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Unilateral versus bilateral percutaneous balloon kyphoplasty for osteoporotic vertebral compression fractures

A systematic review of overlapping meta-analyses

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Abstract

Background: Unilateral and bilateral percutaneous balloon kyphoplasty (PKP) are 2 main approaches for the treatment of patients with osteoporotic vertebral compression fractures (OVCFs). Numerous published systematic reviews and meta-analyses evaluating the effectiveness of 2 approaches remain inconclusive. In order to propose a significant principle to make decisions for comparing clinical safety and efficacy of unilateral versus bilateral PKP for treating OVCFs patients based on the currently best available evidence, a systematic review of overlapping meta-analysis was conducted.

Methods: Three electronic databases, Pubmed/Medline, Embase2 and the Cochrance Library, were searched systematically to retrieve and identify all eligible systematic reviews and meta-analyses comparing unilateral and bilateral PKP for the treatment of patients with OVCFs. Only systematic reviews or meta-analyses with an exclusively pooled analysis of randomized controlled trials (RCTs) met the minimum eligibility criteria in this investigation. The Oxford Levels of Evidence, Jadad algorithm and Assessment of Multiple Systematic Reviews (AMSTAR) instrument were adopted for evaluation of the methodological quality for each included literature to select currently best available evidence.

Results: Screening determined that out of 2159, 9 meta-analyses with level II or III of evidence met the inclusion criteria in the systematic review of overlapping meta-analyses. The multiple systematic reviews scores ranged from 8 to 9 with a mean of 8.55 (median 8.5). According to the search process and selection strategies of the Jadad algorithm, a meta-analysis by Feng et al with the best available evidence (12 RCTs and an AMSTAR score of 9) demonstrated that unilateral and bilateral PKP are both nice choices for the treatment of patients with OVCFs, and no significant differences were revealed in clinical scores, radiological outcomes, and quality of life with long-term follow-up. However, compared with bilateral PKP, unilateral PKP produced a shorter surgery time, smaller dosage of cement, lower risk of cement leakage, and relieved a higher degree of intractable pain at short-term follow-up after surgery.

Conclusion: Unilateral percutaneous balloon kyphoplasty is more advantageous and superior to bilateral percutaneous kyphoplasty, and should be considered an effective option for the treatment of patients with osteoporotic vertebral compression fractures.

Abbreviations: AMSTAR = Assessment of Multiple Systematic Reviews, NOF = National Osteoporosis Foundation, ODI = Oswestry Disability Index, OVCF = osteoporotic vertebral compression fracture, PKP = percutaneous kyphoplasty, PMMA = polymethylmethacrylate, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses, PVP = percutaneous vertebroplasty, RCT = randomized controlled trials, SF-36 = 36-Item Short Form Health Survey, VAS = Visual Analog Scale, VH = vertebral height.

Keywords: kyphoplasty, osteoporotic vertebral compression fractures, overlapping meta-analysis, postoperative pain, randomized controlled trials, systematic review

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1. Introduction

With the advancement of world population aging, the incidence of osteoporosis, the most common metabolic bone disease with low bone mass and a significantly increased risk of fracture, has been increasing in recent decades.[1] The National Osteoporosis Foundation (NOF) released updated prevalence data estimating that approximately 10 million Americans suffer from osteoporosis and an additional 44 million have low bone mass. It is estimated that 50% of women and 25% of men older than 50 years will suffer from an osteoporotic fracture in their lifetime.[2] Unsurprisingly, more than 2 million osteoporotic fractures occur each year, which result in economic costs in hospitalization is greater than that of myocardial infarction, stroke, or breast cancer in the United States.[3,4] Vertebral compression fractures (VCFs) are the most common complication of osteoporosis, which are more likely to occur in the elderly population.[5] These osteoporotic vertebral compression fractures (OVCFs) often contributes to multiple concomitant symptoms and complications including spinal misalignment, particularly kyphosis, low life quality, and intractable pain which has been widely recognized as significant complaint of patients with OVCFs.[6]

Nowadays, there are multiple treatment choices for patients with OVCFs, such as conservative treatment, percutaneous vertebroplasty (PVP), as well as percutaneous balloon kyphoplasty (PKP). Initial conservative treatment including oral analgesics, bed rest and physical support were main therapeutic regimen before the application of percutaneous minimally invasive surgery. Although 64 percent of OVCFs gradually improved with initial conservative treatment, multiple above-mentioned concomitant symptom and complications have emerged.[7–9] The earliest studies by Galibert et al[10] (1987) reported PVP for patients with hemangiomas as a minimally invasive method. Since then, the technique was immediately introduced into treating OVCFs and was considered the optimal method for OVCFs, but subsequently, it failed to restore the decreased vertebral height.[11] Therefore, in order to relieve pain and restore vertebral height, PKP, developed from PVP is a new minimally invasive technique with the help of a balloon tamp inserted into the destructed vertebral body by a transpedicular approach to restore vertebral height, and using polymethylmethacrylate (PMMA) bone cement to support the height of fracture vertebral body.[12–14]

Historically, Garfin et al[13] (2001) compared the effectiveness of PKP and PVP for the treatment of OVCFs patients and suggested that PKP with obvious advantages was considered as a standard technique. Subsequently, PKP has been widely recognized as an effective and safe procedure to relief pain of VCFs and restore vertebral height, which had significantly greater benefit than conservative treatment and PVP, even through the best choice partly depends on characteristics of fractures.[7–9,15] Previously, a Bayesian-framework network meta-analysis[16] of 5 RCTs to compare 3 treatments (PVP, PKP, and conservative treatment) for treating OVCFs patients was performed, which demonstrated that PKP was the best method to reduce the risk of discontinuation in elderly population.

