

KYPHOPLASTY VERSUS VERTEBROPLASTY IN VERTEBRAL COMPRESSION FRACTURES: A META-ANALYSIS

CIFOPLASTIA VS. VERTEBROPLASTIA EM FRATURAS POR COMPRESSÃO VERTEBRAL: UMA METANÁLISE

CIFOPLASTIA VERSUS VERTEBROPLASTIA EN FRACTURAS POR COMPRESIÓN VERTEBRAL: UN METAANÁLISIS

WILLIAM ZARZA¹ , NELSON ASTUR¹ , LEANDRO KIM¹ , LUCAS MIOTTO¹ , RODRIGO GÓES MEDÉA DE MENDONÇA¹ , ALBERTO O. GOTTFRYD¹ ,
MARIA FERNANDA S. CAFFARO¹ , ROBERT MEVES¹ 

1. Hospital de Misericórdia Santa Casa de São Paulo, Orthopedics and Traumatology Department, Spine Diseases Group, São Paulo, São Paulo, Brazil.

ABSTRACT

Introduction: Vertebral fracture is the main complication of osteoporosis and is common among the elderly. Conservative treatment is the first choice for osteoporotic vertebral compression fractures (OVCF) but for persistent painful cases, percutaneous vertebral cement augmentation techniques, such as vertebroplasty and kyphoplasty, are indicated. We performed a systematic review to compare clinical and radiological outcomes of both methods. **Methods:** A systematic review was performed according to the PRISMA and Cochrane Handbook for Systematic Reviews of Interventions. The PICO search strategy consisted of the following terms: Population- Patients with OVCFs; Intervention- Kyphoplasty; Control- Vertebroplasty; Outcomes- Pain, Cement Leakage, Vertebral Body Height, Adjacent level fractures, Oswestry (ODI) and SF36. **Results:** Seven articles were included in the qualitative analysis, selecting only randomized controlled trials. Four hundred and fifty patients were treated with vertebroplasty (VP) and 469 with kyphoplasty (KP). The leakage rate of the VP group was 63% versus 14% for the KP group. However, these results were without statistical significance. The Visual Analogue Scale (VAS), ODI and SF-36 outcomes were evaluated based on the 6-month and 1-year follow-up results, and we were unable to find any significant differences between treatments. For restoration of vertebral height, the values of the KP group were, on average, 0.71 cm higher than those of the VP group, with 95% CI. **Conclusion:** Based on this systematic review, kyphoplasty is superior to vertebroplasty for achieving gains in vertebral body height. As regards cement leakage and other clinical outcomes, neither method showed statistically significant superiority. **Level of Evidence I; Systematic review.**

Keywords: Kyphoplasty; Vertebroplasty; Meta-Analysis; Spinal Fractures.

RESUMO

Introdução: A fratura vertebral é a principal complicação da osteoporose e ocorre com frequência em idosos. O tratamento conservador é a primeira escolha para fraturas compressivas vertebrais por osteoporose (FCVO), mas para casos dolorosos persistentes, as técnicas de cimentação vertebral, como vertebroplastia e cifoplastia, são indicadas. Realizamos uma revisão sistemática para comparar os resultados clínicos e radiológicos de ambos os métodos. **Métodos:** Uma revisão sistemática foi realizada de acordo com o PRISMA e o Manual Cochrane de Revisões Sistemáticas. A estratégia de busca PICO foi: População - Pacientes com FCVOs; Intervenção - Cifoplastia; Controle - Vertebroplastia; Resultados - Dor, Extravazamento de Cimento, Altura do Corpo Vertebral, Fraturas em Nível Adjacente, Oswestry (ODI) e SF36. **Resultados:** Sete artigos foram incluídos na análise qualitativa, somente ensaios clínicos randomizados. Quatrocentos e cinquenta pacientes foram tratados com vertebroplastia (VP) e 469 com cifoplastia (CP). A taxa de extravazamento de cimento do grupo VP foi de 63% contra 14% do CP, no entanto, não atingiu significância estatística. Os desfechos da Escala Visual Analógica (EVA), ODI e SF-36 foram avaliados considerando os resultados de seis meses e um ano de seguimento e não pudemos apontar diferenças entre os tratamentos. Por fim, a CP apresenta valores médios 0,71 cm maiores do que a VP para a restauração da altura do corpo vertebral, com IC de 95%. **Conclusão:** Nesta revisão sistemática a cifoplastia foi superior à vertebroplastia para ganho de altura do corpo vertebral. Não houve superioridade estatisticamente significativa entre os dois métodos para extravazamento de cimento e outros resultados clínicos. **Nível de Evidência I; Revisão sistemática**

Descritores: Cifoplastia; Vertebroplastia; Metanálise; Fraturas da Coluna Vertebral.

RESUMEN

Introducción: La fractura vertebral es la principal complicación de la osteoporosis y ocurre con frecuencia en los ancianos. El tratamiento conservador es la primera opción para las fracturas vertebrales por compresión debidas a la osteoporosis (FCVO), pero para los casos de dolor persistente están indicadas las técnicas de cementación vertebral, como la vertebroplastia y la cifoplastia. Se realizó una revisión sistemática para comparar los resultados clínicos y radiológicos de ambos métodos. **Métodos:** Se llevó a cabo una revisión sistemática de

Study conducted at the Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, Brazil.

