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## Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures: a systematic review

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**Abstract** The aim of this study is to evaluate the efficacy and safety of balloon kyphoplasty (BK) in the management of vertebral compression fractures (VCFs). This study is based on a systematic review of the literature (until October 2004) and meta-analysis of clinical studies assessing the efficacy and safety of BK in the treatment of VCFs. Estimates of effect were based on a random effects model. Meta-regression analyses were carried out where required. A total of 26 studies met the inclusion criteria. Although studies displayed considerable methodological limitations, the results of the clinical series indicate significant improvements in pain intensity, vertebral height, sagittal alignment, functional capacity, and quality of life. Compared with conventional medical management, BK afforded significant improvement in pain intensity and mobility. Likewise, a significant reduction was observed in vertebral collapse, kyphotic deformity, the development

of new vertebral fractures, and hospital stay. Compared with vertebroplasty, the technique reduced the loss of height and the degree of kyphotic deformity, and afforded a significantly lower leakage rate—with no differences in relation to other variables. Regarding adverse effects, leakage affected 7% of all levels treated, while complications were recorded in 2% of the patients, and new vertebral fractures in 16%. The available evidence suggests that BK can be effective and safe in application to VCFs. However, existing studies evince substantial methodological limitations and relatively short follow-up periods. Better clinical research is required to determine the capacity of BK to avoid the functional and physiological sequelae of VCFs and to define the true role of the technique among the existing therapeutic options.

**Keywords** Balloon kyphoplasty · Evidence · Meta-analysis · Vertebral compression fractures

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### Introduction

The growing prevalence of vertebral compression fractures (VCFs) [44, 52], the confirmation of their serious physiological, functional, and psychological repercussions [23, 32, 38, 46, 48], and a large number of patients' refractory to habitual treatment [38, 39, 50] have favored the development of minimally invasive surgical techniques such as balloon kyphoplasty (BK)—the aim of

which is not only to improve the patient symptoms but also to reduce the biomechanical alterations of the spine produced by fracture, thereby avoiding its long-term consequences [2, 19, 40, 60].

The term “kyphoplasty” was introduced by Kyphon Inc. to describe balloon-assisted vertebroplasty. The technique is carried out in the operating room by means of a specific fracture reduction system (The KyphX®, Kyphon Inc.), and comprises several phases: trans- or

extrapedicular bone access until reaching the vertebral body; placement of the inflatable bone impactor within the bone; balloon insufflation under manometric control, elevating the vertebral plate, and creating a cavity within the vertebral body; balloon deflation and filling of the cavity with viscous radiopaque bone cement under low pressure (PMMA KyphX®) through a bone filling device to stabilize the fracture.

The procedure was first used in 1998, and unlike vertebroplasty, it aims not only to secure fracture fixation and stabilization but also to reconstruct the vertebral anatomy and correct the spinal deformity, with the aim of avoiding the medical sequelae of VCFs. While BK has been introduced to clinical practice, no firm conclusions have yet been drawn as to the efficacy and safety of the technique [24, 36, 54]. For this reason, and considering the rate at which the procedure is being diffused and incorporated to clinical practice, the present systematic review aims to analyze the collected body of evidence regarding the efficacy and safety on BK in the treatment of VCFs.

## Methods

For the identification of studies, we performed a systematic review of the literature up until October 2004, involving the following databases: Medline (WebSPIRS, SilverPlatter); CINAHL (WebSPIRS); CC Search Life/Clin, Pollution & Toxicology; The Cochrane Library; Serline: Biomedical Journals; Science citation index expanded (sci-expanded), INAHTA (NHS, DARE, EED, HTA). The search strategy has been: #1: (kyphoplasty) or (vertebroplasty), #2: (fracture\*) or (vertebra\*) or (osteop\*) or (tumor\*), #3: #1 and #2. Likewise, bibliographies of relevant articles were manually examined for additional studies and the industry has been contacted to identify still unpublished material. There were no language restrictions. However, we explicitly excluded proceedings of meetings or congresses.

### Selection of studies

All articles identified were evaluated by two reviewers. For inclusion, the studies were required to meet the following criteria: (a) design: studies conducted in ten or more patients that contained relevant primary clinical data. Since the aim was to analyze the available clinical evidence on BK, no other limitations were imposed—inclusion being made of both experimental and observational designs [45]; (b) population: patients with VCFs of osteoporotic and/or tumoral origin; (c) intervention: BK; (d) comparator: any other medical or surgical procedure; (e) outcomes: the studies were required to include quantitative information relating to at

least one of the following primary interest variables: pain, vertebral height, kyphotic deformity, functional capacity, quality of life (QoL), cement material leakage, complications, and the development of new vertebral fractures. The use of health care resources was included as a secondary variable.

The studies that met the inclusion criteria were exhaustively and independently examined by two reviewers to discard publication duplicity or redundancy. During the trial selection and data extraction, we were not masked to authors, institutions, journal, or interventions assessed.

### Quality assessment

Methodological quality and grade of scientific evidence was evaluated for each selected paper using previously validated recommendations [37]. The possible presence of systematic errors has been analyzed following the recommendations of the Cochrane Collaboration [7].

### Data analysis

The principal characteristics of each of the studies included are detailed in the corresponding tables. To obtain a global measure of the effect of BK upon the variables of interest, use was made of meta-analytical techniques based on the Intercooled Stata 8 program (StataCorp LP Texas USA 1984–2005). The studies were combined according to their clinical homogeneity and outcome measures [16], using a random effects model. Prior to inclusion, we confirmed that all variables were comparable and adequate. The estimation of effect is expressed, in the case of dichotomous variables, as an Odds Ratio (OR) (with a 95% confidence interval, 95% CI) or as a proportion with its corresponding 95% confidence interval. In the case of continuous variables, the estimation of effect is expressed as the difference of means (WMD with 95% CI) between the values at baseline and after BK—estimating the difference of variances by standard formulas [47]. When the original study failed to provide the standard deviation of a continuous variable, it was estimated from the publication data (range or *P* value) [47]. When the original study provided standard error instead of standard deviation, this was calculated using ordinary formulas.

Statistical heterogeneity was analyzed by means of the  $\chi^2$  statistic. The potential reasons for heterogeneity were explored by meta-regression techniques using as analytical variables the etiology of VCF, its estimated age, and the duration of the follow-up period. In those cases where because of the study characteristics or the way in which the results were expressed it proved impossible to apply meta-analytical procedures, an

individual analysis was carried out. Results were deemed significant at a value of  $P < 0.05$ . Because of their limitations and potential misleading results [51], funnel plots were not used to analyze the possibility of publication bias.

## Results

Figure 1 summarizes the search for relevant studies, the excluded studies, and the studies finally included after eliminating the redundancies attributable to the use of several databases. No studies were found that formally analyzed the costs related to BK.

Of the studies located, 26 satisfied the inclusion criteria. Of these, 25 have been published in complete form, and one [15] consists of the case registry corresponding to the formulas submitted to the United States Food and Drug Administration (FDA) (510 kd). This latter study was supplied by the company that owns the system (Kyphon Inc.) without any restrictions on the content of the manuscript.

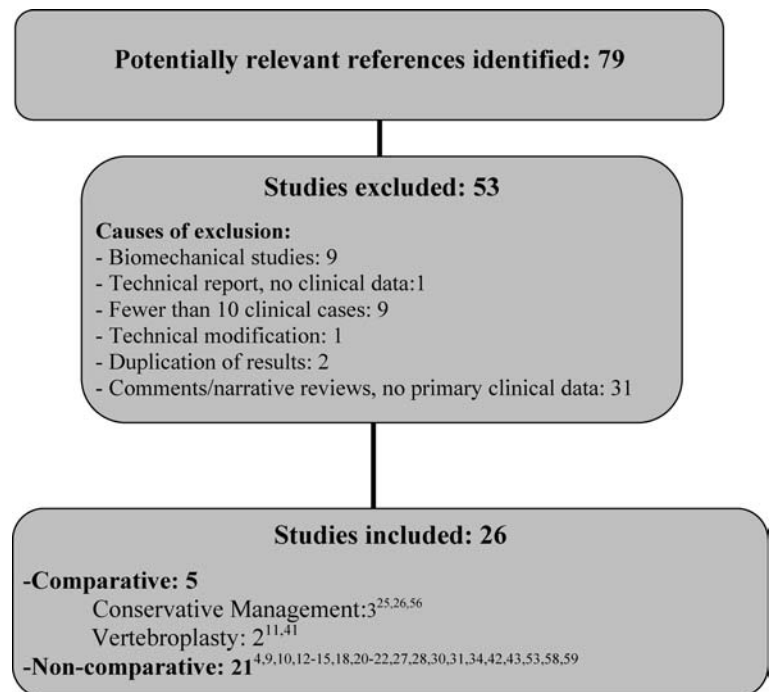
The 21 noncomparative studies include 1,490 patients and 2,637 treated levels. Five studies [11, 25, 41, 56] are comparative and include 220 patients, of which 118 were subjected to BK. Although the number of VCFs per patient is not uniform, most studies involve only a single procedure per patient (generally under general anesthesia). The population mostly comprises women over 65 years of age with painful VCFs secondary to osteoporosis and/or multiple myeloma and located between

T4 and L5. The individual characteristics of studies are shown in Tables 1 and 2.