A study by Garfin et al[13] demonstrated that the standard technique for PKP involved a bilateral approach using 2 balloon tamps. Recently, comparing with bilateral approach, unilateral PKP for VCFs was reported to achieve the same therapeutic effect,[11] sometimes even better.[17] A short-term (minimum 1-year follow-up) prospective study by Chung et al[18] supported that the bilateral approach had a greater advantage in the reduction of kyphosis and the loss of reduction was less than the unilateral approach for treating OVCFs. However, in a long-term study (minimum 2-year follow-up) Chen et al[19] deemed that, in the long run, the unilateral PKP can maintain the same effectiveness, comparing bilateral PKP. Whether one method was superior to the other in clinical outcomes was inconclusive, needing well-designed clinical and biomechanical studies.

Fortunately, on this hot topic, numerous systematic reviews and meta-analyses[20–28] have been conducted in the past 5 years. The earliest meta-analysis performed by Lin et al[24] (2013) demonstrated that evidence was insufficient to support the use of unilateral better than bilateral PKP for treating OVCFs patients. Although several updated meta-analyses[22,25] supported this result, some[20,21,23] refuted it and suggested unilateral PKP yielded significantly better outcomes. These inconsistent meta-analyses made clinicians relapse into terrible predicaments in clinical choice of OVCFs. In order to obtain more reliable clinical outcomes and recommended a best method for treating OVCFs based on the currently available evidence, we systematically retrieved all published meta-analyses though evaluating the methodology and reporting quality of included meta-analyses, investigating the source of discordant results.

2. Materials and methods

2.1. Inclusion and exclusion criteria

A targeted systematic review or meta-analysis must meet 4 eligible criteria related to 4 systematic review or meta-analysis with quasi-randomized clinical trial (RCTs) or RCTs; literatures comparing unilateral and bilateral PKP for treating OVCFs; one of contrast ratios, Visual Analog Scale (VAS), Oswestry Disability Index (ODI) score, surgery time, complication of adjacent vertebral fractures, or cement leakage and so on, being assessed in the included literatures; combined results data (I-square and final results) of meta-analysis provided in literatures; all subjects for study involving in clinical patients.

Literatures were excluded if they were a conventional review, non-RCT, systematic review no reporting the combined outcomes of meta-analysis, animal experiments, and meeting abstracts and correspondence because of half-baked data of methodological quality.

2.2. Search strategy and selection process

A comprehensive search of 3 electronic medical databases, PubMed/Medline, EMBASE, and the Cochrance Library were conducted until November 30, 2017 with no restrictions of language and search. The search keywords were as follows: "osteoporotic vertebral compression fracture," "OVCF," "vertebral compression fracture," "VCF," "kyphoplasty," or "PKP" AND "systematic review" or "meta-analysis." Subsequently, in order not to omit any potential literatures, a hand research was carried out to retrieve and screen the relevant reference lists of reviews, systematic reviews, meta-analysis, and included literatures.

After systematically searching in three databases, the feasible titles and abstracts of searched literatures were scanned and excluded if the topic was not relevant to research target. All that's left were subsequently retrieved and downloaded full-text. Two reviewers (FXL and GQT) independently and in duplicate conducted the selection process. In order to minimize potential bias, the process of searching process for included literatures were conducted by two reviewers (FXL and GQT), and checked by a third one (DSZ). All disagreements were resolved by discussion and consensus of a third reviewer (DSZ).

2.3. Data extraction and methodological quality

Independently, meaningful data were extracted utilizing 3 steps. First, basic information of included literatures were extracted, such as the first author's surname, year and journal of publication, databases, language and the latest retrieval date of searching, data of acceptation and publication, numbers of included RCTs, and quasi-RCTs. Subsequently, quality information of included literatures were extracted, such as the first author's surname and year of publication of primary RCTs and quasi-RCTs, which were included into the targeted meta-analysis, primary study design, level of evidence, software utilized for meta-analysis, and whether the risk of bias, GRADE, sensitivity analysis, publication bias, and PRISMA were utilized or evaluated. Finally, the combined results, effect indexes, and corresponding I^2 were carefully extracted from each original literature into a standardized Excel file (Microsoft, WA).