Correspondence: William Zarza Santos. Rua Dr. Cesário Motta Júnior, 112, Vila Buarque, Departamento de Ortopedia e Traumatologia, 2º andar, Sala do Grupo de Afecções da Coluna Vertebral, São Paulo, SP, Brazil. 01221-020. willzarza@yahoo.com.br



acuerdo con la declaración PRISMA y el Manual Cochrane de Revisiones Sistemáticas. La estrategia de búsqueda PICO fue: Población: Pacientes con FCVO; Intervención: Cifoplastia; Control- Vertebroplastia; Resultados: Dolor, Extravasación del cemento, Altura del Cuerpo Vertebral, Fracturas de Nivel Adyacente, Oswestry (ODI) y SF36. Resultados: Se incluyeron siete artículos en el análisis cualitativo, sólo ensayos clínicos aleatorios. Cuatrocientos cincuenta pacientes fueron tratados con vertebroplastia (VP) y 469 con cifoplastia (CP). La tasa de extravasación de cemento en el grupo VP fue del 63% frente al 14% en el CP, sin embargo, no alcanzó significancia estadística. Los resultados de la Escala Visual Analógica (EVA), ODI y SF-36 se evaluaron teniendo en cuenta los resultados de 6 meses y 1 año de seguimiento y no pudimos señalar diferencias entre los tratamientos.. Finalmente, el CP presenta valores promedios 0,71 cm superiores al VP para restaurar la altura del cuerpo vertebral, con un IC del 95%. Conclusión: En esta revisión sistemática, la cifoplastia fue superior a la vertebroplastia para el aumento de altura del cuerpo vertebral. No hubo una superioridad estadísticamente significativa entre los dos métodos para la extravasación del cemento y otros resultados clínicos. **Nivel de Evidencia I; Revisión sistemática.**

Descriptor: Cifoplastia; Vertebroplastia; Metaanálisis; Fracturas de la Columna Vertebral.

INTRODUCTION

Vertebral fracture is the main complication of osteoporosis¹. It presents clinically as back pain, and radiographically as a compressive fracture in the vertebral body, usually located at the thoracolumbar transition.² Osteoporotic vertebral compression fractures (OVCF) are common among the elderly, especially in postmenopausal women,³ and it is estimated that 30% to 50% of women and 20% to 30% of men aged over fifty will develop vertebral fractures during their lives, with half of these people having multiple lesions.⁴⁻⁶

Conservative treatment is the first choice for OVCF, and is very efficient in most cases.⁷ However, where there is severe pain or functional limitation, percutaneous vertebral cement augmentation techniques, such as vertebroplasty (VP) and kyphoplasty (KP), are indicated, primarily to reduce the back pain and improve the patient's functional status and secondarily, to stabilize the fractured vertebra.⁸

Unlike vertebroplasty, kyphoplasty has the advantage that it uses a balloon, producing a space within the vertebral body, which theoretically reduces cement leakage during the procedure and also allows for the restoration of vertebral body height.⁹

Although some systematic reviews comparing kyphoplasty and vertebroplasty to treat vertebral compression fractures have been published previously, they do not provide reliable evidence due to their flawed methodologies, and the fact that they include articles other than randomized clinical trials.¹⁰⁻¹³ Some of the conclusions reported by previous systematic reviews are biased by the inclusion of low quality and conflicting papers, including prospective cohorts, retrospective and non-randomized studies.¹⁰⁻¹³ Although kyphoplasty is widely used to treat vertebral compression fractures in most osteoporotic patients, and is preferred by surgeons as a newer and safer option to traditional vertebroplasty, there is still no clear evidence that it presents better clinical outcomes or fewer complication rates.

In this study, we perform a meta-analysis of only randomized clinical trials, comparing kyphoplasty versus vertebroplasty to treat OVCF.

METHODS

A systematic literature review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)¹⁴ and Cochrane Handbook of Systematic Reviews.¹⁵

Eligibility Criteria

Inclusion criteria: defined by the PICO search strategy that specifies the population to be evaluated, the intervention, the control, and the desired outcomes. Only Randomized Controlled Trials (RCT) were considered for analysis. The research questions based on PICO were:

- Do patients with OVCFs submitted to kyphoplasty have better pain scores compared to those submitted to vertebroplasty?
- Do patients with OVCFs submitted to kyphoplasty present better vertebral body height restoration compared to those submitted to vertebroplasty?
- Do patients with OVCFs submitted to kyphoplasty present more adjacent level fractures compared to those submitted to vertebroplasty?

- Do patients with OVCFs submitted to kyphoplasty present more cement leakage compared to those submitted to vertebroplasty?
- Do patients with OVCFs submitted to kyphoplasty have better disability scores compared to those submitted to vertebroplasty?
- Do patients with OVCFs submitted to kyphoplasty present better quality-of-life outcomes compared to those submitted to vertebroplasty?

Sources of Information

Two authors (WZS) (LMJ) independently reviewed articles available in the MEDLINE (PubMed), Embase, Lilacs, and Cochrane Central Register databases of randomized assays. The search terms kyphoplasty, vertebroplasty, osteoporosis and vertebral fractures were used, both individually and in combination. Articles on vertebroplasty and kyphoplasty for painful OVCF, published between January 1987 and March 2019, were downloaded and studied. Only articles written in English and approved for publication were included.

Search

The search strategy for PubMed is shown in Appendix 1. One author (N.A.) assessed and guided the results of the electronic literature survey, and any divergences were resolved by group discussion.

Study Selection

The retrieved articles were first assessed based on their titles; the titles identified were reevaluated based on the abstracts, and for the selected abstracts, the papers were then assessed in full. All the authors also searched for cross-references.

Data collection process

Data was extracted independently by two reviewers (WZ and LK), both of whom are board certified in spine surgery. Any disagreements that arose were discussed and resolved by consensus. The following items were included in our form and collected for every RCT: study design, number of patients assigned and assessed at the end of the study, participant's age, and study intervention. The primary outcomes assessed were pain relief, improvement in disability and quality-of-life scores, cement leakage and vertebral body height.

Risk of bias in individual studies

Two of the reviewers (W.Z.S) (L.D.K) independently assessed the methodological quality of the included studies, in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Figure 1).

