SPINE Volume 34, Number 11, pp 1228–1232

Percutaneous Treatment of Vertebral Compression Fractures

A Meta-analysis of Complications

Michael J. Lee, MD, Mark Dumonski, MD, Patrick Cahill, MD, Tom Stanley, MD, Daniel Park, MD, and Kern Singh, MD

Study Design and Objective. This study performs a meta-analysis to compare complication rates from vertebroplasty (VP) and kyphoplasty (KP).

Summary of Background Data. Recently, the development of VP and balloon KP has been shown to provide symptomatic relief and restoration of sagittal alignment of vertebral compression fractures refractory to medical therapy. Complications in treatment of vertebral compression fractures are rare, however can be potentially devastating. Fortunately, clinical sequelae are rare; however, severe clinical complications from cement extravasation have been reported.

Methods. Using PubMed and Ovid, we performed a literature search for "kyphoplasty," "vertebroplasty," and "vertebral augmentation." This search was performed in December 2006. Case reports and reports not available in English were excluded. We categorized complications in 3 categories: (1) procedure-related complications, (2) medical complications, and (3) new vertebral fracture. Cement leakage, asymptomatic and symptomatic, and its locations were recorded. We performed a meta-analysis of complications of all studies. We then repeated the meta-analysis examining only prospective studies. We then used proportion analysis to determine statistical significance. We defined statistical significance as a P value less than 0.05.

Results. We identified 121 reports of KP and/or VP that specifically addressed complications. Of these studies, 33 addressed KP and 82 addressed VP (6 reports addressed complications of both). There were 29 reports in which the data appeared to be collected prospectively. Of these, 9 addressed KP and 21 addressed VP.

VP was found to have a significantly increased rate of procedure-related complications than KP in the analysis of all studies and only prospective studies. VP also appears to have a significantly higher rate of symptomatic and asymptomatic cement leakage than KP ($P < 0.05$). The incidence of medical complications was significantly higher in the KP procedure; however, this difference was not observed when analyzing only prospective studies. The incidence of new fracture was significantly higher in the VP procedure; however, this was not observed when analyzing only prospective studies.

Conclusion. VP and KP are 2 minimally invasive procedures that have been shown to be effective in the treatment of symptomatic vertebral compression fractures. Although the incidence of adverse events for both VP and KP are low, it appears that VP is associated with a statistically significant increased rate of procedure-related complications and cement extravasation (symptomatic and asymptomatic). Future prospective studies with large patient enrollment will be needed to further validate the finding of this meta-analysis

Key words: compression fracture, vertebroplasty, kyphoplasty. **Spine 2009;34:1228–1232**

Vertebroplasty (VP) and balloon kyphoplasty (KP) have been shown to provide symptomatic relief of vertebral compression fractures refractory to medical therapy.[1–3] Brace treatment and open surgical intervention are less desirable in this population because of the associated medical comorbidities. As such, VP and balloon KP have been advocated as minimally invasive treatment options for symptomatic compression fractures. VP involves the injection of less viscous cement into the fractured vertebra. KP, on the other hand, involves the inflation of a balloon to restore vertebral height followed by the injection of more viscous cement under lower pressure.

Perioperative complications related to the treatment of vertebral compression fractures are rare; however, when they occur, they can be potentially devastating.[4,5] Cement extravasation has been reported with both procedures. Fortunately, clinical sequelae are rare. Injection of cement into the paravertebral vessels can result in pulmonary emboli, while extravasation of cement posteriorly into the neural foramen or spinal canal can result in neurologic deficit.[4,5] It has been suggested that extravasation of cement into the disc space increases the likelihood of adjacent level fracture.[6,7] Other procedural complications that have been reported with vertebral augmentation include fractured transverse processes or ribs, dural tears, discitis, and subcutaneous hematomas.

In general, complications after VP and KP have been case reported. Furthermore, events that are considered complications may vary considerably from study to study. The purpose of this study was to analyze the available literature for complication rates from both VP and KP.

Materials and Methods

Using PubMed and Ovid, we performed a literature search using the terms "kyphoplasty," "vertebroplasty," and "vertebral augmentation" (see Appendix, Supplemental Digital Content 1, http://links.lww.com/A1032). This search was performed in December of 2006. Only studies that were in the English language were included. Case reports or series were excluded unless they included a denominator of total number

From the Rush University Medical Center, Chicago, IL.
Acknowledgment date: April 9, 2007. Revision date: August 18, 2007. Acceptance date: October 8, 2007.
The manuscript submitted does not contain information about medical device(s)/drug(s).
No funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.
Address correspondence and reprint requests to Kern Singh, MD, 1725 W Harrison St #1063, Chicago IL 60612; E-mail: kern.singh@rushortho.com

Table 1. Fracture Etiology

	Osteoporotic	Pathologic	Mixed
All studies	71	21	35
Prospective studies	17	4	8

of patients treated. Unless a study specifically addressed complications it was not included in the analysis.