This systematic review of overlapping meta-analysis was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[29] Ethical approval or patient consent is not required for conducting this meta-analysis. The methodological quality of included meta-analyses was evaluated independently by two reviewers (FXL and GQT) according to the Assessment of Multiple Systematic Reviews (AMSTAR) instrument[30–33] and the Oxford Levels of Evidence[34–36], which was used in the similar study.[37] The AMSTAR composed of 11 items is a valuable measurement tool with good reliability, validity, and responsibility for evaluating the methodological quality of systematic reviews and meta-analyses. While the Oxford Levels of Evidence is a hierarchy of the likely best evidence, which was designed and used as a short-cut for busy clinicians, researchers, or patients to find the likely best evidence. It could provide the most reliable answers for treatment benefits and harms in systematic reviews of randomized trials.

2.4. Heterogeneity assessment and application of Jadad decision algorithm

Heterogeneity of mean difference across studies was assessed using the I I^2 statistic, a quantitative measure which described the percentage of total variation due to heterogeneity. Higher I^2showed higher heterogeneity.[38] If $I^2 \leq 50\%$, heterogeneity across studies was tolerant in a systematic review or meta-analysis based on the Cochrane Handbook.[39] Otherwise, 2 reviews evaluated whether the original literature presented sensitivity analyses and publication bias for assessing the stability of pooled estimations to explore possible sources of heterogeneity.

Jadad Decision Algorithm reported by Jadad[33] presented currently that it was a methodology for providing best treatment recommendations to identify discordant meta-analyses. Multiple source of discordance of systematic reviews or meta-analyses included different clinical question, inclusion and exclusion criteria, search strategy, selection process, information extraction, quality assessment, and data synthesis analysis. Three authors (FXL, GQT, and DSZ) reached a consensus to choose literatures presented the best currently available evidence using the algorithm.

3. Results

3.1. Selection process

The detailed literature search and study selection process are summarized as a flow diagram in Figure 1. In total, 2159 relevant

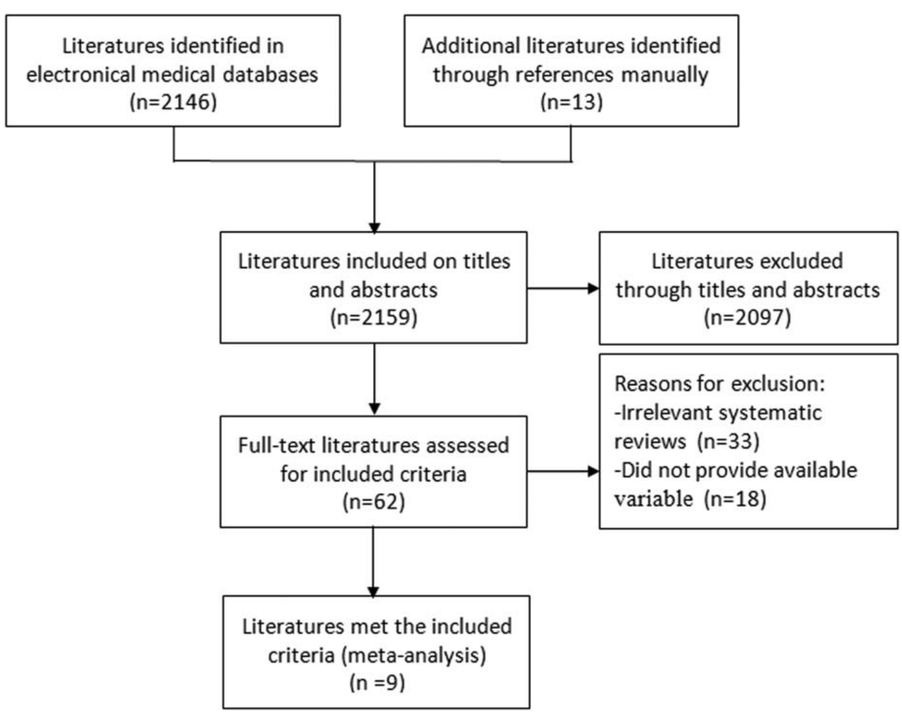

Figure 1. Flow chart summarizing the selection process of meta-analyses.

Table 1

Main characteristics of each included meta-analysis.

Study, year	Journal of publication	Date of last literature search	Language of search	Date of acceptation	Date of publication	Numbers of included RCTs /no-RCT
Li et al[23] 2013	Chin Med J	March 2013	No restrictions	28 May 2013	October 2013	7/0
Lin et al[24] 2013	Pain Physician	July 2012	No restrictions	31 October 2012	September/October 2013	3/0
Yang et al[25] 2013	Pain Physician	September 2012	No restrictions	25 February 2013	July/August 2013	4/0
Chen et al[21] 2014	ORTHOPEDICS	April 2013	English	30 January 2014	9 September 2014	4/10
Huang et al[22] 2014	Clin Orthop Relat Res	June 2013	English	4 June 2014	26 June 2014	5/0
Feng et al[20] 2015	J Orthop Res	January 2015	No restrictions	30 May 2015	29 June 2015	12/0
Cheng et al[26] 2016	Eur Spine J	April 2015	No restrictions	15 January 2016	27 January 2016	7/1
Chang et al[27] 2017	Medicine	November 2016	NR	26 March 2017	April 2017	7/7
Yang et al[28] 2017	Acta Orthopaedica et Traumatologica Turcica	October 2014	NR	21 February 2017	21 June 2017	14/0

NR = not reported, RCT randomized controlled trials.

literatures were retrieved by screening the titles and abstracts, of which 2097 failed to meet the selection criteria and were excluded for various reasons (reviews, correspondence, conference summary, case report, or irrelevant to the analysis). After all the full-texts of potentially relevant studies were downloaded, 62 literatures resulted in further exclusions where a total of 51 literatures did not conduct meta-analyses or pooled data, and remains were irrelevant systematic reviews or meta-analyses. After careful selection, eventually, a total of 9 meta-analyses[20–28] were consistent with the inclusion criteria and were selected for the meta-analysis.