Summary measures

A meta-analysis were performed using the inverse variance method, with the DerSimonian-Laird estimator for τ^2 . The analyses were performed using the software R 3.5.1 (R Core Team, 2019) with the meta package (Schwazer, 2013). Binary events (such as Cement Leakage and Adjacent Level Fractures) were meta-analyzed in rate ratios, and continuous outcome comparisons (VAS, VBH, ODI, SF36) were presented as mean differences.

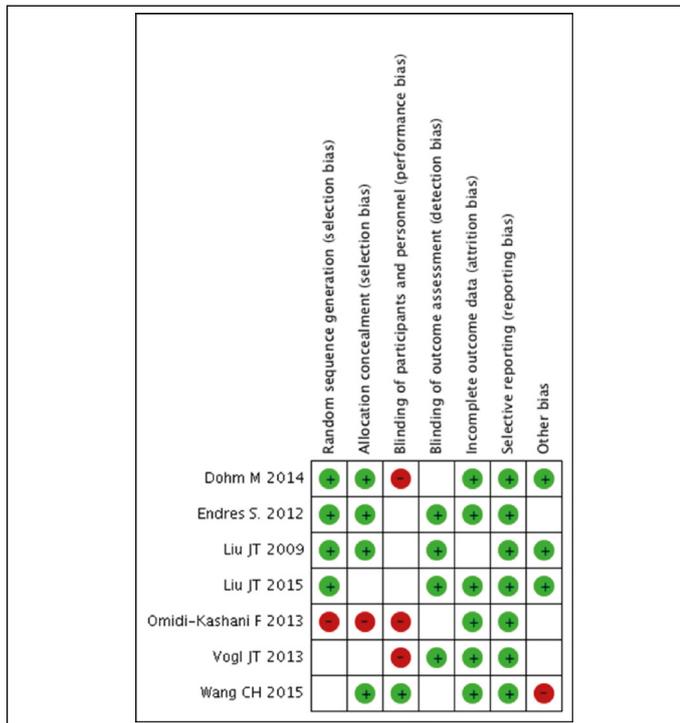


Figure 1. Risk of bias Summary.

Summary of results

All the meta-analyses were presented according to random and fixed effect models. The I² index was reported, in order to assess heterogeneity between studies.

RESULTS

After the full literature search, six hundred and fifty-seven articles were identified. One hundred and twenty-one duplicate articles were excluded. Based on a review of the abstracts, five hundred and thirteen articles were excluded. After applying the exclusion criteria, a further sixteen articles were excluded. In total, seven articles were included in the qualitative synthesis.¹⁶⁻²³

The mechanism for inclusion of articles is shown in the Flow-chart-PRISMA Guidelines (Figure 2).

The results were comprised of seven randomized controlled trials. We identified a total of 919 patients. Of these, 450 patients were treated with vertebroplasty (VP) and 469 with kyphoplasty (KP). The characteristics and patient demographics of the included studies (age, sex, and the outcomes assessed) are summarized in Table 1.

Cement leakage was analyzed in five studies.¹⁶⁻²⁰ The leakage rate of the VP group was 63% versus 14% for the KP group. However, considering the fixed model result given the high variability of the results (I²=85%), it was not possible to indicate, with a significance level of 5%, that the treatments differed as regards Cement Leakage (CL) rate. The RR was estimated at 0.78 [95% CI 0.44 - 1.39]. The graphical analysis of this outcome is represented in Figure 3.