Quality assessment of studies is presented in Tables 3 and 4. These are studies with observational designs (cohorts, cases and controls, and clinical series), and the evidence they provide can be regarded as corresponding to degree II–III [37]. As Tables show, the quality of studies appears to be good on the basis of some biases but only mild in terms of others [7]. Additionally, in many cases the risk of bias is unclear as the studies failed to provide methodological details. Thus, many studies make no reference to concomitant treatments in order to assess performance bias. Same lack of information is revealed as to blind or independent outcome measurement. Further, in only a minimum number of cases is it specified that evaluation is made by professionals not implicated in carrying out the procedure. In some cases the measurement instruments used are unknown. While the duration of follow-up varies from 3 to 24 months, it generally does not exceed 10–12 months—and an important number of losses are also seen during this period. In effect, in some studies [11] the final populations do not reach 20% of the patients actually treated. Only one study [25] explicitly indicates that analysis of the results is made on an intention to treat basis.

Additionally, heterogeneity was also observed in the criteria used for the selection of patients, the estimated age of the fractures, the functional class, the degree of progression of the disease, and refractoriness to previous treatments. Moreover, some studies include fractures secondary to osteoporosis and malignancy, without

**Fig. 1** Study selection and inclusion process



**Table 1** Description of the noncomparative studies

Author	Design/etiology VCF	Patient/levels	Age	VCF <sup>a</sup>	Follow-up	Pain	Vertebral height	Kyphosis	QoL/functional capacity
Wong et al. [59]	R/O	85/143	NK	NK	5 months	Improvement: 94% of patients Worse: one patient	Pre: 79 ± 22%/Post: 99 ± 13%	NK	NK
Garfin et al. [14]	R/O	340/ 603	NK	NK	18 months	Improvement: 90%	Anterior: Pre: 83 ± 14%/Post: 99 ± 13% Middle: Pre: 76 ± 14%/Post: 92 ± 11% Posterior: Pre: 74 ± 12%/Post: 88 ± 14% P < 0.05 Percentage of mean lost height restored: 35% Mean height gained: 2.9 mm	NK	Improvement: 90%
Lieberman et al. [30]	P/O-T (M)	30/70	5.9 months	5.9 months	6.7 months	Improvement: 100%	NK	NK	SF-36: significant improvement except global health and emotional role
Lane et al. [27]	R/O	17/33	NK	NK	NK	Relief > 50%; 85% patients	NK	NK	NK
Theodorou et al. [53]	P/O	15/24	14 weeks	14 weeks	6-8 months	Post: Improvement 100% 6-8 months: 93% of patients	Pre: 78.6 ± 15.6%/Post: 91.5 ± 11% P = 0.00 % restoration: Anterior: 52 ± 32.2% P < 0.0001 Middle: 65.7 ± 36.2% P < 0.0001 Posterior: 53.4 ± 49.1% P < 0.0001	Pre: 25.5 ± 10° Post: 15.6 ± 6.7° P = 0.000	NK
Coumans et al. [9]	P/O-T(M)	78/188	7 months	7 months	18 months	VAS (0-10): Pre: 7/Post: 3.2 P < 0.0001 End follow-up: 3.4 P < 0.0001	NK	NK	SF-36: significant improvement except global health. ODI: Pre: 48/Post: 35 P < 0.01
Garfin [15]	P/O	155/ 214	18 weeks	18 weeks	≤ 24 months	VAS (0-20) Pre: 15.2 ± 4/2 years: 5.9 ± 6.1 P < 0.01	Anterior: % loss Pre: -31.9 ± 20.4/Post: -26.9 ± 17.5 P < 0.01 % restoration: -13.3 ± 94.1 NS Middle: % loss Pre: -29.5 ± 18.4/Post: -22.3 ± 17% P < 0.01 % restoration: 38.2 ± 105.5 P < 0.01 % estimated height: Pre: Anterior: 66%, Middle: 65% 1 y: Anterior: 85%, Middle: 90% P < 0.01	NK	Back function index Pre: 1.4 ± 0.7 2 years: 0.4 ± 0.6 P < 0.01 SF-36: after 2 years significant improvement on all subscales
Ledlie and Renfro [28]	R/O-T (Mx)	96/133	2.4 months	2.4 months	12 months	VAS (1-10) Pre: 8.6/Post: 2.7 P < 0.001 End follow-up: 1.4 P < 0.001	NK	NK	Walking: significant recovery in all patients
Lieberman and Reinhardt [31]	NK/T (MMx)	63/264	NK	NK	M: 4.5 months Mx: 1 month	VAS (0-10) Pre: 6.18/Post: 2.84 P < 0.0001	NK	NK	SF-36 improvement except global health and emotional role
Phillips [40]	P/O	29/61	3.8 months	3.8 months	12 months	VAS (0-10) Pre: 8.6/Post: 2.6 P < 0.001 1 year: 1 P < 0.004	NK	Pre: 17.5° Post: 8.7° P < 0.0001	Improvement: 29 patients. Restored function: 18

**Table 1** (Contd.)

Author	Design/etiology VCF	Patient/levels	Age VCF <sup>a</sup>	Follow-up	Pain	Vertebral height	Kyphosis	QoL/functional capacity
Wilhelm et al. [58]	P/O	34/56	9.7 weeks	6 months	VAS (0–100) Pre: 64±4/Post: 21±5 $P<0.001$	NK	Pre: 11.5° Post: 5° $P=0.003$	Karnovsky: Pre: 40% (32–70) Post: 70% (52–80) $P<0.001$ NK
Berlemann et al. [4]	R/O	24/27	1 month	12 months	VAS (0–10) 3.48±2.3 $P<0.01$ 1 year: 1.5±1.8 $P<0.001$	NK	Reduction: 8±4.7° Reduction %: 47.7±24.6% <10 weeks Pre: 15°/Post: 8° $P(0.001)$	
Crandall et al. [10]	P/O	47/86	<10 weeks: >4 months: 46	18 months	VAS (0–10) <10 weeks: Pre: 7.3±2.1/Post: 4.3±2.7 $P<0.001$ >4 months: Pre: 7.3±1.6/Post: 4.3±2.3 $P<0.001$	<10 weeks: Pre: 58% estimated/Post: 86% $P(0.001)$ >4 mo. Pre: 56% estimated/Post: 79% $P(0.001)$ Difference between groups: $P=0.01$		
Fribourg et al. [12]	R/O	38/47	NK	8 months	NA	NA	NA	NA
Gaitanis et al. [13]	P/O-T	32/61	NK	18 months	VAS: Pre: 8.5/Post: 2.5 cm $P=0.001$	Anterior: Pre: 22.4 mm/Post: 26.8 $P=0.001$ Middle: Pre: 22.1 mm/Post: 27 $P=0.001$ % restitution 49% (0–92.9%) % restitution 51.7% (0–91%) Increase to 90% estimated normal value	Pre: 15.8° Post: 7.9° $P=0.001$	Pre: 60/1 month: 28 $P=0.001$ Walk independently: 100% (8/8)
Grohs and Krepler [18]	R/O-T	101/101	≤3 months	12 months	VAS (0–10): Pre: 7.2/Post: 2.5		Pre: 12°/ Post: 7°	ODI Pre: 60 Post: 26 $P<0.05$ NA
Harrop et al. [20]	R/O	115/ 225	NK	11 months	NA	NA	NA	NA
Heini and Orier [21]	R/O	24/27	NK	12 months	Improvement 23 patients	NK	Mean reduction of 8° or 47%	NK
Hillmeier et al. [22]	P/O-T	99/173	<1 month	12 months	VAS spine (0–100): Improvement: 87% cases	Mean increase: 16% Osteoporotic VF: 11%	NK	Improvement function: 87% cases NK
Masala et al. [34]	P/O-T	16/16	NK	NK	VAS (0–10) Pre: 8.2/Post: 2.4 $P<0.05$ VAS		NK	NK
Rhyne et al. [43]	R/O	52/82	31 weeks	9.25 months	Pre: 9.16/Post: 2.91 $P<0.005$	Anterior: Pre: 19.6 mm/Post: 24.2 $P<0.05$ Middle: Pre: 16.8 mm/Post: 20.7 $P<0.05$ Posterior: Pre: 25.8 mm/Post: 26.1 NS	Pre: 22.5°/Post: 19 $P<0.05$ reduction: 14%	Roland-Morris: Pre: 19.3 (12– 23), Post: 8.1 (1–20) $P<0.05$