3.2. Study characteristics

The main characteristics of the meta-analyses utilized in the systematic review are summarized in Table 1.[20–28] Meta-analyses were published between 2013 and 2017, with the sizes of included studies ranging from 5 to 14 RCTs or quasi-RCTs. Among them, 5 meta-analyses[20,23–25,27] had no restrictions of language search, 2[21,22] only included meta-analysis published in English, and others did not report relevant data. The latest retrieval and publication date was November, 2016 and 26 March 2017, respectively, which were presented in a meta-analysis performed by Chang et al.[27] Two meta-analyses[24,25] were published in *Journal of Pain Physician*, and remains were published in different magazines including *Chinese Medical Journal, Orthopedics, Clinical Orthopaedics and Related Research, Journal of Orthopaedic Research, Acta Orthopaedica et Traumatologica Turcica,* and *Medicine*. Each primary RCTs or quasi-RCTs from 9 meta-analyses were list in Tables 2[20–28] and 3[20,21,23,27,28]. In total, 2 studies[20,39] were all included in this 9 meta-analyses, 4 studies[11,40–42] included 8 meta-analyses, and 1 study[43] included 6 meta-analyses. Of the primary RCTs or quasi-RCTs in 9 meta-analyses, 9 primary studies[11,18,20,39–44] were published in English, and others in Chinese.

3.3. Search methodology

Details of databases applied by literature searches of each included meta-analysis were presented in Table 4.[20–28] In total, 9 meta-analyses[20–28] were conducted with a comprehensively searching for original literatures in PubMed and the Cochrane Library. Of the 9 meta-analyses, 7[20–22,24–27] searched Embase, only 2[22,23] for Web of Knowledge, 2[25,26] for OVID, 2[23,28] for Wanfang data, and 4[21,23,27,28] searched CBM. There was inconsistent as to whether literatures searched CINAHL, Web of Science, Bandolier, SinoMed, CNKI, and China Academic Journals Full-text Database.

3.4. Methodological quality

Detailed methodological information was presented in Table 5.[20–28] All 9 included meta-analyses included RCTs or quasi-RCTs with level II or III of evidence. Among them, 2 meta-analyses[21,22] declared that they adopted GRADE in the research process, 6[21–25,28] followed PRISMA, 7[20–22,24–26,28] performed pool analyses using Revman, and only 2[23,27] used Stata/SE software (StataCorp, CollegeStation, TX).

Table 2

Primary RCTs published in English were included in meta-analyses.

Study, year	Chung 2008	Song 2009	Chen CM 2010	Chen CM 2011	Chen L 2011	Wang 2012	Rebolledo 2013	Yan 2014	Wang 2015
Li et al[23] 2013	√		√	√	√		√		
Lin et al[24] 2013	√			√	√				
Yang et al[25] 2013	√		√	√	√				
Chen et al[21] 2014	√		√	√	√		√		
Huang et al[22] 2014	√		√	√	√		√		
Feng et al[20] 2015	√		√	√	√		√	√	
Cheng et al[26] 2016	√	√	√	√	√	√	√		√
Chang et al[27] 2017	√		√	√	√		√		
Yang et al[28] 2017			√		√				

RCT = randomized controlled trials.

Table 3

Primary RCTs published in Chinese were included in meta-analyses.

Study, year	Gu 2009	Jiang 2010	Feng 2012	He 2012	Li Q 2012	Li GZ 2012	Luo 2012	Zhang 2012	Mao 2013	Huang 2013	Zhai 2013	Zeng 2013	Zhou 2013	Lin 2014	Liu 2014	He 2014	Li 2014
Li et al[23] 2013	√						√										
Chen et al[21] 2014	√	√	√	√	√	√	√	√		√							
Feng et al[20] 2015			√						√		√			√	√	√	
Chang et al[27] 2017															√		√
Yang et al[28] 2017	√					√		√	√			√	√				

RCT = randomized controlled trials.

Table 4

Databases applied by literature searches of each included meta-analysis.

