

Risk factors of the Secondary Fractures for Osteoporotic Vertebral Compression Fractures after Percutaneous Vertebroplasty

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Abstract

Background Percutaneous vertebroplasty related postoperative secondary fractures risk factors were not consistent in patients with osteoporotic vertebral compression Fractures. The purpose was to identify the risk factors of the secondary fractures for osteoporotic vertebral compression fractures after percutaneous vertebroplasty.

Methods Potential academic articles were identified from Cochrane Library, Medline, PubMed, Embase, ScienceDirect and other databases. The time range we retrieved from was that from the inception of electronic databases to August 2019. Gray studies were identified from the references of included literature reports. STATA version 11.0 (Stata Corporation, College Station, Texas, USA) was used to analyze the pooled data.

Results Fourteen studies involving 1910 patients, 395 of whom had secondary fracture following the surgery were included in this meta-analysis. The results of meta-analysis showed the risk factors of the secondary fractures for osteoporotic vertebral compression fractures after percutaneous vertebroplasty was related to bone mineral density [WMD= -0.518, 95%CI(-0.784,-0.252), P=0.000], cement leakage [RR=0.596, 95%CI (0.444,0.798), P=0.001] and kyphosis after primary operation [WMD=4.510, 95%CI (3.061,6.004),P=0.000], but not to gender, age, body mass index (BMI), cement volume, thoracolumbar spine, and cement injection approaches.

Conclusions BMD, cement leakage and kyphosis after primary operation are the risk factors closely correlative to the secondary fracture after percutaneous vertebroplasty. There has not been enough evidence to support the association between the secondary fracture and gender, age, body mass index, cement volume, thoracolumbar spine, and cement injection approach.

Introduction

Osteoporosis is a systemic disease with progressive dicalcium and bone structure abnormality, which could result in compression fracture even under a slight external force (falling, lifting heavy objects, coughing violently).[1, 2] Spine, hip and distal radius are the predilection sites of osteoporotic fracture, but osteoporotic vertebral compression fracture (OVCF) is the most common one, accounting for more than 1/3[3–5]. Patients with OVCF could have a series of symptoms such as back pain and kyphosis, which can seriously affect the quality of life of patients.[6] Furthermore, the OVCF has a slow healing, accompanied by a high rate of disability and death.[7] The traditional treatment methods include bed rest, drug analgesia, bracing external fixation, resulting in a vicious circle of decalcification of bone, progresses of severe pain, kyphotic deformity and increasing mortality[8]. Percutaneous vertebroplasty (PVP) can be used as early as possible in an emergency once OVCF is diagnosed and the patient's physical condition permits. Due to small trauma, less time in bed, quick relief of the pain. PVP, a technique of injecting bone cement into the target vertebral body, currently has become the characteristics of the main clinical treatment of OVCF, which obtained the identification of orthopedic

physicians and patients.[9, 10] However, numerous clinical data have been confirmed that the incidence of non-surgical vertebral fractures was 8%-52%, and 41%-69% of the secondary fractures occurred in the adjacent segment of the vertebral body.[11–13] Lin et al.[14] believe that the stiffness and other biomechanical factors of the injured vertebral bone cement injection lead to changes in biomechanics of the whole spine, resulting in significant changes in the pressure of adjacent vertebral body. Though, the bulk of the data showed that the gender (significantly more women than men), age (mainly 60 to 80 years old), bone mineral density (BMD), cement volume, cement leakage are the underlying inducements. PVP related risk factors of postoperative secondary fractures were not consistent in patients with OVCF.[15, 16] Therefore, we collected literatures on the related factors of vertebral fracture after PVP of OVCF patients, assessed the effects of these factors on vertebral secondary fractures through meta-analysis.

Materials And Methods

Literature and search strategy

The retrieved object was the research literature on the analysis of secondary fractures of OVCF following PVP operation published publicly in the electronic databases including PubMed, Cochrane Library, EMBASE, and Web of Science from the inception of electronic databases to August 2019. We retrieved the following keywords in combination with Boolean logic: osteoporosis, vertebral compression fracture, percutaneous vertebroplasty, subsequent fracture, secondary fractures. Beyond that, the research of the appraisal reference list was manually checked to determine other potential qualification trials. The process iterates until no more articles could be determined. The meta-analysis was based on acknowledged PRISMA guideline (the prioritized reported items for systematic review and meta-analysis).