Individual results are shown as reported in the original publications

I/C/F Vertebral compression fracture; R Retrospective design; P Prospective design; T Tumor; M Multiple myeloma; Mx Metastasis; NK Not known; NA Not applicable; NS Not significant O Osteoporosis

<sup>a</sup>Estimated mean age of VCF

**Table 2** Description of the comparative studies

Author	Design/etiology VCF	Patients/levels	Age VCF <sup>a</sup>	Follow-up	Pain	Vertebral height	Kyphosis	QoL	Leakage	Adverse effects	New VF
Weisskopf et al. [56]	R BK: O-T CMT: O	BK 22/37 CMT: 20/ 35	> 3 months	3 months	Mean reduction pain intensity: BK: None						81.5 ± 27.9%; CMT: 41.6 ± 35.5% <i>P</i> < 0.0001
NK	11% levels global mean 1.8°	NK	14%	NK	None						
Kasperk et al. [25]	P/O	BK 40/72 CMT20/ 33	> 12 months	6 months	Validated VAS BK: Pre: 26.2 ± 2 Post: 44.2 ± 3.3 CMT: Pre: 33.6 ± 4.1 Post: 58.0 ± 2.2 35.6 ± 4.1 <i>P</i> = 0.007	BK: Pre: 59.3 ± 1.7 Post: 65.3 ± 1.2 CMT: Pre: 63.3 ± 2.2 Post: 58.0 ± 2.2 <i>P</i> < 0.001	BK: Pre: 8.7 ± 0.8 Post: 8.3 ± 0.9 CMT: Pre: 7.1 ± 1.2 Post: 12 ± 1.1 <i>P</i> < 0.001	EVOS BK: Pre: 43.8 ± 2.4 Post: 54.4 ± 2.7 CMT: Pre: 39.8 ± 4.5 Post: 43.8 ± 4.6 <i>P</i> = 0.031	9.7%	None	BK: 12.5% CMT: 30%
Komp et al. [26]	P/O	BK 21/21 CMT: 19/ 19	1 month	6 months	VAS (0-100): BK: Pre: 91 (80-100) Post: 25 (0-30) CMT: Pre: 91 (80-100) Post: 83 (35-100) <i>P</i> < 0.05	BK: 11 levels increase to 2/3 of adjacent level Ten levels increase of 50% CMT: 16 levels larger deformity	NK	NK	9.7%	BK: two cases perforation fractured lamina CMT: change in medication ten cases intolerance/difficulty with corsets: nine cases	BK: 33% CMT: 58%
Fourney et al. [11]	R/T	BK 15 V 34	3.2 months	4.5 months	VAS pain relief Complete: V8, C1 Improvements: V22, C11 Same: V3, C1 Worse: V 0, C 0 No data: V2, C2	Restored height: 4.5 ± 3.6 mm <i>P</i> = 0.01 vs. baseline % restoration: 42 ± 21	Pre: 25.7 ± 9.7° Post: 20.5 ± 8.7° <i>P</i> = 0.001	Functional improvement: NS	BK: 0% V: 9.2%	BK: exacerbatation prior CHF V: paraplegia after 13 days due to progressive epidural metastasis	No specified by technique
Phillips [40]	P/O	20/20	4.5 months	NA	NA	NA	NA	NA	BK: 60% V: 100%	NA	NA

Individual results are shown as reported in the original publications

R Retrospective; P Prospective; O Osteoporotic; T tumoral; BK Balloon Kyphoplasty; CMT Conventional medical treatment; V Vertebroplasty; NK Not known; NA Not applicable;

NS Not significant

<sup>a</sup>Estimated mean age of VCF



**Table 3** Summary of quality assessment of noncomparative studies

	Number of studies (references)
Selection bias	
Is the study based on a representative sample selected from a relevant population?	Yes: 15 [4, 9, 12, 15, 20, 22, 28, 30, 34, 42, 53, 58] Not reported: 6 [14, 18, 21, 27, 31, 59]
Consecutive cases	Yes: 9 [9, 10, 12, 20, 30, 42, 58] Not reported: 12 [4, 14, 18, 21, 27, 31, 34, 53, 59]
Performance bias	
Presence of cointerventions	Yes: 8 [4, 9, 12, 20, 28, 30, 53] No: 13 [13–15, 18, 21, 27, 31, 34, 42, 58, 59]
Detection bias	
Before/after analysis	Yes: 21 [4, 9, 12, 18, 20, 27, 30, 34, 42, 53, 58, 59]
Blind or independent evaluation	Yes: 4 [15, 22, 42, 43] No: 1 [28] Not reported: 16 [4, 9, 12, 18, 20, 27, 30, 34, 53, 58, 59]
Validated/objective outcomes assessed	Yes: 18 [4, 9, 12, 15, 18, 20, 28, 30, 34, 42, 53, 58] Not reported: 3 [14, 27, 59]
Attrition bias	
Follow-up $\geq 80\%$ of patients	Yes: 6 [4, 12, 20, 30, 43, 53] No: 6 [9, 13, 15, 22, 28, 42] Not reported: 9 [10, 14, 18, 21, 27, 31, 34, 58, 59]

**Table 4** Summary of quality assessment of comparative studies

	Weisskopf et al. [56]	Kasperk et al. [25]	Komp et al. [26]	Fourney et al. [11]
Design	Retrospective analysis	Controlled prospective cohort	Prospective cohort	Retrospective analysis
Inclusion/exclusion criteria specified	No	Yes	Yes	Yes
Groups similar at baseline	No	Yes	Yes	No
Concomitant treatment specified	No	Yes	No	Yes
Independent assessment of results	Not reported	Not reported	Not reported	Yes
Intention-to-treat analysis	Not reported	Yes	No	Not reported
Losses specified [%]	Not reported	Yes (0)	Yes (10%)	Yes (84%)

identification of the results corresponding to each etiological group. The time points and instruments used to assess response differ and there is no standard criterion regarding the definition of treatment response or success. Due to this lack of homogeneity, the units in which the results are expressed vary among studies (Tables 1, 2). Only exceptionally are the statistical comparisons made fitting for the baseline values of age, sex, and number of fractures, with an analysis of the lost values and the adoption of specific correction measures when performing multiple comparisons.

## Efficacy

### Noncomparative studies

**Pain:** The 18 studies that analyze this variable before and after BK report significant reductions in pain intensity that is moreover maintained during follow-up (Table 1). The combined analysis of the studies that contribute data shows that kyphoplasty affords a significant reduction in pain score using a visual analog