Study, year	PubMed	Embase	Cochrane Library	Web of Knowledge	Web of Science	OVID	CINAHL	Bandolier	SinoMed	CBM	CNKI	Wanfang Data	VIP	China Academic Data	By hand
Li et al[23] 2013	√		√	√						√		√			√
Lin et al[24] 2013	√	√	√				√	√							√
Yang et al[25] 2013	√	√	√			√									√
Chen et al[21] 2014	√	√	√		√					√					√
Huang et al[22] 2014	√	√	√	√											√
Feng et al[20] 2015	√	√	√						√		√				√
Cheng et al[26] 2016	√	√	√		√	√									√
Chang et al[27] 2017	√	√			√					√					
Yang et al[28] 2017	√		√		√					√		√	√	√	

AMSTAR outcomes for each item from 9 included meta-analyses were presented in Table 6.[20–28] AMSTAR scores of included 9 meta-analyses varied from 8 to 9 with a median of 8.55 (mean 8.5), of which 4 meta-analyses[20,21,25,26] receiving 8 scores, and others[22–24,27,28] receiving 9. Finally, a meta-analysis by Feng et al[20] met 9 items of eleven criteria of the AMSTAR with the highest quality literature.

3.5. Heterogeneity assessment and publication bias

Of the 9 meta-analyses, 6[20,21,23,25,27,28] used Funnel-plot and Egger's test to identify publication bias and 8[20–23,25–28] performed risk of bias. All 9 included meta-analyses used the I^2 value as a statistic measure to evaluate heterogeneity across studies. I^2 value for each result of 9 meta-analyses was demonstrated in Table 7.[20–28] Heterogeneities (I^2 <50%) of the majority variables in 9 meta-analyses were tolerant. Meanwhile, 4 meta-analyses[22,23,25,27] performed sensitivity analyses to test whether the results would qualitatively change if a different assumption was used.

3.6. Results of Jadad decision algorithm

The pooled outcomes of all included meta-analyses are summarized in Fig. 2. Three reviewers (LFX, TGQ and ZDS) independently applied the Jadad decision algorithm to evaluate which of the included meta-analyses provides the best currently available evidence from which to stipulate recommendations for the treatment of patients with OVCFs. Given that each included meta-analysis focused on the same topic, comprising the different studies based on the similar search process and selection strategy, and the inclusive criteria were discordant. The determination was thus made that the best available evidence should be selected based on the publication status and the methodological quality of primary studies, whether language restrictions and data analysis for individual patients. Eventually, a meta-analysis[20] including more RCTs was selected as a high-quality reporting (Fig. 3). This selected meta-analysis suggested that unilateral PKP was better than bilateral in the treatment of OVCFs in respects of VAS scores (short-term), the dosage of PMMA, surgery time, cement leakage, physical function, and role physical (short-term). The similar

Table 5

Methodological information for each included meta-analysis.

Study, year	Included study design	Level of evidence	Software	Assessment of study quality	Risk of Bias	GRADE use	Sensitivity analysis	Publication bias	PRISMA
Li et al[23] 2013	RCT	Level II	Stata/SE 10.0	Cochrane Back Review Group	Yes	No	Yes	Yes	Yes
Lin et al[24] 2013	RCT	Level II	RevMan version 5.1	Jadad scale	No	No	No	No	Yes
Yang et al[25] 2013	RCT	Level II	RevMan version 5.1	Cochrane review criteria	Yes	No	Yes	Yes	Yes
Chen et al[21] 2014	RCT and no-RCT	Level III	RevMan version 5.2	Cochrane Handbook	Yes	Yes	No	Yes	Yes
Huang et al[22] 2014	RCT	Level II	RevMan version 5.1	Cochrane Handbook	Yes	Yes	Yes	No	Yes
Feng et al[20] 2015	RCT	Level II	RevMan version 5.2	Cochrane review criteria	Yes	No	No	Yes	No
Cheng et al[26] 2016	RCT and no-RCT	Level III	RevMan version 5.3	Cochrane review criteria	Yes	No	No	No	No
Chang et al[27] 2017	RCT and no-RCT	Level III	Stata/SE 11.0	Newcastle Ottawa Scale	Yes	No	Yes	Yes	No
Yang et al[28] 2017	RCT	Level II	RevMan version 5.0	Cochrane Handbook	Yes	No	No	Yes	Yes

PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RCT = randomized controlled trials.

Table 6

AMSTAR criteria for each included meta-analysis.

Items	Li et al[23] 2013	Lin et al[24] 2013	Yang et al[25] 2013	Chen et al[21] 2014	Huang et al[22] 2014	Feng et al[20] 2015	Cheng et al[26] 2016	Chang et al[27] 2017	Yang et al[28] 2017
Was an a priori design provided?	0	0	0	0	0	0	0	0	0
Was there duplicate study selection and data extraction?	1	1	1	1	1	1	1	1	1
Was a comprehensive literature search performed?	0	1	1	1	1	1	1	1	1
Was the status of publication (ie, grey literature) used as an inclusion criterion?	1	1	1	1	1	1	1	1	1
Was a list of studies (included and excluded) provided?	0	0	0	0	0	0	0	0	0
Were the characteristics of the included studies provided?	1	1	1	1	1	1	1	1	1
Was the scientific quality of the included studies assessed and documented?	1	1	1	1	1	1	1	1	1
Was the scientific quality of the included studies used appropriately in formulating conclusions?	1	1	1	1	1	1	1	1	1
Were the methods used to combine the findings of studies appropriate?	1	1	1	1	1	1	1	1	1
Was the likelihood of publication bias assessed?	1	0	1	1	0	1	0	1	1
Was the conflict of interest stated?	1	1	1	1	1	1	1	1	1
Total scores	8	8	9	9	8	9	8	9	9

Table 7

I^2 statistic value of each variable in each included meta-analysis.