Inclusion and exclusion criteria

The articles will be incorporated into the present meta-analysis if the literatures meet the following principles: (I) OVCF patients undergoing PVP surgery; (II) analysis of related risk factors for postoperative patients with secondary fractures; (III) one or more adequate data of the outcomes could be conducted statistical analysis;(IV) Non-English language publications, case reports, comments, letters, editorials, protocols, guidelines, and review papers were excluded; (V) animal studies were excluded.

Data extraction and outcome measures

Two of the reviewers respectively extracted data from the included studies. The following essential information was captured—the first author names, publication year, samples size, study design, and outcomes and other relevant data. The extracted data (median, range and the size of the trial, and MD and SD) was input into the designed standardized table 1. When there are differences of opinion, another authority author has the final decision. The outcome measurements were gender, age, body mass index

(BMI), bone mineral density (BMD), cement volume, cement leakage, thoracolumbar spine, cement injection approach, kyphosis after primary operation.

Quality assessment and Statistical analysis

Tool of Cochrane Bone, the Joint and Muscle Trauma Group and Newcastle-Ottawa Scale (NOS) were respectively conducted to evaluate the quality assessment of the included RCTs and non-RCTs. The literature quality evaluation was conducted separately by two reviewers. Consensus was reached through consultation for divergence. We use the STATA version 11.0 (Stata Corporation, College Station, Texas, USA) for statistical analyses. When $I^2 \geq 50\%$, we consider the data has obvious heterogeneity, and We conduct an meta-analysis using random-effect model according to Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0). Otherwise, fixed-effect model was performed. The results of continuous outcomes (age, BMI, BMD, cement volume) were expressed as mean difference (MD) with 95% confidence intervals (CIs). For discontinuous various outcomes (gender, cement injection approach, kyphosis after primary operation, thoracolumbar spine, cement leakage) risk ratio (RR) with 95% CIs was applied for the assessment.

Results

Search results

A total of 216 studies were identified as potentially relevant literature reports. 58 reports were removed because of duplication. By scanning the title and abstract, 130 reports were excluded according to the eligibility criteria. 14 reports are eliminated after browsing the full text. No additional studies were obtained after the reference review. Ultimately, 14 studies [14, 16-28] were eligible for data extraction and meta-analysis. The searching process is shown in Figure1.

Outcomes of meta-analysis

Bone mineral density (BMD)

We extracted the BMD value from three included articles. The results show that BMD was the risk factors closely correlative to the secondary fractures after percutaneous vertebroplasty (Heterogeneity $P = 0.908$, $I^2 = 0.0\%$, MD = -0.518, 95% CI: -0.784 to -0.252, $P = 0.000$; Figure2).

Cement leakage

Six articles have been demonstrated the relationship between the cement leakage and secondary fractures rate. There is no significant heterogeneity in the statistical results of the pooled literature ($I^2=42.4\%$, $P=0.123$). The result of the fixed effect model showed that the cement leakage could increase the incidence of new fractures ($RR = 0.596$, 95% CI: 0.444 to 0.798, $P = 0.001$; Figure3).

Kyphosis

Three publications focus on the effect of postoperative kyphosis after primary operation on secondary fractures. Similar to the results described above, postoperative kyphosis angle of vertebra is closely related to the secondary fractures (Heterogeneity $P = 0.472$, $I^2 = 0.0\%$, MD =4.510, 95% CI: 3.016 to 6.004, $P = 0.000$; Figure4).

Gender

In eleven publications, 97 males and 248 females were enrolled in our meta-analysis respectively. No significant difference between the risk factor and the gender was found (Heterogeneity $P = 0.830$, $I^2 = 0.0\%$, $RR=0.962$, 95% CI: 0.768 to1.204, $P = 0.733$; Figure5).

Age

The results of the meta-analysis showed that the age had no effect on postoperative new fractures of OVCF patients following PVP operation (Heterogeneity $P = 0.724$, $I^2 = 0.0\%$, MD = 1.127, 95% CI: -0.013 to 2.267, $P = 0.053$; Figure6).

Cement volume

No significant differences were observed between the cement volume and new fractures rate of OVCF patients following PVP operation (MD= -0.506, 95% CI-1.171 to 0.158; $P = 0.135$, Figure 7) with obvious heterogeneity (heterogeneity $P = 0.0000$, $I^2 =90.8\%$).