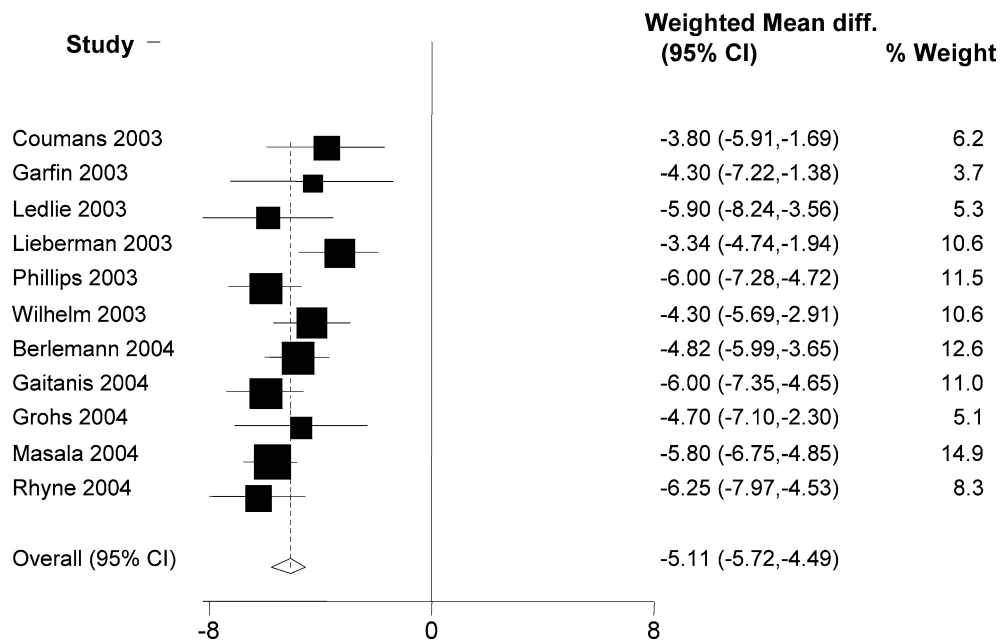
scale (VAS) both in the postoperative period (Fig. 2) and at the end of follow-up (Table 5). The heterogeneity among studies observed in this latter case seems to be related to the duration of the follow-up period ( $P = 0.06$ ) in the meta-regression analysis. Likewise, the results of individual studies show that BK produces significant improvement in variables that indirectly measure pain symptoms, such as the need for opiates [10], the number of days during which pain interferes with daily life activities [15], and the number of days of bedrest because of pain [15] (Table 5).

As to the behavior of acute versus chronic vertebral fractures, the results of a single study [10] show that BK significantly and similarly reduces pain intensity in both groups (Table 1).

**Vertebral height:** The studies that analyze this variable report an effect significantly in favor of BK. Regarding the percentage of levels in which the technique proves able to increase vertebral height, the results of various studies [10, 13, 28, 30] yield values in the range of 70–96%.

The combined analysis of the studies that contribute data on the pre- and postoperative values shows that the technique significantly increases vertebral height

**Fig. 2** Visual analog scale (VAS). Changes in pain score versus baseline. Results of the meta-analysis



regardless of the segment subjected to measure (Table 5). Figure 3 shows the combined results of balloon kyphoplasty on anterior region of vertebral body. All the studies include VCFs of osteoporotic origin, and in the meta-regression analysis it is seen that the heterogeneity among studies appears to be related to the different estimated ages of the treated fractures ( $P=0.005$ ).

Various studies [10, 15] indicate that the increase in vertebral height is related to the estimated age of the

VCFs—with superior results in fractures less than 2–3 months old. Thus, the results obtained by Garfin [15] indicate that in patients with a baseline loss of height equivalent to over 15% of the estimated normal value, the favorable effects of the technique only reach statistical significance in the case of fractures less than 60 days old. On the other hand, the results of a prospective study [10] specifically contrasting the results of BK in acute VCFs (defined as being less than 10 weeks

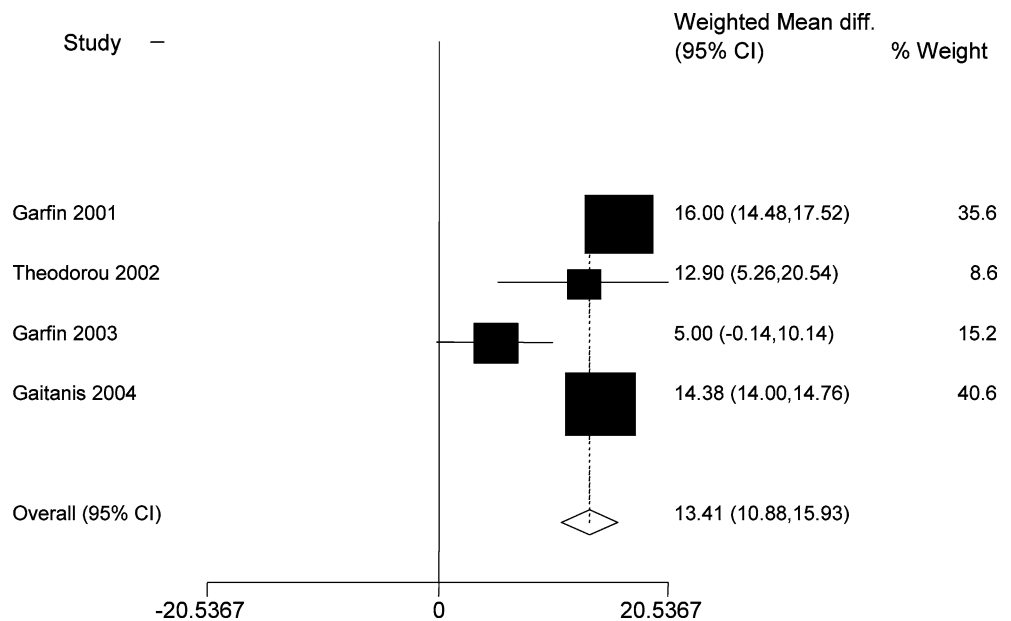
**Table 5** Efficacy of balloon kyphoplasty. Noncomparative studies

	Number of studies/patients' levels	Heterogeneity test, $P$ value	Size of effect WMD (95% CI), $P$ value
<b>Pain:</b>			
VAS score			
Basal-postoperative (VAS 0–10)	11 <sup>4,9,13,15,18,28,31,34,42,43,58</sup> /665	$\chi^2$ 17.2, .07	-5.11 (-5.72, -4.49), .000
Baseline-1 year (VAS 0–10)	5 <sup>4,9,15,28,42</sup> /378	$\chi^2$ 38.85, .00	-6.10 (-7.47, -4.48), .000
Baseline-2 years (VAS 0–20)	1 <sup>15</sup> /100		-9.3 (-10.65, -7.94), .000
Opiate use	1 <sup>10</sup> /47		-1.8 (-2.77, -0.89), .000
Interference DLA	1 <sup>15</sup> /100		-11.3 (-13.09, -8.69), .00
Days in bed	1 <sup>15</sup> /100		-6.8 (-9.57, -4.02), .00
<b>Vertebral height:</b>			
Percentage of increase in height			
Anterior region	4 <sup>13,14,15,53</sup> /784	$\chi^2$ 17.2, .001	13.41 (10.9, 15.9), .001
Middle region	3 <sup>13,14,15</sup> /760	$\chi^2$ 12.06, .002	14.56 (12.4, 16.7), .002
Posterior region	2 <sup>14,28</sup> /639	$\chi^2$ 13.06, .000	18.52 (9.7, 27.3), .000
Restitution percentage			
Anterior region	2 <sup>15,53</sup> /132	$\chi^2$ 0.35, .55	37.48 (-3.5, 78.5), .07
Middle region	2 <sup>15,53</sup> /132	$\chi^2$ 0.47, .49	46.08 (2.4, 89.8), .039
Posterior region	1 <sup>53</sup> /24		20.31(10.6, 29.7), .000
<b>Kyphotic deformity:</b>			
Cobb angle (°)	7 <sup>4,10,13,18,42,43,53</sup> /430	$\chi^2$ 5.65; .46	-7.68 (-9.34, -6.03), .00
Reduction (%)	2 <sup>4,53</sup> /51	$\chi^2$ .24; .6	57.8 (30.7, 84.8), .00

WMD Weighted mean difference; DLA Daily live activities



**Fig. 3** Mean difference in vertebral height before versus after balloon kyphoplasty: anterior region of vertebral body. Results of the meta-analysis



old) versus chronic fractures (with an estimated age of over 4 months) show that in both cases the vertebral height is significantly greater than the preoperative height, though the degree of restitution achieved is greater in the former group (Table 1). Likewise, the data obtained indicate that in 60% of the acute fractures and in 26% of the chronic fractures, the restitution achieved exceeds 89% of the height lost ( $P=0.01$ ), while in 8 and 20% of the acute and chronic fractures, respectively, the restitution obtained does not exceed 10%—no significant differences being observed between the two groups [OR (95% CI): 3 (0.75, 11.97),  $P=0.12$ ].

**Spinal sagittal alignment:** The results of each of the nine studies [4, 10, 13, 18, 21, 42, 53, 58] that consider the absolute value of the Cobb angle show the latter to decrease after kyphoplasty, though the mean reduction varies between  $-1.8^\circ$  and  $-9.9^\circ$ . The combined examination of the studies [4, 10, 13, 18, 42, 53] that contribute data amenable to analysis confirms that following BK, the absolute value of this angle decreases significantly (Fig. 4). In Table 5 it can also be seen that kyphoplasty produces a significant percentage correction of the kyphotic deformity, though the number of levels that can be subjected to analysis is limited [4, 53].