Outcomes	Li et al[23] 2013 (%)	Lin et al[24] 2013 (%)	Yang et al[25] 2013 (%)	Chen et al[21] 2014 (%)	Huang et al[22] 2014 (%)	Feng et al[20] 2015 (%)	Cheng et al[26] 2016 (%)	Chang et al[27] 2017 (%)	Yang et al[28] 2017 (%)
Preoperative VAS score	0	46	–	–	–	–	–	–	–
Short-term VAS score	0	0	0	0	0	0	0	0	0
Mid-term VAS score	–	–	–	–	–	0	–	–	0
Long-term VAS score	0	0	0	0	0	0	0	0	–
Preoperative ODI score	57.3	–	–	–	–	–	–	0	–
Short-term ODI score	<50	–	–	72	–	36	31	0	–
Long-term ODI score	<50	–	–	91	–	–	–	0	–
PMMA dosage	50.4	0	–	38	–	44	96	85	–
Surgery time	94.7	17	0	32	0	14	95	68	–
Cement leakage	39.9	45	28	27	41	0	23	0	–
Adjacent vertebral fracture	–	–	34	–	39	0	34	0	–
X-ray exposure	–	–	–	–	–	–	98	97.3	–
Preoperative kyphosis angle	0	–	–	–	–	–	–	–	–
Kyphosis angle Reduction	0	–	–	–	85	85	–	85.3	–
Kyphosis angle Restoration	94.3	–	–	42	–	–	–	–	–
Loss of reduction kyphosis angle	92.6	–	–	–	–	–	–	–	–
Cobb's angle recovery	–	–	–	–	–	50	–	–	–
VH lost rate	–	–	68	–	–	0	–	–	–
Anterior VH	–	–	–	0	91	–	–	–	–
Short-term Anterior VH restoration	–	–	–	–	–	0	–	–	–
Long-term Anterior VH restoration	–	–	–	–	–	18	–	–	–
VH restoration	–	–	–	–	–	94	0	–	–
Middle VH	–	–	–	25	–	–	–	–	–
Short-term middle VH restoration	–	–	–	–	–	0	–	–	–
Long-term middle VH restoration	–	–	–	–	–	0	–	–	–
Short- and long-term physical function	–	–	–	–	–	0/0	–	–	–
Short- and long-term role physical	–	–	–	–	–	67/62	–	–	–
Short- and long-term bodily pain	–	–	–	–	–	9/0	–	–	–
Short- and long-term general health	–	–	–	–	–	0/0	–	–	–
Short- and long-term vitality	–	–	–	–	–	0/15	–	–	–
Short- / long-term social function	–	–	–	–	–	0/0	–	–	–
Short- / long-term role emotional	–	–	–	–	–	9/0	–	–	–
Short- / long-term mental health	–	–	–	–	–	0/0	–	–	–

ODI = Oswestry Disability Index, PMMA = polymethylmethacrylate, VAS = Visual Analog Scale, VH = vertebral height.

Outcomes	Li et al. 2013	Lin et al. 2013	Yang et al. 2013	Chen et al. 2014	Huang et al. 2014	Feng et al. 2015	Cheng et al. 2016	Chang et al. 2017	Yang et al. 2017
Preoperative VAS score	6	3	2	?	?	?	?	?	?
Short-term VAS score	5	3	2	6	3	8	6	4	5
Mid-term VAS score	?	?	?	?	?	3	?	?	2
Long-term VAS score	5	3	2	6	4	6	6	5	2
Preoperative ODI score	3	?	?	?	?	2	?		?
Short-term ODI score	3	?	?	2	2	2	2	2	1
Long-term ODI score	3	?	?	3	2	?	?		1
PMMA dosage	3	3	?	10	?	6	6	5 5	?
Surgery time	5	2	2	12	4	6	6	6 5	?
Cement leakage	4	3	3	6	4	8	5	10	?
Adjacent vertebral fracture	1	?	2	?	2	5	2	5	?
X-ray exposure	?	?	?	?	?	?	2	2 3	?
Preoperative kyphosis angle	4	?	?	?	?	?	?	?	?
Kyphosis angle reduction	2	?	?	?	3	3	?	2 2	5
Kyphosis angle restoration	2	?	?	9	?	?	?	?	?
Loss of reduction kyphosis angle	2	?	?	?	?	?	?	?	?
Cobb's angle recovery	?	?	?	?	?	4	?	?	?
VH lost rate	?	?	2	?	?	2	?	?	4
Anterior VH	?	?	?	7	2	?	?	?	?
Short-term anterior VH restoration	?	?	?	?	?	5	?	?	?
Long-term anterior VH restoration	?	?	?	?	?	4	?	?	?
VH restoration	?	?	?	?	?	4	2	?	?
Middle VH	?	?	?	6	?	?	?	?	?
Short-term middle VH restoration	?	?	?	?	?	3	?	?	?
Long-term middle VH restoration	?	?	?	?	?	2	?	?	?
Short- and long-term physical function	?	?	?	?	?	2 2	?	?	1
Short- and long-term role physical	?	?	?	?	?	2 2	?	?	1
Short- and long-term bodily pain	?	?	?	?	?	2 2	?	?	1
Short- and long-term general health	?	?	?	?	?	2 2	?	?	1
Short- and long-term vitality	?	?	?	?	?	2 2	?	?	1
Short- and long-term social function	?	?	?	?	?	2 2	?	?	1
Short- and long-term role emotional	?	?	?	?	?	2 2	?	?	1
Short- and long-term mental health	?	?	?	?	?	2 2	?	?	1