The outcome of the Visual Analogue Scale (VAS) was evaluated

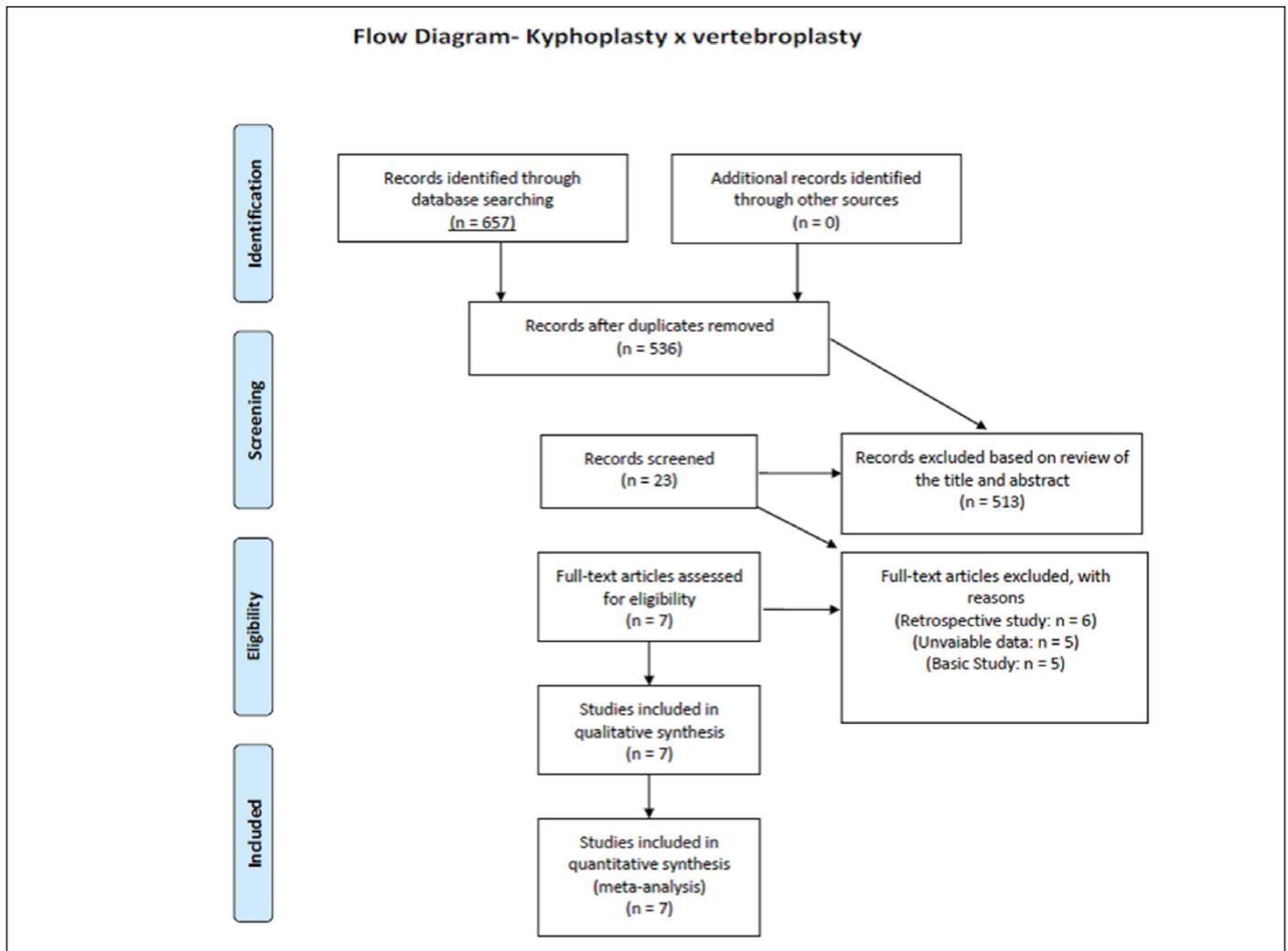


Figure 2. Flowchart – PRISMA Guideline.

considering the 6-month and 1-year follow-up results.^{17-19,22} Mean and standard deviations were estimated for both groups. We were not able to demonstrate differences between treatments at a significance level of 5% ($I^2=23.2\%$). This result is represented by Figure 4.

Regarding the results for the Oswestry Disability Index (ODI) and Short Form 36 (SF-36) scores, for both the 6-month and 1-year follow-up groups, in the fixed and mixed models, there was insufficient evidence to conclude that the KP group was superior to the VP group. This is demonstrated graphically in Figures 5 and 6 (I^2 : 61.7% and 91.6%, respectively).

Finally, in relation to Vertebral Body Height (VBH),^{21,22} the values for the KP group were, on average, 0.71 cm higher than those of the VP group, with 95% CI [0.61; 0.81] (I^2 : 0.0%). This superiority is represented in Figure 7.

DISCUSSION

This study compares clinical and radiographic results, including complications, of two different vertebral augmentation methods to treat osteoporotic vertebral compression fractures. Therefore, we performed a systematic review and meta-analysis with a strict methodology, including only randomized clinical trials, which was not done in previous published reviews on the same subject.¹⁰⁻¹³

Due to conflicting results of research on kyphoplasty and vertebroplasty, the theoretical advantage of one technique over the other is controversial. While kyphoplasty promises effectiveness in gaining vertebral height, and less complications such as cement leakage, vertebroplasty is more cost-effective compared to the more expensive, improved technique. Supported by the literature, there is a tendency for surgeons to change their practices, with kyphoplasty becoming more popular. However, we still do not have clear evidence of the superiority of kyphoplasty over vertebroplasty, and it appears that its advantage in restoring vertebral height is not accompanied by clinical improvement.

After performing a meta-analysis of seven randomized controlled trials comparing both techniques, we found no significant difference between them for most of the outcomes analyzed, including clinical outcomes such as VAS, ODI and SF-36, and cement leakage. The most feared complication of vertebral cement augmentation is leakage of cement into the spinal canal or blood vessels, which can have severe and major complications, such as spinal cord injury, paraplegia, or thromboembolic events. Although kyphoplasty delivers a controlled, low-pressure injection of cement into a previously prepared cavity in the vertebral body, there is no statistical evidence that it reduces cement leakage when compared to vertebroplasty. Wang et al.,¹⁰ Gu et al.,¹¹ and Xiao et al.,¹² published previous

Table 1. Characteristics of the Included Studies.

Author(s)	Year	Location	Study Design	N KP	N VP	Total	Sex (F/M) KP	Sex (F/M) VP	Age KP – mean (SD)	Age VP – mean (SD)	Outcome
1. Vogl JT.	2013	Germany	RCT	49	28	77	36/13	19/9	72,0 (10,2)	74,0 (11,5)	CL / ALF / VBH
2. Endres S.	2012	Germany	RCT	20	21	41	14/6	12/8	63,3	71,3	CL / ALF / VBH / VAS / ODI
3. Omid	2013	Iran	RCT	29	28	57	22/7	22/6	72,1 (6,2)	72,4 (8,2)	CL / ALF / VAS / SF-36
4. Liu JT.	2009	Taiwan	RCT	50	50	100	39/11	38/12	72,3 (7,6)	73,4 (6,4)	ALF / VAS / VBH
5. Wang CH.	2015	China	RCT	72	68	140	40/14	41/12	68,6 (8,3)	69,4 (8,9)	CL / VAS / VBH / ODI
6. Dohm M.	2014	USA	RCT	199	205	404	154/45	158/47	75,6	75,6	CL / SF-36 / ODI / KC
7 Liu JT.	2015	Taiwan	RCT	50	50	100	39/11	38/12	72,3 (7,6)	74,3 (6,4)	VBH / KC / VAS

RCT: Randomized Clinical Trial; KP: Kyphoplasty; VP: Vertebroplasty; CL: Cement leakage; ALF: Adjacent Level Fracture; VBH: Vertebral body height; ODI: Oswestry; SF-36: Short form 36; KC: Kyphosis correction.