In osteoporotic VCFs, the number of levels in which the kyphotic deformity is reduced varies between 57 [42] and 85% [4]; in this context, it should be taken into account that the authors use different criteria for defining correction.

Regarding the age of VCFs, the results are divergent. Thus, while Crandall et al. [10] report similar reductions in mean kyphosis angle between acute and chronic fractures (Table 1), other investigators [4, 13, 21] indicate that the possibilities for reduction seem to be

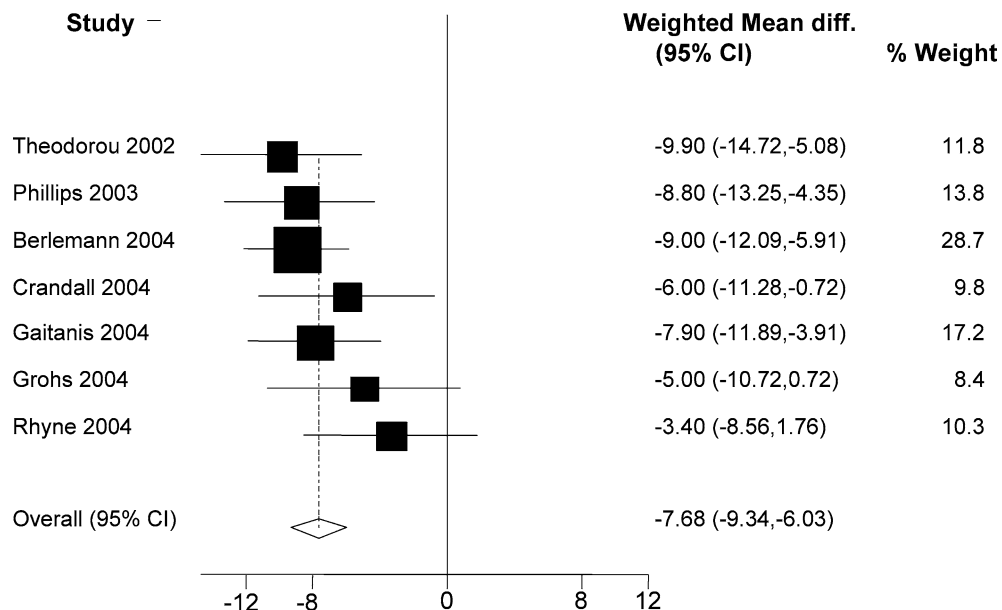
greater the younger the fractures. However, these results are difficult to evaluate, due to the limited number of cases [4] and the lack of data amenable to analysis [13, 21].

The authors of two studies indicate that the degree of reduction of the kyphotic deformity is not correlated to the level treated [4, 42] or to pain relief [4].

**QoL and functional capacity:** Although the instruments used to evaluate these aspects are not always described, the results of each of the studies that take such variables into account reveal evident improvements after kyphoplasty (Table 1). The combined analysis of the studies [9, 15, 30, 31] that analyze the impact of the technique upon QoL based on the SF-36 questionnaire shows (Fig. 5) that statistically significant improvements are afforded on the subscales corresponding to physical function, physical role, body pain, vitality, social function, and mental health. Although considerable statistical heterogeneity is detected among the studies, the meta-regression analysis has been unable to identify the underlying cause—no significant association being observed with any of the variables employed.

The impact on functional capacity has been analyzed in nine studies, though two [22, 42] fail to specify the evaluation approach adopted. The results of individual studies (Table 1) show significant improvements with any of the measurement instruments used, i.e., back function index [15], the Roland–Morris disability questionnaire [43] or walking status [13, 28]. Moreover, the combined analysis of four studies [9, 13, 18, 31] with 263 patients using the Oswestry Disability Index, confirms that BK affords significant improvement [WMD (95% CI):  $-23.8$  ( $-34.0$ ,  $-13.55$ ),  $P=0.00$ ].

**Fig. 4** Spinal sagittal alignment. Changes in absolute Cobb angle values versus baseline ( $^{\circ}$ ). Results of the meta-analysis



### Comparative studies

#### *BK versus conventional medical treatment*

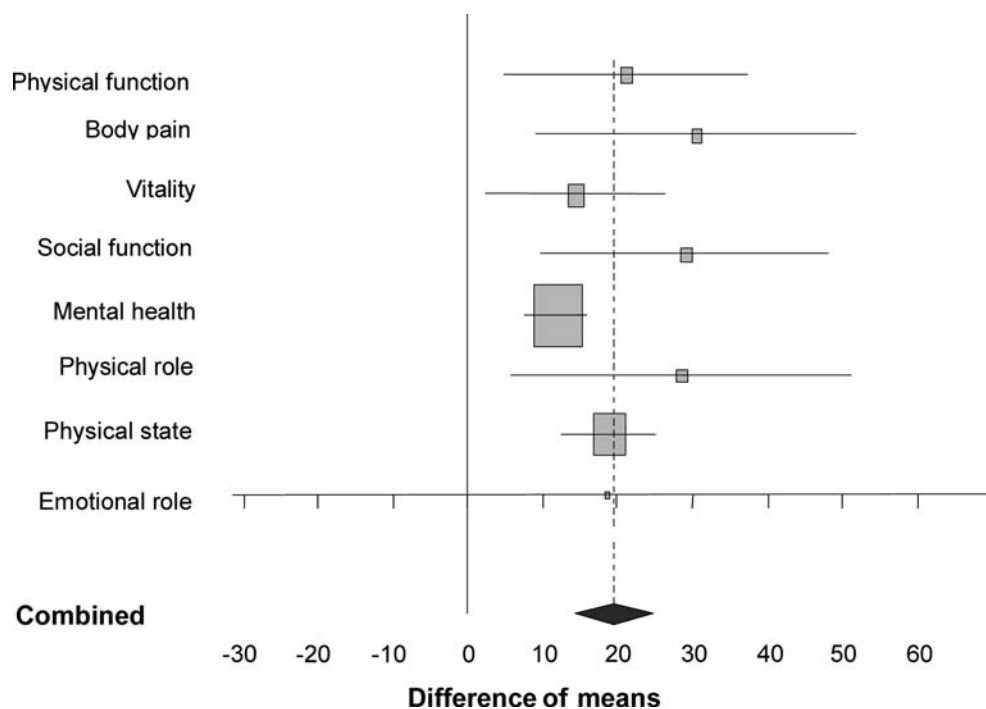
**Pain:** The results of each of the studies (Table 2) show significant improvements with BK both in the postoperative evaluation and during follow-up. Regarding the percentage reduction in pain intensity, the combined analysis of the studies that contribute data [25, 26, 56], with 83 and 59 patients in the of treatment and control

groups, respectively, shows BK to yield a mean reduction in pain intensity 55.6% greater than that afforded by conservative management (Table 6).

The results of a study [25] indicate effects favorable to BK in relation to other variables such as the need for opiates or the number of medical visits because of pain in 6 months (Table 6).

**Vertebral height:** The results of a controlled study [25] show that 6 months after treatment, vertebral height increases in the patients subjected to BK and decreases

**Fig. 5** Changes in the SF-36 subscales. Results of the meta-analysis



in the control group—the difference being statistically significant (Table 6). However, the authors indicate that there is no significant correlation between the improvement in vertebral height and other variables such as pain relief or mobility. Komp et al. [26] reported significant differences favorable to BK—though they afford no data amenable to analysis (Table 2).

**Spinal sagittal alignment:** Two studies [25, 56] describe the results in relation to this variable. Weisskopf [56] found that in only 11% of the levels was it possible to correct the kyphotic deformity, though he contributed no data on its evolution in the comparator group. Kasperk [25] found that 6 months after treatment, the kyphosis angle remained relatively constant in the group subjected to BK but increased gradually in the control group—the difference between both groups being significant (Table 6).

**QoL and Functional capacity:** The results of Kasperk [25] show that after 6 months of follow-up, the QoL score among the patients subjected to BK is better than in the control group, although the differences did not reach the required level of significance (Table 6). The same study reports a statistically significant improvement in mobility in the group subjected to kyphoplasty ( $P=0.03$ )—though no significant correlation is observed between such improvement and the degree of recovery of vertebral height.