Figure 2. Outcomes of effective indexes from each included meta-analysis. Red means favoring unilateral percutaneous kyphoplasty; green means no difference; yellow means not reporting; and blue means favoring bilateral percutaneous kyphoplasty. Arabic numerals mean the number of included randomized clinical trials. ODI = Oswestry Disability Index, PMMA = polymethylmethacrylate, VAS = Visual Analog Scale, VH = vertebral height.

findings emerged in VAS scores (mid- and long-term), ODI scores (short-term), adjacent vertebral fracture, kyphosis angle reduction, Cobb's angle recovery, VH lost rate and restoration (short- and long-term), and quality of life (36-Item except physical function and role physical at short-term follow-up). However, the effective of 2 methods in respects of ODI scores (long-term), restoration of kyphosis angle, and loss of reduction kyphosis angel were unclear.

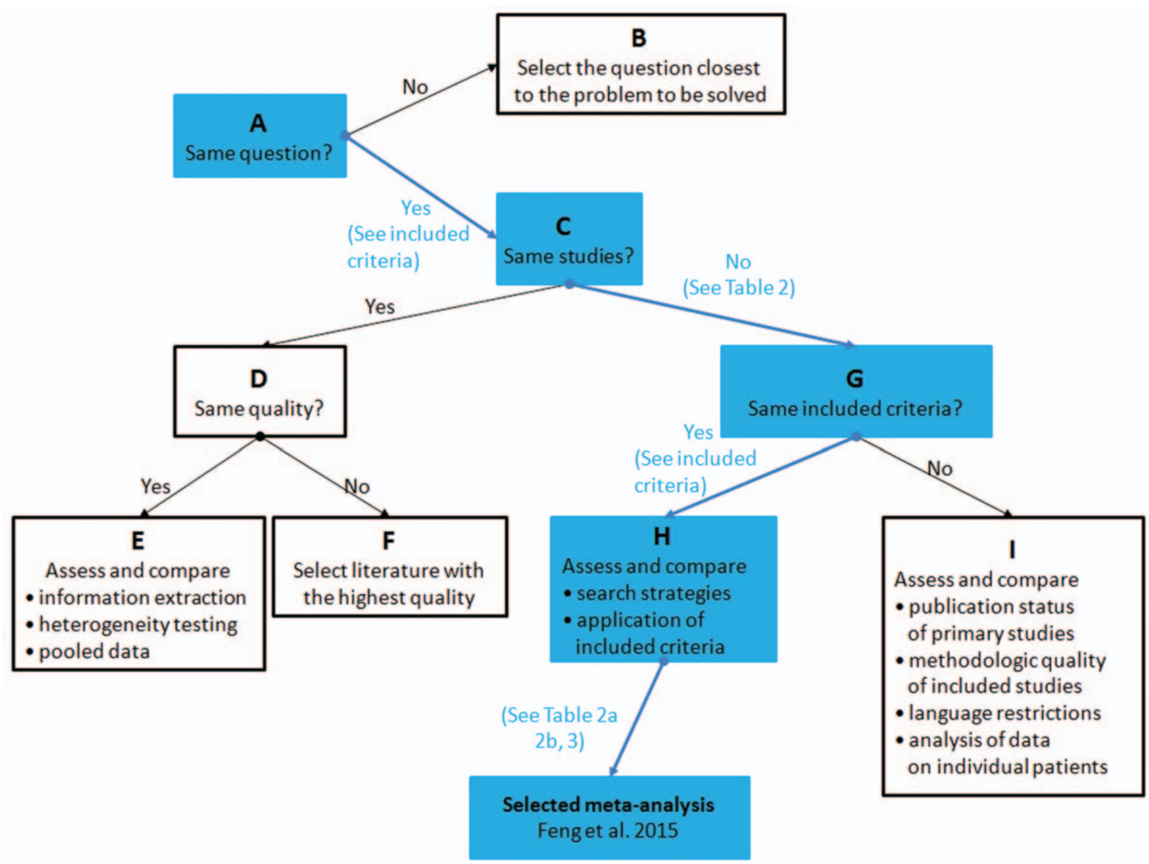

Figure 3. Flow chart of Jadad decision algorithm.