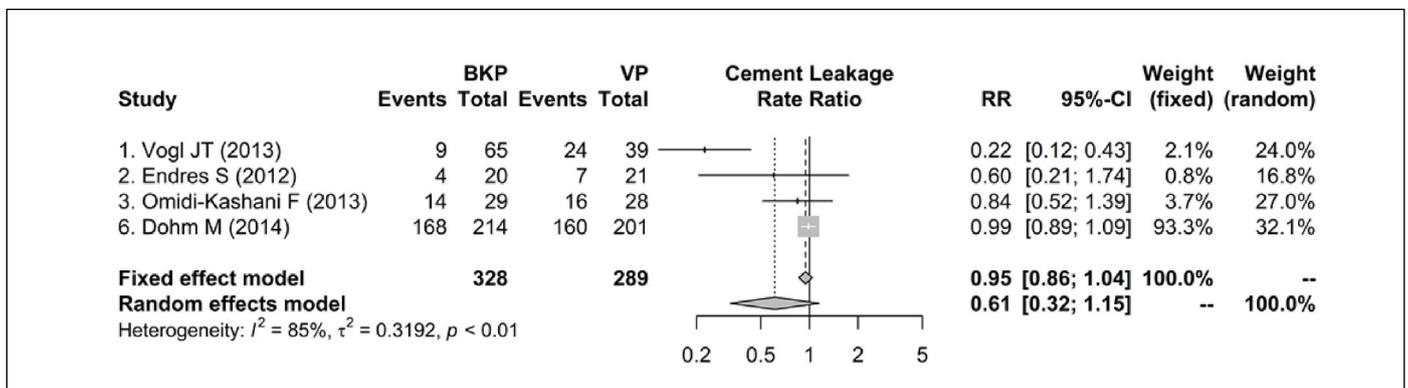


Figure 3. Cement leakage compared for Kyphoplasty versus vertebroplasty.

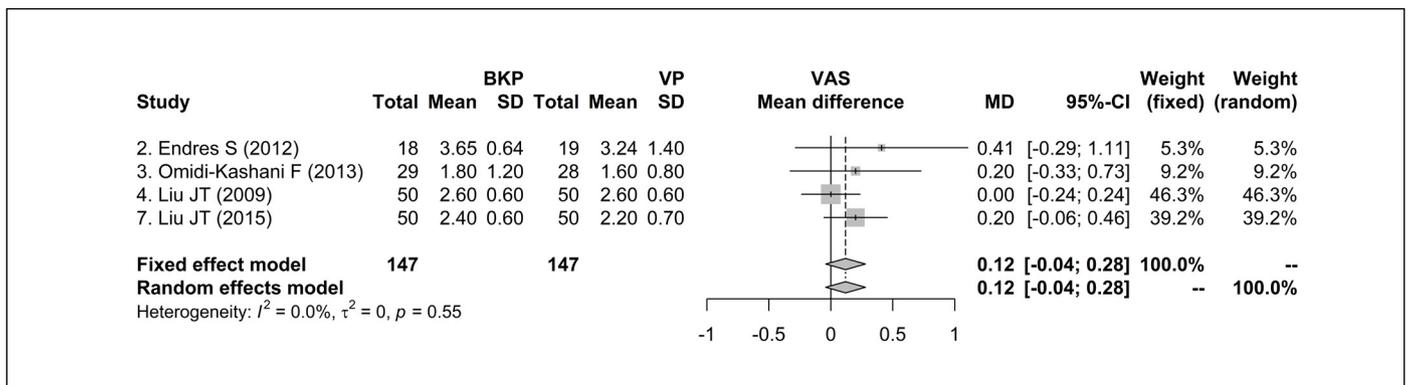


Figure 4. Pain outcome comparison of Kyphoplasty versus Vertebroplasty.

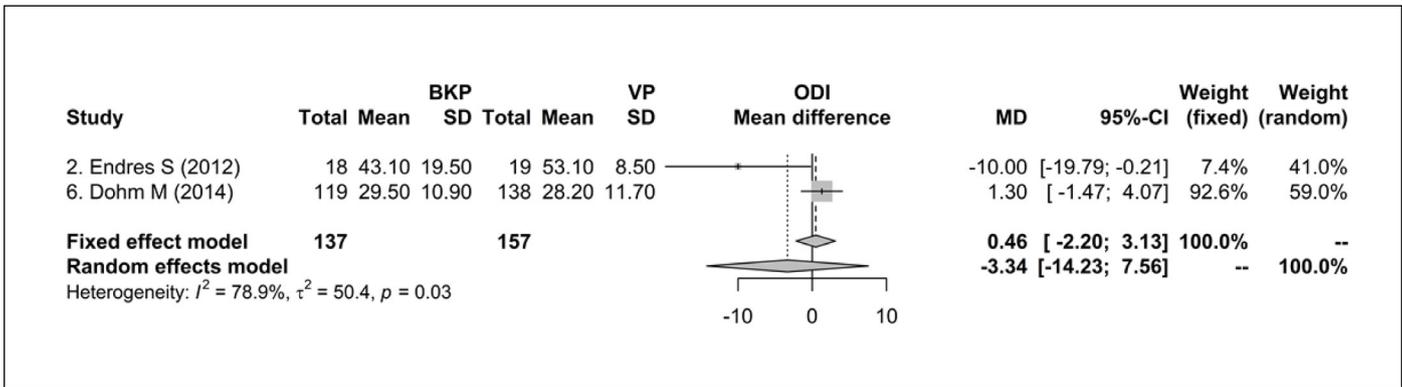


Figure 5. Meta-analysis of the mean difference between the intervention group (KP) and the control group (VP) for ODI.