Body Mass Index (BMI)

The BMI was reported in eight studies. A random-effects model was performed with obvious heterogeneity ($I^2 = 75.4\%$, $P = 0.000$). There is no statistical difference on the BMI (MD = -0.662, 95% CI:

-1.557 to 0.233, P = 0.147; Figure8).

Thoracolumbar spine

Five studies concentrated on whether the primary fracture in thoracic lumbar segment effects on postoperative secondary fractures of PVP operation. There was no obvious heterogeneity ($I^2 = 48.3\%$, $P = 0.101$); therefore, a fixed-effects model was applied. Pooling the results demonstrated that primary fracture in thoracic lumbar segment has no effect on secondary fractures after PVP (RR =0.898, 95% CI: 0.696 to 1.159, $P = 0.409$; Figure9).

Cement injection approach

Two publications compared the secondary fracture rate of different cement injection approaches. The result show that different cement injection approaches are independent of secondary fractures (Heterogeneity $P = 0.489$, $I^2 = 0.0\%$, RR =1.76, 95% CI: 0.795 to 3. 931, $P = 0.163$; Figure10).

Discussion

The aging process of the population has accelerated osteoporosis as one of the common diseases that endanger the health of the elderly, and OVCF are the main complications of the disease.[5] According to the literature, OVCF accounts for about 45% of all osteoporotic fractures.[29] PVP could not only relieve pain rapidly and effectively, but also shorten the hospitalization days and improve the life quality of OVCF patients.[30] Though, PVP has been widely used in the treatment of OVCF, the problem of secondary fractures following PVP surgery is widely concerned. The studies reported that the incidence of new fractures following PVP was 7.4–52%.[31, 32] But PVP related risk factors of postoperative secondary fractures are not consistent in OVCF patients. The results of our meta-analysis show that the new fractures after PVP for OVCF patients was related to BMD, cement leakage and kyphosis after primary operation, but not to gender, age, BMI, cement volume, thoracolumbar spine or cement injection approach.

Mudano et al.[33] believed that the risk of secondary fractures in patients after PVP was significantly higher than that of conservative treatment. By using spinal finite element model, scholars observed that the bone cement injection could reduce the physiological concave of vertebral endplate.[34] This process not only increased the vertebral body pressure by 19%, but also reduced the flexibility of local spinal joints, and the load of adjacent segments increased by 17%. Another explanation for the secondary fractures is that increased daily activity in postoperative patients aggrandize the stress of the vertebral body, resulting in higher risk of secondary fractures.[35]

BMD, an important symbol of bone mass, could reflect the degree of osteoporosis. The study showed that patients with lower BMD were more likely to have secondary fractures after PVP.[35] The result of 104 cases of OVCF patients with PVP follow-up study shows that there are 51.9% of patients of postoperative recurrence of adjacent vertebral fracture. The BMD of the fracture group was - 3.52, the non-fracture group was - 2.91. Logistic regression analysis showed that there was a negative correlation between BMD and the risk of fracture of adjacent vertebral bodies, suggesting that the lower BMD, the higher risk of secondary fractures of the adjacent vertebral bodies.[36] The research of Lu in 155 patients with PVP showed that the probability of new osteoporotic fractures within 2 years after the operation was 27.7%. [19] Furthermore, The BMD in the fracture group was significantly lower than that of no more fracture group(-3.07 versus - 2.24, $p < 0.05$). The results of our meta-analysis confirmed that low BMD was a high-risk factor for postoperative secondary fractures of OVCF patients. It also has a higher risk of secondary fractures even without PVP in OVCF patients. This risk may be the natural progression of osteoporosis.