4. Discussion

OVCFs are a common type of fracture and nowadays, bilateral and unilateral PKP for treating OVCFs patients are both widely-used in clinic. Controversy exists about which of the 2 procedures leads to superior results, complicating clinical decision-making even though multiple original studies have been published to praise 2 clinical intervention measures appropriately. Famously, well-designed meta-analyses including RCTs were generally recognized as the best statistical evidence for clinical decisions; however, inconsistencies in findings among overlapping meta-analyses raise concerns as to whether an effective tool or solution aiming to address a thorny problem truly exists. Fortunately, Jadad et al[33] generalized the potential sources of inconsistency within and across meta-analyses and presented a more efficient solution which summarized the process for exploring and resolving reasons of inconsistencies.

In our review, the comprehensive search of eligible literatures and rigorously screening yielded a total of 9 meta-analyses on this topic. Of included 9 meta-analyses, 4[20,21,23,27] demonstrated that unilateral PKP is superior to bilateral PKP for treating patients with OVCFs, the remains[22,24–26,28] did not show any obvious advantage of either of the 2 surgery methods. According to the Jadad decision tool, a meta-analysis reported by Feng et al[20] was selected into the systematic review of overlapping meta-analysis, which included 12 RCTs with level II evidence, possessing the highest methodological quality. Based on currently available best evidence, the determination was thus made that more advantages could obtain by using unilateral PKP for the treatment of patients with OVCFs.

The main purpose of early surgery for the treatment of patients with OVCFs patients is to relief back algia with satisfactory degree of mobility. VAS and ODI scores were often used as main pain and functional scores. The VAS, a measurement instrument from psychometric response for subjective attitudes that could not be directly evaluated, could be applied in questionnaires. If respondents responded to each item of VAS, the level was specified to be in accordance with a statement by implying a precise position on a continuous line. All chosen meta-analyses regarded VAS scores at a short- and long- term follow-up as the primary outcome, and demonstrated that VAS scores of unilateral PKP was superior to bilateral PKP with a short-term follow-up. Surprisingly, at a long-term follow-up no significant difference was presented. ODI is a questionnaire for rating the severity of back pain, which is currently considered by many as the gold standard for measuring degree of disability and estimating quality of life in a person with low back pain. Among 9 included meta-analyses, 2[20,23] reported ODI scores before operation, 4[21–23,28] and 5[20–23,28] at a short- and long-term follow-up, respectively. Congruously, no difference was found at a short- and long-term follow-up.

Synchronously, included meta-analyses showed no difference of unilateral PKP and bilateral PKP in outcomes of measurement data obtained from images, including kyphosis angle reduction, Cobb's angle recovery, vertebral height lost rate, restoration of general, anterior, and middle vertebral height restoration at a short- or long-term follow-up. Complication rates are of great importance. Cement leakage and adjacent vertebral fracture are common complications after operation of PKP. In this systematic review, 6[20,22,23,25–27] of 9 included meta-analyses investigated adjacent vertebral fracture after unilateral and bilateral PKP and both demonstrated that no difference between 2 methods. However, all 9 targeted meta-analyses, including a high-quality 1 selected according to Jadad tool, noticed cement leakage of 2 surgery methods and suggested that higher cement leakage occurred in bilateral PKP. Another 2 important indexes to evaluate the effect and safety of 2 methods are surgery time and PMMA. The meta-analysis performed by Feng et al[20] demonstrated shorter surgery time and lower dosage of PMMA in unilateral PKP group compared with those in bilateral PKP group.

The 36-Item Short Form Health Survey (SF-36) instrument was utilized as a useful tool to assess the quality of life, which consist of physical function, role physical, bodily pain, general health, vitality, social function, role emotional, and mental health. Only 2 meta-analysis[20,28] with 2 RCTs provided the outcomes of SF-36, and demonstrated that unilateral PKP had a better general health benefit with short-term follow-up after surgery. Statistically significant differences of other items between 2 methods were not presented.

The best available evidence demonstrated that unilateral and bilateral PKP are both nice choices for the treatment of OVCFs, and no significant differences were revealed in clinical scores, radiological outcomes and quality of life with a long-term follow-up. However, compared with bilateral PKP, unilateral PKP resulted in a shorter surgery time, smaller dosage of cement, lower risk of cement leakage, and relieved a higher degree of intractable pain at a short-term follow-up after surgery. Unilateral PKP is more advantageous and superior to bilateral PKP, and should be considered an effective option for the treatment of patients with osteoporotic vertebral compression fractures.

Several limitations exist in this investigation. First of all, we only included English language meta-analyses; some non-English language studies may be omitted. Second, some meta-analyses enrolled and pooled with quasi-RCTs or lower quality RCTs. Although all included meta-analyses were evaluated to ensure the high quality of this systematic review, level evidence included II or III evidence and are lack of I evidence in all included meta-analyses. Last but not least, we might omit some systematic reviews or meta-analyses, which were available for the inclusion criteria even though a computer search was performed as comprehensive as possible.

5. Conclusions

This systematic review of overlapping meta-analyses comparing unilateral versus bilateral PKP for the treatment of patients with OVCFs demonstrated that unilateral PKP provides a lower rate of cement leakage, lower dosage of PMMA, shorter surgery time, and a better quality life. Therefore, we could safely arrive at a conclusion that unilateral PKP is superior to bilateral PKP for patients with OVCFs. However, in some respects, large-scale high-quality randomized controlled trials are still needed to warrant current conclusion.

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