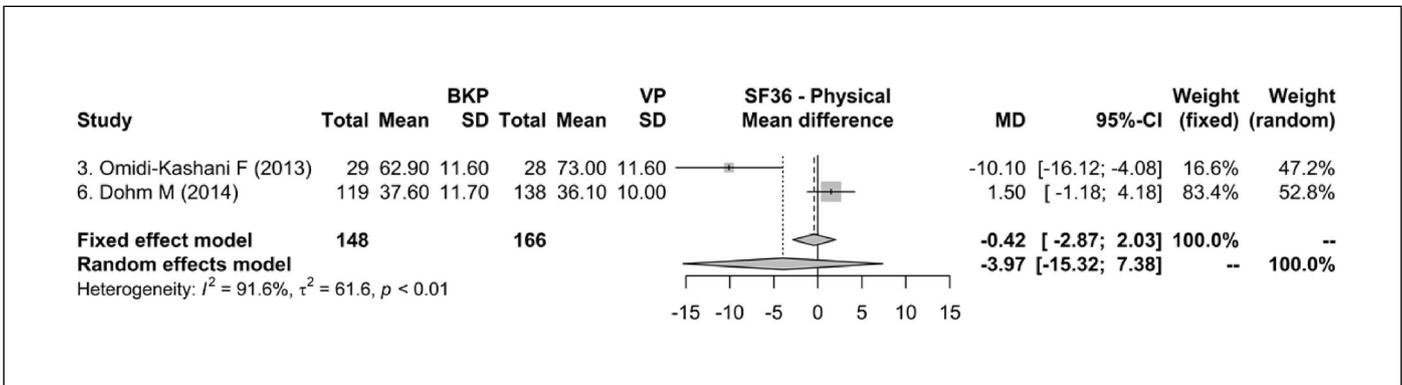


Figure 6. Meta-analysis of the mean difference of the intervention group (KP) versus the control group (VP) for the SF36.

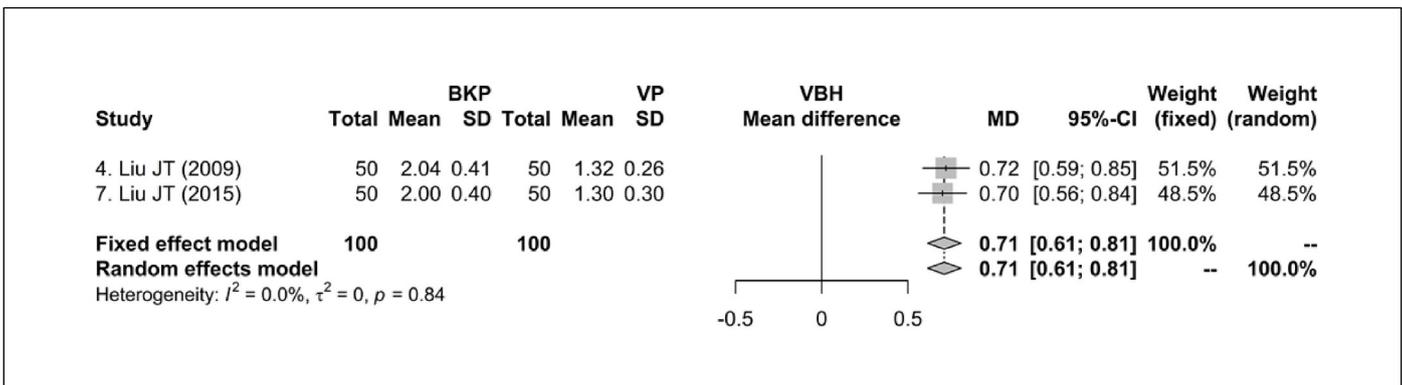


Figure 7. Meta-analysis of the mean difference of the intervention group (KP) versus the control group (VP) for vertebral body height.

systematic reviews comparing both techniques. They concluded that there is significantly less cement leakage in the kyphoplasty technique, but they all included cohorts and retrospective studies in their reviews, and not only RCTs, which may have contributed to biased conclusions. Although we found a higher leakage rate of 63% for the VP group versus 14% for the KP group, this result was not statistically significant. As for the improvement in pain and quality of life Gu et al.,¹¹ and Zhao et al.,¹³ also found equivalence for both treatments in their systematic reviews. Wang et al.,¹⁰ divided their clinical results into short- and long-term follow-up and found similarity between the treatments at both time points. They demonstrated that kyphoplasty showed better results for pain improvement in the short-term follow-up, but there was no statistical difference between the techniques in the long term. The force of evidence of these conclusions is weakened by the inclusion of retrospective, cohort or non-randomized studies. However, the results of our systematic review, which found practically no differences between kyphoplasty versus vertebroplasty, also presents a bias, as the randomized clinical trials included in our analysis presented high heterogeneity.

The only statistically significant difference between the two surgical techniques was the gain in vertebral height. The origin of the term kyphoplasty is obviously based on the theoretical ability of this technique to restore vertebral alignment and height by inflating a balloon in the vertebral body. The balloon lifts the superior endplate, correcting or mitigating the kyphosis created by the compression fracture. The power of kyphosis correction by balloon kyphoplasty depends on the time and degree of vertebral collapse of the fracture. A chronic vertebral compression fracture will present great rigidity and less potential for restoration of height than an acute and more mobile fracture. A severe collapse of body height might be an obstacle to the introduction of the percutaneous balloon into the vertebra, or could limit its inflation. Vertebroplasty is based on the pure injection of cement into the vertebral body without any previous preparation, which provides structural support to the fractured vertebra but does not restore its height. This outcome is usually presented with statistical significance in all trials and systematic reviews comparing kyphoplasty with vertebroplasty or non-surgical treatment. Otherwise, this radiographic improvement is not related

to clinical improvement, as there was no statistical significance in VAS, SF 36 and ODI.

