend



**Figure 5.** A 78 year old female with multiple fractures in the thoraco-lumbar and lumbar spine due to multiple myeloma (green arrow denotes a vacuum cleft in L1). A 5-level kyphoplasty (T11-L4) was performed; shortly after the 2.5 hour operation she experienced sudden death attributed to pulmonary embolism or cardiac syncope (relatives did not give consent for necropsy).

augmentation of up to 4 or 5 levels per session [7, 12, 20], while on the same time, there have been various studies in the literature reporting on successful multilevel vertebral augmentations (of more than 5 levels) in a single operative session [9, 10, 13-15]. Mailli et al in a comparative study of patients undergoing few level (up to three) vs. more than 4 levels found no difference between groups in terms of pain control, performance status, or complication rate including cement leakage [13]. Audat et al stud-

ied 14 myeloma patients, who received multilevel augmentation of the thoracolumbar spine (mean of 14.7 levels in a single session). The authors reported on good results, although one patient (7.1%) died from pulmonary embolism the day of surgery, possibly related to the prolonged operation and the large amount of PMMA (Polymethylmethacrylate) instilled [10].

BKP/ VP are considered safe and effective procedures with minimal complications. However silent pulmonary cement embolism may be present in up to one fourth of the patients undergoing VP (VERTOS II study [21]). Asymptomatic cement leakage in prevertebral veins, intervertebral disc or even epidural space happens frequently (on average around 10-20% [2]). Serious complications are rare although well documented in the literature in the form of case reports. Pneumo/ hemothorax, cardiac tamponade and fatal embolism may ensue [22-28]. A reasonable hypothesis is that multilevel/ prolonged operations may lead to catastrophic results; the FDA back in 2004 highlighted this small risk “especially when multiple vertebral levels are treated in one setting” [29]. This is also suggested by our study.

The detrimental cardiovascular effects of bone cement (Polymethylmethacrylate- PMMA) are well documented in the arthroplasty literature [30-34]. For vertebral augmentation procedures where PMMA is instilled inside the vertebral body, animal studies suggest that cardiovascular parameters deteriorate during cement injection. Aebli et al reported that with augmentation of four vertebrae (VP) there is a significant decrease in mean blood pressure along with hypoxemia and hypercapnia; this is an accumulated phenomenon that becomes more prominent with increasing vertebrae treated, possibly due to increase in intraosseous pressure and fat microembolism; therefore continuous invasive monitoring during VP is recommended [35]. Benneker et al also found that fat embolism along with increase in mean arterial pulmonary pressure was significant in a sheep model after VP, whereas a pulsed jet-lavage technique (that removes intravertebral fat) alleviated this phenomenon [36]. In human studies transient hypotension after VP has also been reported [37]; Kaufmann et al found a statisti-

cal but not clinically significant drop of oxygen saturation 10 minutes after VP[38]. However, this study included single or 2-level procedures which in general are very well tolerated. On the other hand Uemura and colleagues noticed that PaO<sub>2</sub> decreased during percutaneous VP which strongly correlated with the number of treated vertebral bodies. Reasons for this pulmonary compromise include fat or cement emboli, increased oxygen desaturation from prolonged administration of sedative drugs, decrease in functional residual capacity as a result of thoracic compression attributable to the prone position etc [16]. Although we did not measure cardiovascular markers in our patient cohort, we did find that cement leakage is proportional to the number of treated vertebrae, a factor that may theoretically predispose to complications (along with the bigger cement volume instilled). The higher incidence of cement leakage found in our patients, compared to the reported incidence in the literature, is attributed to the higher percentage of malignant fractures which have a higher propensity of leakage than osteoporotic ones [2]. Another factor is that cement leakage was assessed with respect to operative sessions, rather than to levels treated, leading to a factitious higher incidence.

The results of our study are in accordance with the BKP literature regarding pain control and sagittal balance correction. Serious complications were rare and strongly correlated with the number of treated vertebrae. This led us to modification of our therapeutic strategy and we have abandoned the lengthy multilevel procedures. We stop at 4 levels which is translated to a less than 2-hour operation, thereby minimizing our complication rate. To our knowledge, this is the first series to deal with the optimal number of levels that should be augmented on a single session in a more evidenced based way. Vertebrae plana may also predispose to complications since accuracy is needed in the trajectory of the needle, bipedicular approach is fostered most of

the times because the lateral pillars of the vertebral body are generally better preserved and penetration of the body/ cement extravasation or encroachment of the foramen or canal is more likely to happen. It is not advisable for unexperienced operators to undertake severely collapsed vertebrae.

The retrospective design, the small number of patients, as well as the small number of complications that were encountered are important limitations that reduce the power of the present study. However, it is a single surgeon series with patients being treated in a uniform way. Additionally, it is our belief that the safety issue hereby studied is rather important and interesting, and guidelines on this matter are missing; surgeons have reported augmenting up to sixteen levels at one session[10]. Larger prospective trials may shed more light on this controversial topic.

In conclusion we believe the surgeon should avoid the temptation of performing more than a 4-level operation and prefer to return subsequent times to the operating theatre. Also meticulous approach and careful planning is needed in severely deformed vertebrae. In this manner, life threatening complications may be avoided. 

#### **Conflict-of-interest statement**

*On behalf of all authors, the corresponding author states that the work presented here is original and has not been concurrently submitted or published in another journal/media. The authors declared no conflict of interest: no benefits have been or will be received from a commercial party related directly or indirectly to the subject matter of this article.*

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