#### *BK versus vertebroplasty*

The results of a retrospective analysis contrasting BK versus vertebroplasty in tumoral VCFs [11] show that, globally, no significant differences are found between the

two techniques in terms of pain relief [OR (95% CI): 0.89 (0.29–2.67);  $P=0.8$ ] or the degree of functional improvement achieved. BK produced a significant increase ( $P=0.01$ ) in vertebral height, with a mean value of  $4.5 \pm 3.6$  mm—which implies a  $42 \pm 21\%$  restoration of the height lost. Likewise, statistically significant improvement is observed in local kyphosis [WMD (95% CI):  $-5.2$  ( $-9.71, -0.89, P=0.02$ )]. The authors contribute no data on the degree of kyphosis or vertebral height of the levels subjected to vertebroplasty.

#### Safety

##### *Filler material leakage*

The analysis of the 19 studies that contribute data [4, 9, 13, 15, 18, 21, 25, 28, 30, 34, 42, 53, 56, 58] (Fig. 6) shows a total of 134 cement leakages in 1,742 treated levels, i.e., a proportion of 7.13% (95% CI: 4.83–9.42%). Of these, only two (1.5%) are described as symptomatic or cause clinical sequelae. The heterogeneity observed among the studies is associated to the etiology of VCFs ( $P=0.032$ ), with a greater presence of leakage in the studies that include VCFs of osteoporotic origin [10.49% (6.23–14.7)] than in those that only consider VCFs of tumor origin [3.7% (0.5–6.8)] or both etiologies [4.4% (1.6–7.1)]. The meta-regression also revealed a possible association with the estimated age of VCFs, though the relationship did not reach statistical significance ( $P=0.096$ ).

In comparative studies with vertebroplasty, Fournier et al. [11] recorded no cement leakage in the levels subjected to kyphoplasty, while 9% of the levels subjected

**Table 6** Kyphoplasty versus conventional medical management: efficacy variables

Variable	Studies with data	Conventional medical treatment (number of cases)	Kyphoplasty (number of cases)	Size of effect (95% CI), <u>P</u> value
<b>Pain:</b>				
Reduction intensity %	3 <sup>25,26,56</sup>	( $n=59$ )	( $n=83$ )	WMD: 55.6 (39, 72), $P \leq 0.001$
Opiate needs	1 <sup>25</sup>	Pre 14/Post 13. ( $n=20$ )	Pre 27/Post 22 ( $n=40$ )	OR: 2.95 (.31, 28), $P=0.3$
Number of visits due to pain	1 <sup>25</sup>	8.6/patient	3.3/patient	WMD: $-5.3$ ( $-5.35, -5.25$ ), $P < 0.001$
Post/Pre changes in Vertebral height	1 <sup>25</sup>	$-8.2 \pm 7.4\%$ ( $n=33$ levels)	$+12.1 \pm 19.5\%$ ( $n=72$ levels)	WMD: 20.3% (15.1, 25.5), $P < 0.001$
Post/Pre changes in Cobb angle (°)	1 <sup>25</sup>	$12.0 \pm 6.3$ ( $n=33$ levels)	$8.3 \pm 7.6$ ( $n=72$ levels)	WMD: $-3.7$ ( $-6.48, -.91$ ), $P < 0.001$
Post/Pre changes in QoL	1 <sup>25</sup>	$4 \pm 30.44$	$10.6 \pm 22.37$	WMD: 6.60 ( $-8.42, 21.62$ ), $P=0.4$
New VCF	2 <sup>25,26</sup>	17/39	12/61	OR: 0.35 (0.14, 0.88); $P=0.03$
Days in hospital	1 <sup>56</sup>	$20.4 \pm 13.5$ ( $n=20$ )	$10.4 \pm 7.4$ ( $n=22$ )	WMD: $-10$ ( $-16.7, -3.3$ ), $P=0.003$

Changes in vertebral height, Cobb angle and QoL, and Days in hospital are expressed as mean  $\pm$  standard deviation. WMD (weighted mean difference) is expressed as mean with 95% confidence interval  
OR odds ratio

to vertebroplasty showed leakage. In turn, Phillips et al. [41], in a prospective study, reported a significantly smaller number of contrast extravasations with kyphoplasty than with vertebroplasty [OR (95% CI): .04 (.00–.68)  $P=0.03$ ], as well as a significantly lesser mean score with BK in terms of contrast extravasation considered both globally and for each of the regions analyzed.

#### Major complications

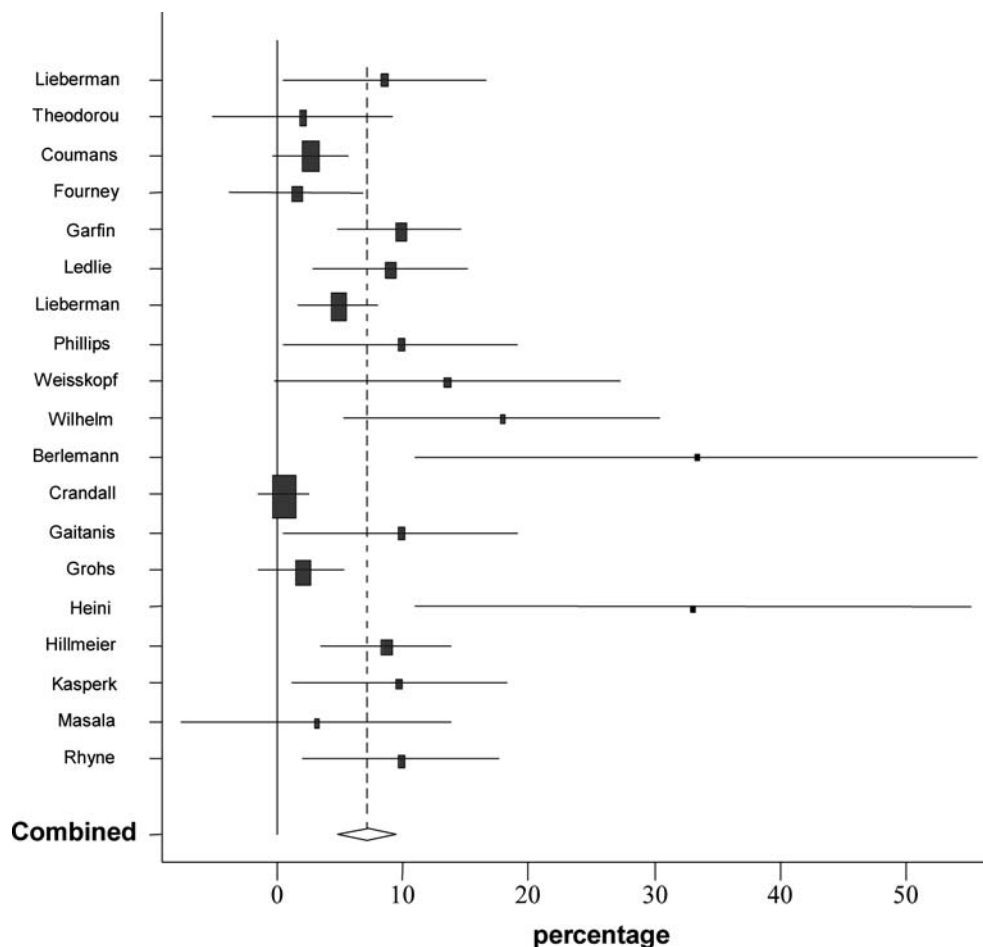
The combined analysis of the 16 noncomparative studies that contribute data [4, 9, 13, 22, 27, 30, 34, 42, 53, 58, 59] reveals 23 complications in 1,154 patients and 1,974 levels treated—this corresponding to a complication rate of 2 and 1.16%, respectively. As can be seen in Table 7, most of the problems were of a cardiopulmonary or neurological nature. In three cases (0.26% of the patients)—comprising partial motor loss [14], epidural hematoma [14], and digestive bleeding [4]—emergency surgery was required.

In comparative studies, Komp [26] reported the presence of two cases of perforation of the fractured lamina without posterior repercussions in the group subjected to BK, while among the patients subjected to conventional medical treatment, changes in medication proved necessary in 10 of 17 patients (in eight cases because of treatment failure and in two because of intolerance). Likewise, intolerance or difficulties with the external fixation systems were reported in nine patients. On the other hand, Fourny et al. [11] reported the need for readmission to hospital due to exacerbation of heart failure in one patient 2 weeks after kyphoplasty, and the development of sudden onset of paraplegia due to progressive epidural metastasis in one patient subjected to vertebroplasty.