The association between the secondary fractures and the correction of vertebral kyphosis is uncertain. KANG et al.[16]found 20 out of 27 cases of secondary fractures were surgical vertebral body fractures. The larger angle of the kyphosis preoperatively was a risk factor for fracture. At the same time, the correction of postoperative kyphosis lead to the imbalance of the stress of the vertebral body, which also increases the risk of vertebral fracture. Lin et al.[14] considered that each degree rectification in the vertebral kyphosis could increase the risk of adjacent vertebral fractures by 9%. However, Lunt et al.[37] reported that kyphosis corrections could reduce the incidence of adjacent fractures. Robert et al. [38]believes that the severity of kyphosis is associated with a subsequent fracture of the adjacent vertebral body. The results of present meta-analysis show that the rates of secondary fractures in patients with larger postoperative vertebral kyphosis is higher. Under normal conditions, the compression load of the spine was perpendicular to the endplate of the vertebral body, and the progressive kyphosis will result in a change in the distribution of the spinal load, thus increasing the incidence of vertebral secondary fractures.[35] Therefore, we believe it is more favorable to correct kyphotic deformity without causing complications.

During the operation of PVP, bone cement could be overflowed through fractures fissure of vertebral body when it is injected into bone cement.[39, 40] The study showed that the leakage of bone cement to the intervertebral space increased the risk of fracture of adjacent vertebral body.[35, 41] The following mechanism of bone cement leakage may lead to a recurrent fracture of the adjacent vertebral body: (I) when the bone cement leaks into the intervertebral space, the stress reduction of the injured vertebral disc leads to an increase in the stress of the adjacent vertebral body. (II) The leakage of bone cement could mechanically stimulate the endplate plate of the adjacent vertebral body, accelerate the degeneration of the disc, and further increase the risk of fracture of adjacent vertebral body. The results of our meta-analysis indicate that bone cement leakage could increase the incidence of vertebral secondary fractures.

The choice of unilateral or bilateral puncture in PVP operation is still controversial. Steinmann et al.[42] hold the point that there is no statistically significant difference in the efficacy and mechanical analysis of PVP by unilateral or bilateral pedicle puncture. VAN-MEIRHAEGHE et al.[43]found that the strength and

stiffness of injured vertebrae could be restored by unilateral injection or bilateral injection, which had no significant effect on the stress of non-operative vertebral body. The present meta-analysis demonstrate that cement leakage is not a risk factors for the new fractures to PVP for OVCF patients.

Kim et al.[44]compared the different volume of bone cement injection in PVP operation showing that there was no correlation between the secondary fractures and volumes of bone cement injection. Our meta-analysis gets the same conclusion. In addition, some scholars believe that the vertebrae which close to the primary fracture site has higher risk, especially the vertebrae at the thoracolumbar junction. [45, 46] However, the result of meta-analysis show that whether the primary fracture is located in the thoracolumbar segment has no effect on the secondary fractures after the PVP. Ahn et al.[47] found that low BMI is a risk factor for new fractures of the hip and spine. Conversely, vertebral fractures are more likely to occur in overweight patients [48].The present meta-analysis show that BMI is not a relevant risk factor. In theory, the elderly women are more likely to develop osteoporosis, which could result in vertebral secondary fractures following PVP operation. However, from our meta-analysis, the age and gender are not an independent risk factor. It may be due to the relatively small sample size of the included literature; the conclusion is still to be proved.

Our research has the following limitations: (I) the included literatures were retrospectively studies (II) The length of the follow-up time is different in each study, and the data collection is not comprehensive (III) The quality of the included literatures is uneven.

Conclusion

BMD, cement leakage and kyphosis after primary operation are the risk factors closely correlative to the secondary fracture after PVP. There has not been enough evidence to support the association between the secondary fracture and gender,age□BMI□cement volume□thoracolumbar spine, and cement injection approach.

Declarations

Acknowledgments

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None.

Conflict of Interest

The authors have declared that no competing interests exist.

Abbreviations

RCT = randomized controlled trial, MD = mean difference, RD = Risk difference, CI= confidence intervals, SD = standard deviation, NOS=Newcastle-Ottawa Scale, PVP= percutaneous vertebroplasty, OVCF= osteoporotic vertebral compression fracture, RCS= retrospective controlled study, BMD =Bone mineral density, BMI= Body Mass Index, PKP= percutaneous kyphoplasty.

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Table

Table 1 Cohort characteristics.