The widespread acceptance of kyphoplasty by spine surgeons led to the development of new augmentation techniques by the industry that promised the ability to restore vertebral height, and these techniques are gaining in popularity.^{24,25} However, none has proven superiority over the other. Surgical strategies to decrease cement leakage have been proposed: slower injection of cement under low pressure; previous injection of contrast into the cavity created in the vertebrae, performed under fluoroscopic control, to observe leakage; and waiting a longer period between preparing the cement and applying the injection, to achieve higher viscosity. New cement with higher viscosity has also been developed for vertebroplasty, and has demonstrated less leakage rate and higher safety.²⁶

This is a meta-analysis of a systematic review that included only RCTs, with very strict control over the quality of the articles included. Previous meta-analyses on this topic have included articles with weak quality of evidence, such as cohort studies, non-randomized trials, and retrospective studies. Despite our highly selective inclusion criteria, we found some weaknesses and methodological flaws in the studies included, especially in relation to sample size, randomization, allocation/concealment mechanism, implementation, and blinding. Furthermore, only three of the seven RCTs presented discussion of their study limitations, evaluation of possible biases, or exposure of inaccuracies, diminishing the credibility of these studies. We understand that performing a RCT of a surgical intervention is cumbersome and expensive, and some biases will be unavoidable, especially when it comes to blinding of surgeons or patients.

Another limitation of this systematic review is that we focus only on the comparison between vertebroplasty and kyphoplasty,

excluding conservative treatment such as medications, brace and physiotherapy, which have demonstrated strong evidence of benefits in vertebral compression fractures in osteoporosis.⁷ While many authors advocate conservative treatment as the treatment of choice for osteoporotic fractures, several studies comparing kyphoplasty and non-surgical management²⁷⁻²⁹ favor surgery with vertebral augmentation, especially in relation to pain improvement in the short-term follow-up. This would lead to decreased lengths of hospital stay and/or bed restriction of elderly patients with fractures, reducing associated complications.³⁰

CONCLUSION

This systematic review and meta-analysis showed superiority of kyphoplasty over vertebroplasty only in relation to the gain in vertebral body height gain. But for clinical outcomes and cement leakage, there was no statistically significant superiority of one method over the other. Further homogeneous randomized clinical trials are needed, using a better methodology, to elucidate the benefit of one technique over the other.

ACKNOWLEDGMENTS

The authors would like to thank the Brazilian Spine Society for financial and academic incentive to this research and Lucas Damiani for his help with statistical analysis.

All authors declare no potential conflict of interest related to this article.

CONTRIBUTIONS OF THE AUTHORS: Each author made significant individual contributions to this manuscript. WZS: data writing and analysis; RM: data analysis and review; MFSC: data analysis and review; AOG: data analysis and review; NA: data analysis, data writing and review; RGMM: data analysis and review; LDJ: data analysis and review; LMJ: data analysis and review.

REFERENCES

- Gaitanis IN, Hadjipavlou AG, Katonis PG, Tzermiadianos MN, Pasku DS, Patwardhan AG. Balloon kyphoplasty for the treatment of pathological vertebral compressive fractures. *Eur Spine J*. 2005;14(3):250-60.
- Ensrud KE, Schousboe JT. Clinical practice - Vertebral Fractures. *N Engl J Med*. 2011;364(17):1634-42.
- Voormolen MHJ. Kyphoplasty. *Neuroradiol*. 2011;53(Suppl 1):S203-5.
- Nanes MS, Kallen CB. Osteoporosis. In: *Semin. Nucl. Med.* Springer International Publishing; 2014. p 1-13.
- McConnell CT, Wippold FJ, Ray CE, Weissman BN, D Angevine P, Fries IB, et al. ACR appropriateness criteria management of vertebral compression fractures. *J Am Coll Radiol*. 2014;11(8):757-63.
- Chandra RV, Meyers PM, Hirsch JA, Abruzzo T, Eskey CJ, Hussain MS, et al. Vertebral augmentation: Report of the Standards and Guidelines Committee of the Society of NeuroInterventional Surgery. *J Neurointerv Surg*. 2014;6(1):7-15.
- Lee HM, Park SY, Lee SH, Suh SW, Hong JY. Comparative analysis of clinical outcomes in patients with osteoporotic vertebral compression fractures (OVCFs): Conservative treatment versus balloon kyphoplasty. *Spine J*. 2012;12(11):998-1005.
- Wang H, Sribastav S, Sen, Ye F, Yang C, Wang J, Liu H, et al. (2015) Systematic Review Comparison of Percutaneous Vertebroplasty and Balloon Kyphoplasty for the Treatment of Single Level Vertebral Compression Fractures: A Meta-analysis of the Literature. *Pain Physician*. 2015;18(3):209-22.
- Gu CN, Brinjikji W, Evans AJ, Murad MH, Kallmes DF. Outcomes of vertebroplasty compared with kyphoplasty: A systematic review and meta-analysis. *J Neurointerv Surg*. 2015;8(6):636-42.
- Xiao H, Yang J, Feng X, Chen P, Li Y, Huang C, et al. Comparing complications of vertebroplasty and kyphoplasty for treating osteoporotic vertebral compression fractures: a meta-analysis of the randomized and non-randomized controlled studies. *Eur J Orthop Surg Traumatol*. 2014;25(Suppl 1):77-85.
- Zhao S, Xu CY, Zhu AR, Ye L, Lv LL, Chen L, et al. Comparison of the efficacy and safety of 3 treatments for patients with osteoporotic vertebral compression fractures: A network meta-analysis. *Med (Baltimore)*. 2017;96(26):e7328.
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:1006-12.
- Higgins J, (ed). *Cochrane Handbook for Systematic Reviews of Interventions*. Hoboken, NJ: Cochrane; 2008.
- Vogl TJ, Pflugmacher R, Hierholzer J, Stender G, Gounis M, Wakhloo A, et al. Cement directed kyphoplasty reduces cement leakage as compared with vertebroplasty: Results of a controlled, randomized trial. *Spine (Phila Pa 1976)*. 2013;38(20):1730-6.
- Endres S, Badura A. Shield kyphoplasty through a unipedicular approach compared to vertebroplasty and balloon kyphoplasty in osteoporotic thoracolumbar fracture: A prospective randomized study. *Orthop Traumatol Surg Res*. 2012;98(3):334-40.
- Omid-Kashani F, Samini F, Hasankhani EG, Kachooei AR, Toosi KZ, Golhasani-Keshtan F. Does percutaneous kyphoplasty have better functional outcome than vertebroplasty in single level osteoporotic compression fractures? A comparative prospective study. *J Osteoporos*. 2013:1-5.
- Wang CH, Ma JZ, Zhang CC, Nie L. Comparison of high-viscosity cement vertebroplasty and balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. *Pain Physician*. 2015;18(2):E187-94.
- Dohm M, Black CM, Dacre A, Tillman JB, Fueredi G, KAVIAR investigators. A randomized trial comparing balloon kyphoplasty and vertebroplasty for vertebral compression fractures due to osteoporosis. *Am J Neuroradiol*. 2014;35(12):2227-36.
- Liu JT, Li CS, Chang CS, Liao WJ. Long-term follow-up study of osteoporotic vertebral compression fracture treated using balloon kyphoplasty and vertebroplasty. *J Neurosurg Spine*. 2015;23(1):94-8.
- Liu JT, Liao WJ, Tan WC, Lee JK, Liu CH, Chen YH, et al. Balloon kyphoplasty versus vertebroplasty for treatment of osteoporotic vertebral compression fracture: A prospective, comparative, and randomized clinical study. *Osteoporos Int*. 2010;21(2):359-364.
- Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 Statement : updated guidelines for reporting parallel group randomised trials. *BMC Med*. 2010;8:18.
- Otten LA, Bornemann R, Jansen TR, Kabir K, Pennekamp PH, Wirtz DC, et al. Comparison of balloon kyphoplasty with the new Kiva(R) VCF system for the treatment of vertebral compression fractures. *Pain Physician*. 2013;16(5):E505-12.
- Kruger A, Oberkircher L, Figiel J, Floßdorf F, Bolzinger F, Noriega DC, et al. Height restoration of osteoporotic vertebral compression fractures using different intravertebral reduction devices: a cadaveric study. *Spine J*. 2013;15(5):1092-8.
- Zhang L, Wang J, Feng X, Tao Y, Yang J, Wang Y, et al. A comparison of high viscosity bone cement and low viscosity bone cement vertebroplasty for severe osteoporotic vertebral compression fractures. *Clin Neurol Neurosurg*. 2015;129:10-6.
- Meirhaeghe J Van, Bastian L, Boonen S, Ranstam J, Tillman JB, Wardlaw D. A Randomized Trial of Balloon Kyphoplasty and Nonsurgical Management for Treating Acute Vertebral Compression Fractures Vertebral Body Kyphosis Correction and Surgical Parameters. *Spine (Phila Pa 1976)*. 2013;38(12):971-83.
- Boonen S, Van Meirhaeghe J, Bastian L, Cummings SR, Ranstam J, Tillman JB, et al. Balloon kyphoplasty for the treatment of acute vertebral compression fractures: 2-year results from a randomized trial. *J Bone Miner Res*. 2011;26(7):1627-37.
- Movrin I. Adjacent level fracture after osteoporotic vertebral compression fracture: A non-randomized prospective study comparing balloon kyphoplasty with conservative therapy. *Wiener Klin Wochenschr*. 2012;124(9-10):304-11.
- Borgström F, Olafsson G, Ström O, Tillman JB, Wardlaw D, Boonen S, et al. The impact of different health dimensions on overall quality of life related to kyphoplasty and non-surgical management. *Osteoporos Int*. 2013;24(7):1991-9.