#### New vertebral fractures

Noncomparative studies: The results of eight studies [4, 12, 15, 20, 31, 42, 43] show that 87 of the 450 patients included developed new vertebral fractures during the

**Fig. 6** Balloon kyphoplasty. Combined analysis of bone cement leakage



follow-up period. The combined analysis of these studies shows (Fig. 7) that 16.5% (95% CI: 10.7–22%) of the patients suffered new vertebral fractures 1 year after treatment. There is evident heterogeneity among the studies ( $\chi^2 = 20.17$ ,  $P = 0.00$ ), which in the meta-regression analysis was found to be independent of the duration of follow-up ( $P = 0.19$ ) and the estimated age of the fractures ( $P = 0.58$ ), and appeared to be associated to fracture etiology ( $P = 0.02$ ). Thus, the studies that include only osteoporotic VCFs show a new fracture rate of 17.8% (95% CI: 11.7–24%)—this figure being clearly greater than the percentage recorded in the studies that include patients with tumor VCFs [(7.4% (95% CI): 0–17%)]. On the other hand, the results of a retrospective study involving 115 patients with osteoporotic VCFs and a follow-up duration of over three months [20] indicate that the risk of new fractures is significantly greater in the cases of secondary osteoporosis (17/35 patients vs. 9/80,  $P < 0.001$ ).

In five studies [4, 12, 20, 42] it was seen that 33 of the patients developed new fractures in levels adjacent to the treated levels, and two of these studies [12, 13] report that most such fractures occur in the first 2 months after BK.

Comparative studies: As can be seen in Table 6, the combined analysis of two studies [25, 26] indicates that patients subjected to kyphoplasty are at a significantly lesser risk of suffering new fractures 6 months after the procedure than patients in the comparator group

subjected to medical management. There are no data to allow comparison of this variable between BK and vertebroplasty.

#### Use of health care resources

The estimated mean duration of the procedure is about 1 h per level [15, 22, 26, 53, 56, 58].

Regarding hospital stay, the great majority of studies [4, 9, 11, 14, 18, 25, 27, 30, 42, 58] report stays of between 1 and 3 days after the procedure, while only 10–15% of the patients remain in hospital for more than 72 h. These latter cases are moreover attributed to the presence of disorders unrelated to the technique [4, 28].

The results of a comparative study with historical controls [56] show that hospital stay to be significantly shorter in patients subjected to BK versus conventional medical treatment [WMD:  $-10$  ( $-16.7$ ;  $-3.3$ );  $P = 0.003$ ], though in both cases the duration of stay was longer than reported in other studies ( $10.4 \pm 7.4$  days in the BK group;  $20.4 \pm 13.5$  days in the control group).

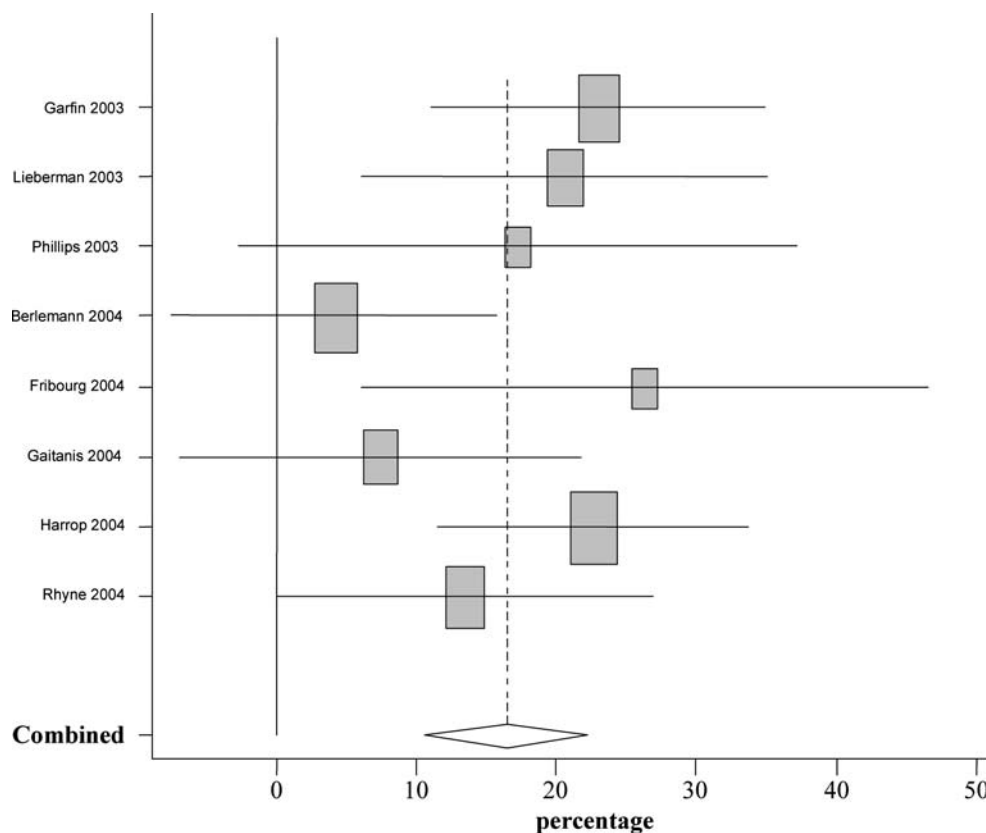
The results of a comparative and controlled study [25] indicate that in the 6 months after BK, the number of medical visits due to pain is significantly lower than in the control group (8.6 vs. 3.3 visits/patient,  $P = 0.01$ ).

**Table 7** Safety of balloon kyphoplasty. Noncomparative studies

Author	Leakage	Adverse effects	New VCF
Wong et al. [59]	NK	Spinal infarction, Deep venous thrombosis	NK
Garfin et al. [14]	NK	Transient fever and hypoxia, Epidural hematoma, Partial motor loss, Anterior cord syndrome	NK
Lieberman et al. [30]	8.6%	Rib fractures 2, Acute myocardial infarction 1	NK
Lane et al. [27]	NK	None	NK
Theodorou et al. [53]	None	None	NK
Coumans et al. [9]	2.7%	Acute myocardial infarction MI 1	NK
Garfin [15]	10%	Rib fracture 1, Arrhythmia 1	11.5%
Ledlie and Renfro [28]	9%	Respiratory failure, Deep venous thrombosis	NK
Lieberman and Reinhardt [31]	<5%	NK	21%
Phillips [40]	9.8%	Acute myocardial infarction, Arrhythmia, Urinary retention	17%
Wilhelm et al. [40]	17.8%	Transient lesion of L2	NK
Berlemann et al. [4]	33%	Digestive bleeding	4%
Crandall et al. [10]	None	Arrhythmia	NK
Fribourg et al. [12]	NA	NA	26%
Gaitanis et al. [13]	9.8%	Transient fever	7.4%
Grohs and Krepler [18]	2%	NK	11%
Harrop et al. [20]	NA	NA	23%
Heini and Orler [21]	33%	None	NK
Hillmeier et al. [22]	9%	Epidural hemorrhage, Transient spinal cord lesion	NK
Masala et al. [34]	None	None	NK
Rhyne et al. [43]	9.8%	None	13.5%

NK Not known; NA Not applicable

**Fig. 7** Noncomparative studies: incidence of new vertebral fractures



## Discussion

The results of this review, which includes 26 studies with primary clinical data, show BK to be effective and safe for the treatment of painful VCFs of both osteoporotic and tumor origin. Likewise, there are data indicating that over the short term, BK may offer greater clinical benefits than conventional medical treatment or vertebroplasty. However, little is known of the long-term effects of the technique and its capacity to avoid the physiological and functional sequelae of VCFs. This fact, and the heterogeneity and methodological limitations of the studies, complicates the definition of the true role of the technique in clinical practice.

The present systematic review includes published and unpublished studies, and data from the FDA [5, 33, 45], and we believe it to be the largest such effort made to date. The results obtained show that BK produces significant reduction in pain intensity, regardless of the method used to evaluate it, and moreover also affords significant improvement in mobility, functional capacity, and quality of life. These benefits are maintained over the course of follow-up. The technique is also able to at least partially restore and correct vertebral height and

the kyphotic deformity produced by VCFs. The results of the noncomparative studies indicate that, globally, BK affords a mean increase in vertebral height of  $15 \pm 5\%$ , though there are variations according to the segment subjected to measurement. Regarding kyphosis, a significant reduction is observed in both the absolute value of the Cobb angle and the degree of kyphotic deformity.