We categorized complications into 3 categories: (1) procedure related, (2) medical, and (3) new vertebral fracture. A complication was deemed "procedure related" if the occurrence was directly the effect of the procedure and not the patient's medical comorbidities. Procedure-related complications include cement embolism, neurologic deficit, fracture (rib, transverse process, and pedicle), discitis, dural tear, pain worse than before surgery, and subcutaneous hematoma. We also separately recorded the occurrence of cement extravasation, asymptomatic and symptomatic, and if reported, the location of the leak. A complication was deemed "medically related" if it was likely secondary to the patient's medical status. Medically related complications include non-cement embolism, temporary respiratory insufficiency, stroke, cardiovascular complications, pneumonia, or fever. We also examined the occurrence of adjacent and remote fractures. An adjacent fracture was defined to be 1 level cephalad or caudad to the treated level. A remote fracture was defined to be at least 2 levels away from the treated level.

Data from all the studies were pooled together controlling for sample size. We also performed a separate analysis for only the studies in which the data were collected in a prospective fashion.

Statistics

We used a proportion analysis to determine statistical significance (χ^2 test). We defined statistical significance as a $P < 0.05$.

■ Results

Study Demographics

We identified 121 reports of KP and/or VP that specifically addressed complications. Of these studies, 33 addressed KP and 82 addressed VP (6 reports addressed complications of both). The number of patients per study ranged from 6 to 868. There were 29 reports in which the data appeared to be collected prospectively. Of these, 9 addressed KP and 21 addressed VP. (One study addressed complications for both.) Fracture etiology per study is summarized in Tables 1, 2, and 3.

Table 2. Fracture Etiology in All Studies

Complications	Procedure (Total Studies)	Osteoporotic	Pathologic	Mixed
Medically related	KP (n = 29)	18	4	7
	VP (n = 71)	39	11	21
Procedure related	KP (n = 29)	18	4	7
	VP (n = 71)	39	11	21
Cement leak	KP (n = 33)	19	7	7
	VP (n = 70)	38	13	19
New fracture	KP (n = 13)	12	1	0
	VP (n = 28)	23	1	4

Table 3. Fracture Etiology in Prospective Studies

Complications	Procedure (Total Studies)	Osteoporotic	Pathologic	Mixed
Medically related	KP (n = 6)	4	0	2
	VP (n = 18)	10	2	6
Procedure related	KP (n = 9)	5	2	2
	VP (n = 29)	21	2	6
Cement leak	KP (n = 7)	4	2	1
	VP (n = 16)	11	1	4
New fracture	KP (n = 2)	2	0	0
	VP (n = 10)	6	1	3

Medical Complications

The rate of medical complications per patient was statistically lower for VP than for KP (0.4% *vs.* 1.6%) when reviewing all studies ($P < 0.001$); however, when reviewing only prospective studies, this difference was no longer statistically significant ($P > 0.05$) (Table 4). When evaluating the rate of medical complications per number of levels treated, the differences for VP and KP were not statistically significant ($P > 0.05$). The differences between mortality rates for VP and KP were not statistically significant (0.6% *vs.* 1.0%, $P > 0.05$) (Table 5).

Procedure-Related Complications

When reviewing all studies, VP had a significantly increased procedural complication rate per number of patients treated compared with KP (3.8% *vs.* 0.6%, $P < 0.001$). This difference continued to be statistically significant when reviewing only prospective studies (2.4% *vs.* 0.4%, $P < 0.001$) (Table 4). When reviewing the procedural complication rate per number of levels treated, VP had a significantly increased rate of complications compared with KP for all and prospective-only studies, respectively (2.8% *vs.* 0.3%, 1.6% *vs.* 0.2%, $P < 0.001$) (Table 5).

Asymptomatic Cement Leakage

In all studies, the rate of asymptomatic cement leaks per number of patients treated was significantly higher for VP than for KP (75% *vs.* 14%, $P < 0.001$). This difference was also observed when evaluating only prospective studies (56.2% VP *vs.* 13.6% KP, $P < 0.001$) (Table 6). The rate of asymptomatic cement leaks per number of levels treated was significantly higher for VP than for KP in all and prospective-only studies (43% *vs.* 8.8%, 38.2% *vs.* 8.1%, $P < 0.001$) (Table 7).