Appendix 1. Search strategy for PubMed.

```
((Osteoporosis[mh] OR osteoporos*[tw] OR osteoporotic*[tw]) AND ("Fractures, Compression"[mh] OR "Compression Fracture"[tw] OR "Compression Fractures"[tw] OR "Spinal Fractures"[mh] OR "Spinal Fractures"[tw] OR "Spinal Fracture"[tw] OR "Vertebral Collapse"[tw] OR "vertebral augmentation"[tw] OR "spinal augmentation"[tw] OR "vertebral fracture"[tw] OR "vertebral fractures"[tw] OR OVCFS[tw] OR ((spinal[tw] OR spine[tw] OR Spine[mh] OR "Spinal Column"[tw] OR "Vertebral Column"[tw] OR espinal*[tw] OR vertebra*[tw] OR column*[tw] OR thoracolumbar[tw] OR lumbar[tw]) AND (injur*[tw] OR fractur*[tw] OR compress*[tw] OR traumatism*[tw] OR trauma[tw] OR collaps*[tw]))) AND ((kyphoplasty[mh] OR kyphoplasty[tw] OR "Balloon Vertebroplasty"[tw]) AND (Vertebroplasty[mh] OR Vertebroplast*[tw])) AND (Humans[mh] AND medline[sb] AND (aged, 80 and over[mh] OR aged[mh] OR middle age[mh]))) AND (((Complication* OR "adverse effects" OR "Cement Extravasation" OR "cement leakage" OR "Extravasation of Diagnostic and Therapeutic Materials" OR (extravasa*[tiab] AND (cement*[tiab] OR ciment*[tiab])) OR "Pulmonary Embolism" OR "Pulmonary Thromboembolism" OR sequel*[tiab])) OR (Pain[mh] OR Pain[tiab] OR Pains[tiab] OR ache[tiab] OR aches[tiab] OR Painful[tiab] OR VAS[tiab] OR (Visual[tiab] Analogue[tiab] Scale[tiab]) OR NRS[tiab] OR (Numeric[tiab] Rating[tiab] System[tiab]) OR "Physical Suffering"[tiab] OR "Physical Sufferings"[tiab] OR lumbago[tiab]) OR (function[tiab] OR physiology[Subheading] OR "Disability Evaluation"[mh] OR (height[tiab] AND (column[tiab] OR spinal[tiab] OR vertebra*[tiab] OR thoracolumbar[tiab])) OR (Oswestry[tiab] Disability[tiab] Index[tiab]) OR ODI[tiab]))
```