Assessment of the safety of the procedure reveals the presence of habitually asymptomatic cementing material leakage in 7% of the levels treated. Regarding the complications of the technique, problems were only noted in 2 and 1.16% of the patients and levels treated, respectively, though some of the complications appeared to be serious and required intensive care and/or emergency surgery (three cases). Complications are more frequent in patients with a larger number of underlying comorbidities [27, 28, 42], and with metastatic fractures [31]. Furthermore, in some cases, complications have been associated with both patient positioning maneuvers [15, 30] and insertion of the device during the learning curve of the technique [14]. On the other hand, the results of this review show that, globally, about 16% (95% CI: 10.7–22) of the patients subjected to BK suffer new vertebral fractures 1 year after treatment. The incidence in this case is highest among the patients with osteopo-



rotic fractures. These figures are similar to the percentages (19–24%) described for the general population of patients with VCF [32], and do not confirm the greater risk associated with kyphoplasty postulated by some authors [55, 60].

In addition, the studies analyzed indicate that despite the age and fragility of the population involved, BK is generally well tolerated by the patients, who report high levels of satisfaction, and hospital stay after the procedure is short.

BK appears to be more safe and effective than vertebroplasty in the treatment of tumor VCFs, as it is able to reduce the loss of height and the degree of kyphotic deformity, and generates a lesser leakage rate while affording similar responses in terms of pain reduction and improvement in patient function quality of life [11]. Likewise in osteoporotic VCFs, it has been shown that kyphoplasty offers a significantly lesser contrast leakage rate [41]. These results are in turn ratified on establishing an indirect comparison with the available literature on vertebroplasty, where it is conclusively shown that the cement leakage rates and complications are lower when using BK [1, 6, 17, 29, 57]. On the other hand, the risk of new vertebral fractures appears to be similar with both techniques [1, 6, 17, 29, 57]—though the lack of direct comparisons does not allow us to confirm this entirely.

Compared with habitual medical management, BK at least over the short to middle term affords better management control, with a statistically significant reduction in pain and associated analgesic use, and improved mobility and independence. On the other hand, the fractures treated show no progression toward the vertebral collapse and kyphotic deformity associated with conventional medical treatment [8, 25, 26]. In turn, over the short term, the technique significantly reduces the risk of new fractures in adjacent vertebrae. Likewise, there are data indicating that BK reduces the use of health care resources by shortening both hospital stay and the number of medical consultations due to pain in the 6 months after the application of the technique.

All these considerations define BK as a technique that is both promising and very interesting from the clinical point of view. However, many areas of uncertainty remain that do not allow us to firmly define the true role of the technique in clinical practice. Thus, while it is clear that BK significantly improves both vertebral height and spinal sagittal alignment, the clinical importance and repercussions of these effects have not yet been established, and little is known of their influence upon the medical complications secondary to VCFs. Knowledge is also lacking as to whether or not an association exists between the changes in spinal anatomy and variables of such great clinical importance as patient pain relief or functional capacity. Marked variability is moreover seen in the results of the individual studies. For example, the percentage of levels where kyphoplasty is able to reduce

kyphosis angle is reported to be between 11 [56] and the 85% [4]. Such discrepancy seems attributable not only to the different criteria used to define the outcome threshold [4, 10, 42] and the different methods used to measure it (a lack of consensus being observed on this point), but also to the unequal presence in each study of factors presumed to possess prognostic value—such as the etiology of fracture, baseline vertebral height, the degree of kyphosis, the level treated, and the estimated age of the fracture—the importance of which remains unclear. Regarding safety, uncertainty also exists due at least in part to the methodological limitations of the studies. As an example, the studies made do not allow us to determine whether the risk of new vertebral fractures after kyphoplasty is associated with the etiology of VCFs; whether such risk is really similar to that of the general population of patients with VCFs; or whether there are other possible adverse effects of the technique over both the short and long term.

The literature shows a lack of consensus over the possible indications of BK and the appropriate timing of the technique. At present, possible candidates for the technique are patients with painful VCFs of osteoporotic or tumor origin and, in this latter group, particularly those fractures secondary to multiple myeloma—since their characteristics facilitate tissue displacement to reduce the fracture and create the cement filler space. In other tumors it seems that the technical difficulties are greater [31], and the clinical experience gained is certainly much more limited. As to the selection of the best treatment level, there appears to be some agreement that the choice should be based on the results of the magnetic resonance imaging findings—specifically the presence of edema in the region of the fractured vertebra [55]. However, while some authors consider that the intervention is only indicated in patients with intractable pain refractory to medical management [27], or do not advise the technique in the case of simple osteoporotic fractures with minimal deformity [21], other investigators [10] define BK as the primary treatment of choice for osteoporotic fractures.

A lack of agreement is likewise observed regarding the best timing of the technique. Thus, while some authors do not recommend treatment of fractures estimated to be more than 3 months old [15, 21, 42], there are consistent data suggesting that chronic fractures are also amenable to BK, since the technique significantly reduces the pain and is at least partially able to restore vertebral height [4, 10, 25]. Given the natural course of VCFs [8], an early intervention in theory would afford better correction of the deformity and avoid increased vertebral collapse. However, this could result not only in the over-treatment of patients who would improve with conservative management, but could also pose a risk to their safety by subjecting them to an intervention not without risks and



complications—and whose long-term efficacy has not been firmly established.

Regarding safety, and while acknowledging the important influence of patient age, fragility, and the number of existing comorbidities in the population amenable to treatment with BK, it seems possible to reduce the appearance of complications through the adequate selection of patients, the use of high-quality radiological techniques during insertion of the device, the injection of bone cement in an appropriate state of polymerization, and adequate surgeon training [24, 36, 54, 55]. This latter aspect is of particular importance, for although the procedure is percutaneous, it is also complex and—as reported in the literature—requires skill and experience. Consequently, an adequate learning curve must be observed to ensure satisfactory efficacy and safety performance.

### Limitations of the review

The analysis of the literature on BK reveals a series of limitations that complicate extrapolation of the results to clinical practice. These limitations include a lack of direct comparisons with vertebroplasty with which to draw solid conclusions. On the other hand, many of the studies present methodological shortcomings, with known sources of bias—including poor description of the criteria used for patient selection and their lack of homogeneity due to the inclusion of fractures with different characteristics, etiologies, locations, and evolutive stages. Additional sources of bias include small sample size; scant description of concomitant treatments; the combination of kyphoplasty with other treatment measures (making it almost impossible to establish the differential contribution to the outcome of each technique); the lack of standard measures and the subjectivity of some of the outcome variables; the absence of masking in the assessment of the results; the variability and limited duration of follow-up; the lack of identification of losses and their causes; and poor quality in describing the results obtained [7, 35, 37, 49]. Such heterogeneity and limitations moreover make it impossible to establish a definitive estimate of the global effect of BK, since not all studies analyze the same variable of interest, and not all describe the results on a quantitative basis and in a comparable manner. On the other hand, many outcome

variables are used, and their definition and the instruments used to evaluate them are often not standardized. Moreover, the variables are sometimes subjective or even inadequate due to recall bias. Another problem that cannot be entirely ruled out despite the efforts made is the possibility of publication bias.

Nevertheless, while we are aware of the aforementioned problems, in this review we decided not to limit the analytical setting to studies meeting strict methodological criteria, since this would imply ignoring the reality of the clinical implantation of the technique [3, 5]. Moreover, it was considered that the approach adopted could be useful not only for evaluating the real results of the technique but also for identifying little or incompletely analyzed aspects that could set the bases for new areas of methodologically appropriate research.

### Conclusions

In synthesis, the available evidence reveals the efficacy and safety of BK in the treatment of painful VCFs secondary to osteoporosis or multiple myeloma. However, the uncertainty observed in the literature indicates that there is a particular need for prospective studies of good methodological quality to allow the following: (1) Precise determination of its efficacy in terms of both objective and subjective response, and specifically as regards the clinical repercussion and relevance of the increase in vertebral height and reduction in kyphotic deformity afforded by the technique. (2) Definition of the long-term efficacy of the procedure, and particularly of its influence upon the physiological, functional, and psychological complications secondary to VCFs. In this sense a specific point for evaluation is its impact upon lung function and patient survival. (3) The definition of the prognostic factors associated with response to treatment. (4) Precise determination of the short- and long-term adverse effects and morbidity-mortality associated with the procedure, and particularly of the rate of vertebral fractures adjacent to the treated segments. (5) Comparison between BK and conventional treatments and other percutaneous techniques to facilitate optimum therapeutic decision taking in patients with VCFs. (6) Determination of the costs of the procedure and the utilization of health care resources to assess its economic impact and cost-effectiveness.

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