Symptomatic Cement Leakage

The rate of symptomatic cement leaks per number of patients treated was significantly higher for VP than for KP in all studies (1.48% *vs.* 0.04%, $P < 0.05$). This difference approached statistical significance when evaluating only prospective studies (0.8% VP *vs.* 0% KP, $P < 0.064$) (Table 6). The ratio of symptomatic cement leaks per number of levels treated was significantly higher for VP than for KP in all and prospective-only studies (1.08% *vs.* 0.4%, 0.5% *vs.* 0%, $P < 0.05$) (Table 7).

We then evaluated the incidence of cement leaks per number of levels treated for osteoporotic and pathologic

Table 4. Complications Rate per Number of Patients Treated

	Procedure Type	Procedure-Related Complications	Medical Complications	Mortality
All studies	KP (per no. patients)	0.60% (9/1491)	1.6% (24/1491)	1.0% (15/1491)
	VP (per no. patients)	3.80% (215/5629) $P < 0.001$	0.40% (22/5629) $P < 0.001$	0.60% (24/5629) $P > 0.05$
Prospective	KP (per no. patients)	0.40% (3/631)	3.20% (18/558)	2.30% (13/558)
	VP (per no. patients)	2.40% (29/1190) $P < 0.001$	2.80% (29/1051) $P > 0.05$	2.10% (22/1051) $P > 0.05$

fractures. Some studies did not clearly identify how many patients had which underlying diagnosis and these studies were excluded from this part of the analysis. The ratios of total cement leaks per number of levels treated were significantly higher for VP, after isolating pathologic and osteoporotic fractures ($P < 0.05$). These ratios were also significantly higher for VP when evaluating only symptomatic cement leaks ($P < 0.05$) (Table 8). The rates of cement leaks in KP for pathologic fractures and osteoporotic fractures were 6.07% and 6.89%, respectively ($P > 0.05$); however, in VP, the rate of leakage in the pathologic fracture group was significantly higher than in the osteoporotic group (79.07% *vs.* 20.79%, respectively; $P < 0.05$).

New Fracture

When reviewing all studies, 18% of patients in the VP group and 17% of treated patients in the KP group experienced a fracture at another level ($P > 0.05$). When reviewing only prospective studies, 16.1% of the KP patients and 18.1% of the VP experienced new fractures ($P > 0.05$) (Table 9). The follow-up ranged from 1.5 months to 36 months. When reviewing all studies the ratio of new fractures that occurred per levels treated was significantly higher for the VP group than for the KP group (21% *vs.* 13%, $P < 0.001$); however, this difference was not statistically significant when reviewing prospective-only studies (16.3% VP *vs.* 11.2% KP, $P > 0.05$).

Regarding the effect of the location of fracture, 27 studies specifically described the distribution of the new fracture, 12 for KP, and 25 for VP. In the KP group, 74.8% (116/155) of the new fractures occurred at an adjacent level, whereas 25.2% (39/155) occurred at a remote location. In the VP group, 51.6% (366/709) of the new fractures occurred at an adjacent level and 48.2% (343/709) of the new fractures were considered remote. This difference in distribution of the fractures between the VP and KP groups was statistically significant ($P < 0.001$). This difference persisted when evaluating prospective-only studies. The adjacent-level fracture rate was significantly lower for VP than for KP (45.5% *vs.* 91.6%, $P < 0.001$) (Table 10).

■ Discussion

Complications from VP and KP in the literature are rare and are poorly reported. Previous reports have attempted to pool studies in order to assess pain, function, alignment, and complications.[1,2] The present study is the largest attempt at analyzing the current literature. Two separate analyses were performed in this study. First, we pooled data from all studies and performed a proportion analysis. There were no randomized series; however, there were numerous reports in which the data were collected in a prospective fashion. As such, these were analyzed separately.

In general, vertebral compression fractures occur in an elderly patient population with multiple medical comorbidities. We noted that the incidence of medical complications was higher for KP than for VP ($P < 0.05$) for all studies; however, this difference was not noted in the prospective studies. One possible explanation is that KP is performed with general anesthesia, whereas VP can be done with a local anesthetic. Additionally, the reporting of medical complications may be subject to bias as VP is often an outpatient procedure and complications may not be reported during the hospitalization.

Although the difference in mortality between the 2 procedures was not found to be statistically significant, it should be noted that mortality rates exceeded 2% when evaluating only prospective studies. These rates emphasize the poor overall condition of patients who typically experience compression fractures, osteoporotic, or pathologic.

The incidence of procedure-related complications appears to be less for KP than for VP ($P < 0.001$) when analyzing all studies and prospective-only studies. This trend may in part be explained by historical context. VP was developed before KP. The procedures share the same approach and complications encountered in VP earlier

Table 5. Complications Rate per Number of Levels Treated

	Procedure Type	Procedure-Related Complications	Medical Complications
All studies	KP (per no. levels treated)	0.30% (9/2731)	0.90% (24/2731)
	VP (per no. levels treated)	2.80% (215/7771) $P < 0.001$	0.30% (22/7771) $P < 0.001$
Prospective	KP (per no. levels treated)	0.40% (3/1290)	0.70% (9/1290)
	VP (per no. levels treated)	2.40% (29/1727) $P < 0.001$	0.30% (5/1727) $P > 0.05$

Table 6. Cement Leakage per Number of Patients

	Procedure Type	All Cement Leaks	Symptomatic Cement Leaks
All studies	KP (per no. patients)	14.0% (184/1297)	0.06% (1/1568)
	VP (per no. patients)	75.0% (3078/4097) $P < 0.001$	1.48% (76/5067) $P < 0.001$
Prospective	KP (per no. patients)	13.6% (51/373)	0.0% (0/631)
	VP (per no. patients)	56.2% (401/713) $P < 0.001$	0.80% (6/735) $P < 0.063$

Table 7. Cement Leakage per Number of Levels Treated

	Procedure Type	All Cement Leaks	Symptomatic Cement Leaks
All studies	KP (per no. levels treated)	8.80% (184/2093)	0.04% (1/2794)
	VP (per no. levels treated)	43.0% (3078/7184) $P < 0.001$	1.08% (76/7027) $P < 0.001$
Prospective	KP (per no. levels treated)	8.10% (51/623)	0.0% (0/1297)
	VP (per no. levels treated)	38.2% (401/1047) $P < 0.001$	0.50% (6/1078) $P < 0.05$

may not have been encountered in KP because of the increased technical experience.

In addition to examining all procedural complications, we examined the incidence of cement extravasations, asymptomatic, and symptomatic. Although severe neurologic deficits have been described in case reports for percutaneous treatment of compression fractures,[4,5] almost all symptomatic cement leaks in this study manifested in single level radiculopathy and were treated either with steroid injection or surgical decompression. The significance of an asymptomatic cement leak has been widely debated.[3,6–8] Some authors do not consider asymptomatic leaks to be a complication. Others have suggested that there are long-term sequelae from asymptomatic cement leaks. It has been suggested that cement leakage into the adjacent disc space predisposes the patient to an adjacent-level fracture.[6,7] The incidences of asymptomatic and symptomatic cement leakage are significantly higher with VP than with KP (75% *vs.* 14%, $P < 0.05$). When examining prospective-only studies, this difference continued to be statistically significant (56.2% *vs.* 13.6%, $P < 0.001$). Hulme *et al* reported rates of cement leakage to be 41% and 9% for VP and KP, respectively.[1] In the present study, the rate of symptomatic cement leakage also appeared to be higher for VP ($P < 0.05$). When examining only the prospective studies, we found the rates to be 0.8% and 0% for VP and KP, respectively. Although the difference between the incidences of symptomatic leak per patient was not statistically significant, the difference in the ratios of symptomatic leaks per levels treated was statistically significant ($P < 0.05$). Taylor *et al* reported a symptomatic cement leak rate of 3% and 0% for VP and KP, respectively.[2]

We also examined the rates of cement leakage in the osteoporotic and pathologic fracture populations. VP was associated with a higher rate of cement leakage, symptomatic and asymptomatic, in both osteoporotic and pathologic populations. Furthermore, VP in pathologic fractures was associated with a higher cement leak rate than VP in osteoporotic fractures; however, we did not observe this contrast in the KP group.

It appears that VP may be associated with an increased new fracture rate when compared to KP. This result should be interpreted cautiously as the occurrence of new fractures at previously unaffected levels may be multifactorial. Variability in fracture reporting can confound these results as only symptomatic fractures are likely to be reported. Furthermore, when examining data only from prospective-only studies we did not find a sta-

Table 8. Osteoporotic *Versus* Pathologic Fractures per Number of Levels Treated

	Procedure Type	No. Levels	Cement Leak (Total)	Symptomatic Cement Leak
Pathologic fractures	KP	214	6.07% (13/214)	0.00% (0/214)
	VP	760	79.07% (601/760) $P < 0.05$	0.26% (21/760) $P < 0.05$
Osteoporotic fractures	KP	1901	6.89% (131/1901)	0.05% (1/1901)
	VP	5260	20.79% (1094/5260) $P < 0.05$	0.03% (21/5260) $P < 0.05$

Table 9. New Fracture per Procedure

	Procedure Type	New Fractures	Procedure Type	New Fractures
All studies	KP (per no. patients)	17.0% (123/727)	KP (per no. levels treated)	13.0% (158/1192)
	VP (per no. patients)	18% (490/2781) $P > 0.05$	VP (per no. levels treated)	21.0% (830/3912) $P < 0.001$
Prospective	KP (per no. patients)	16.1% (11/68)	KP (per no. levels treated)	11.2% (12/107)
	VP (per no. patients)	18.1% (122/672) $P > 0.05$	VP (per no. levels treated)	16.3% (154/941) $P > 0.05$

Table 10. Distribution of New Fracture

	Procedure Type	Adjacent Fracture	Remote Fracture
All studies	KP	74.8% (116/155)	25.2% (39/155)
	VP	51.6% (366/709) $P < 0.05$	48.4% (343/709) $P < 0.05$
Prospective	KP	91.6% (11/12)	8.4% (1/12)
	VP	45.5% (70/154) $P < 0.05$	54.5% (84/154) $P < 0.05$

tistically significant difference between the 2 groups ($P > 0.05$). It also appears that KP may have a higher predisposition for adjacent level fracture than VP. This finding, while observed in complete and prospective analysis, should also be interpreted cautiously as it is subject to the same aforementioned biases. Despite these biases, balloon KP does attempt to restore the volume of the fracture compressed level and also involves the injection of more viscous cement. This may result in a more rigid segmental construct that may subsequently lead to greater junctional stresses adjacent to the treated level.

As with any meta-analysis there are limitations to this study. This analysis is dependent on the quality of each of the individual studies, which largely represent retrospective case series. Although an effort was made to isolate prospective studies, it is difficult to quantify study quality and appropriately weigh its influence.

In conclusion, VP and KP are 2 minimally invasive procedures that have been shown to be effective in the treatment of symptomatic vertebral compression fractures. Although the incidence of adverse events for both VP and KP are low, it appears that VP is associated with a statistically significantly increased rate of procedure-related complications and cement extravasation (symptomatic and asymptomatic). Future prospective studies with large patient enrollment will be needed to further validate the finding of this meta-analysis.

■ Key Points

- Complications from KP and VP are rare.
- The incidence of procedure-related complications appears to be lower for KP than for VP.
- The incidence of symptomatic and asymptomatic cement leakage appears to be lower for KP then for VP.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.spinejournal.com).

References

1. Hulme PA, Krebs, Ferguseon SJ, et al. Vertebroplasty and kyphoplasty: a Systematic Review of 69 Studies. *Spine* 2006 31;17:1983–2001.
2. Taylor RS, Taylor JT, Fritzell P. Balloon kyphoplasty and vertebropalsty for vertebral compression fractures: a comparative review of efficacy and safety. *Spine* 2006 31;23: 2747–55.
3. Phillips FM. Minimally invasive treatments of osteoporotic vertebral compression fractures. *Spine* 2003 28;15s:s45–s53.
4. Lee BJ, Lee SR, Yoo TY. Paraplegia as a complication of vertebroplasty with polymethylmethacralate. *Spine* 2002;17:19:E419–22.
5. Harrington KD. Major neurological complications following percutaneous vertebroplasty with polymethylmethacralate: a case report. *JBJS Am* 2001;83: 1070–3.
6. Lin EP, Ekholm S, Hiwatashi A, et al. Vertebroplasty: cement leakage into the disc increases the risk of new fracture of adjacent vertebral body. *AJNR* 2004;25:175–80.
7. Komemushi A, Tanigawa N, Kariya S, et al. Percutaneous vertebroplasty for osteoporotic compression fracture: multivariate study of predictors of new vertebral body fracture. *Cardiovasc Intervent Radiol* 2006;29:580–5.
8. Phillips FM, Todd Wetzel F, Lieberman I, et al. An in vivo comparison of the potential for extravertebral cement leak after vertebroplasty and kyphoplasty. *Spine* 2002;27:2173–8.