Studies	Year	Country	Fractures	Simple size	Age	Type	Follow-up	NOS
Lee WS	2006	Korea	38	244	66.4	RCS	148*	7
Li YA	2012	China	63	166	73.4	RCS	12-60*	6
Lin WC	2008	China	14	29	56-77	RCS	—	8
Lo YP	2008	China	15	220	53-97	RCS	24-36*	8
Lu K	2012	China	34	155	43-94	RCS	124*	8
Martinez	2013	Spain	17	57	73.6±9.3	RCS	6-39*	7
Ren HL	2015	China	21	182	49-91	RCS	6-60*	8
Rho YJ	2012	Korea	27	147	49-93	RCS	12-73*	8
Sun G	2014	China	37	175	70.3±8.2	RCS	112*	8
Kang SK	2011	Korea	27	60	70	RCS	112*	7
Lin H	2008	China	14	29	73.8	RCS	22.4*	8
Voormolen	2006	Dutch	16	66	46-88	RCS	112*	6
Ahn Y	2008	Korea	45	95	69.3	RCS	—	8
Yoo CM	2012	Korea	49	244	48-93	RCS	0.2-61.7*	8

*month

Figures

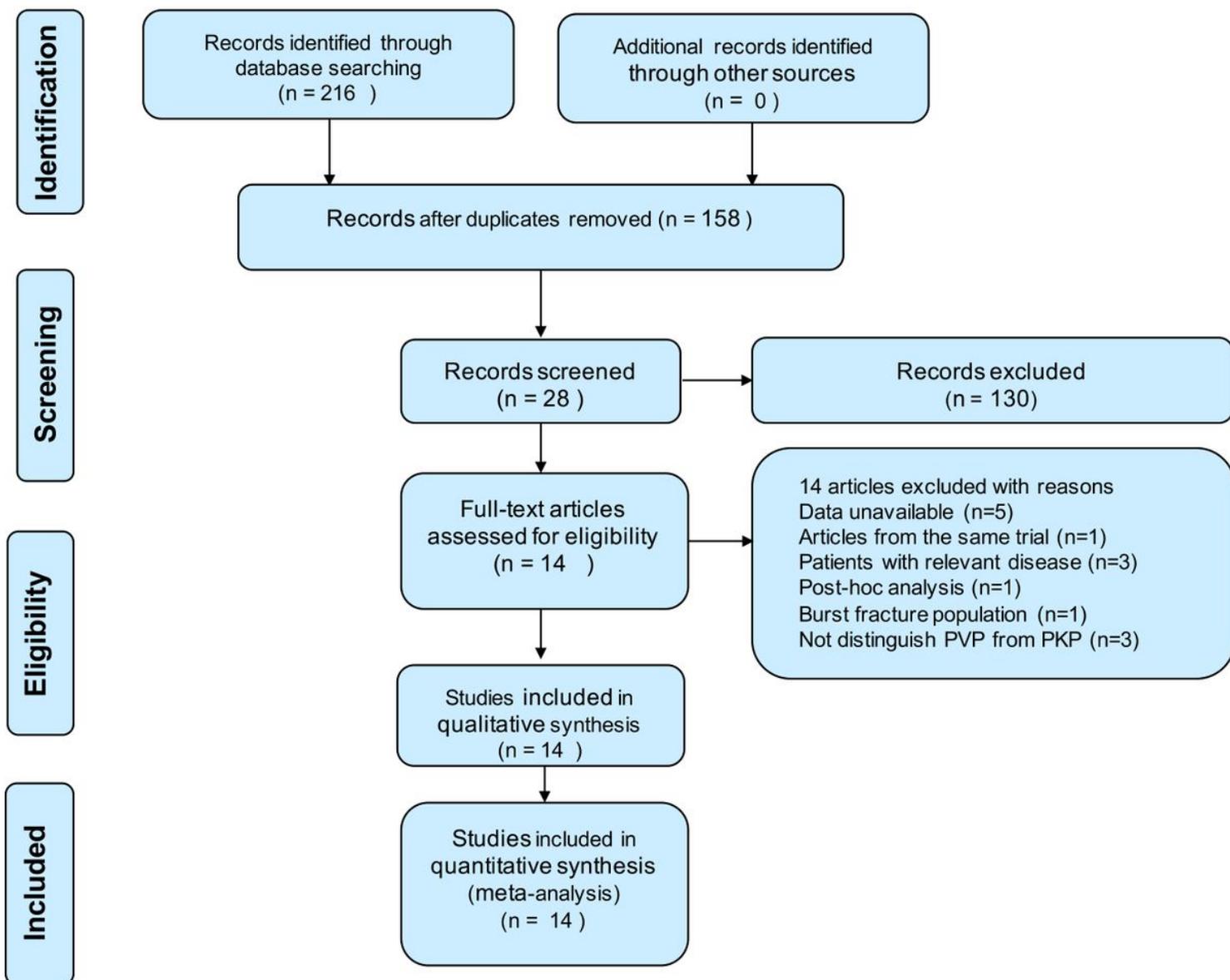


Figure 1

Flowchart of the study selection process

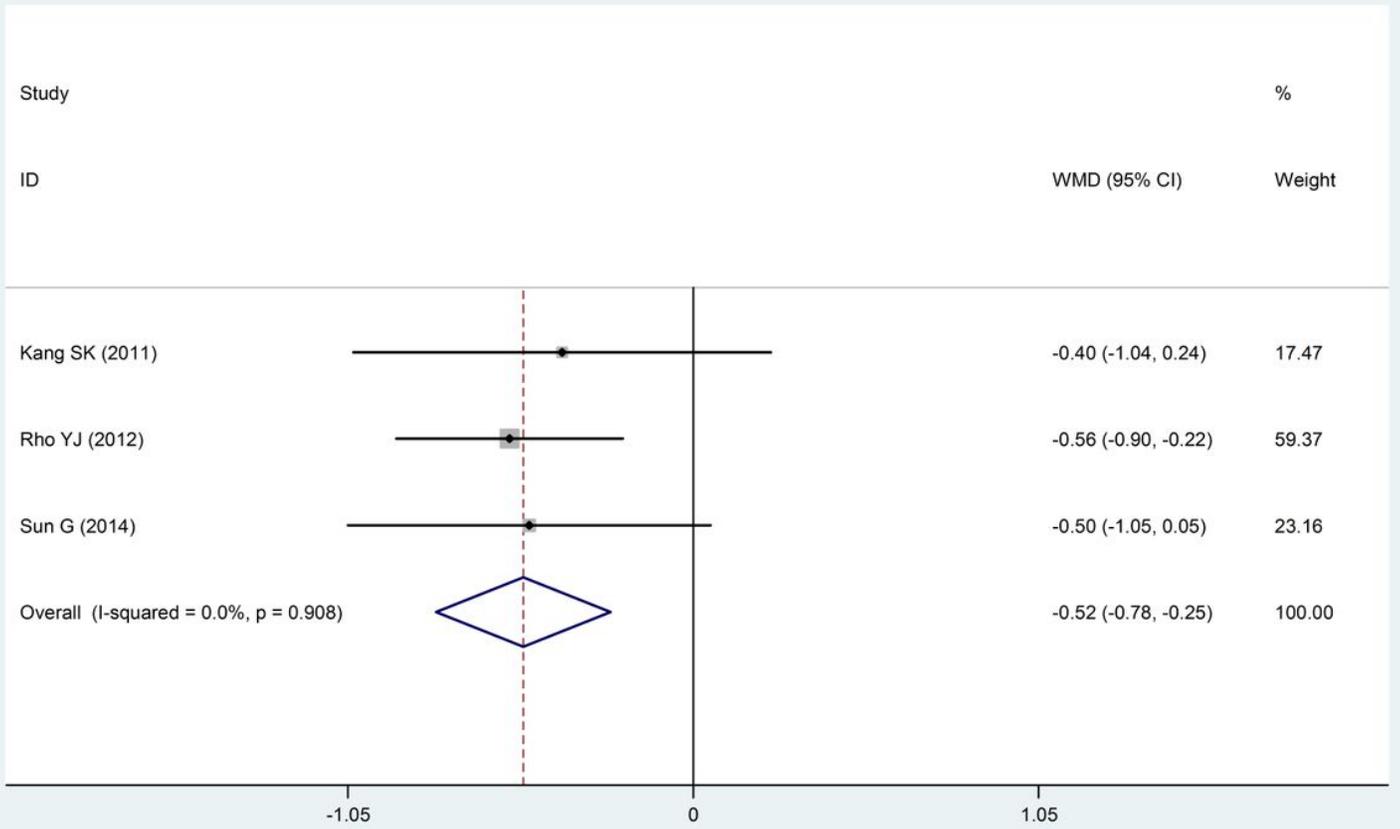


Figure 2

Forest plot diagram showing the BMD

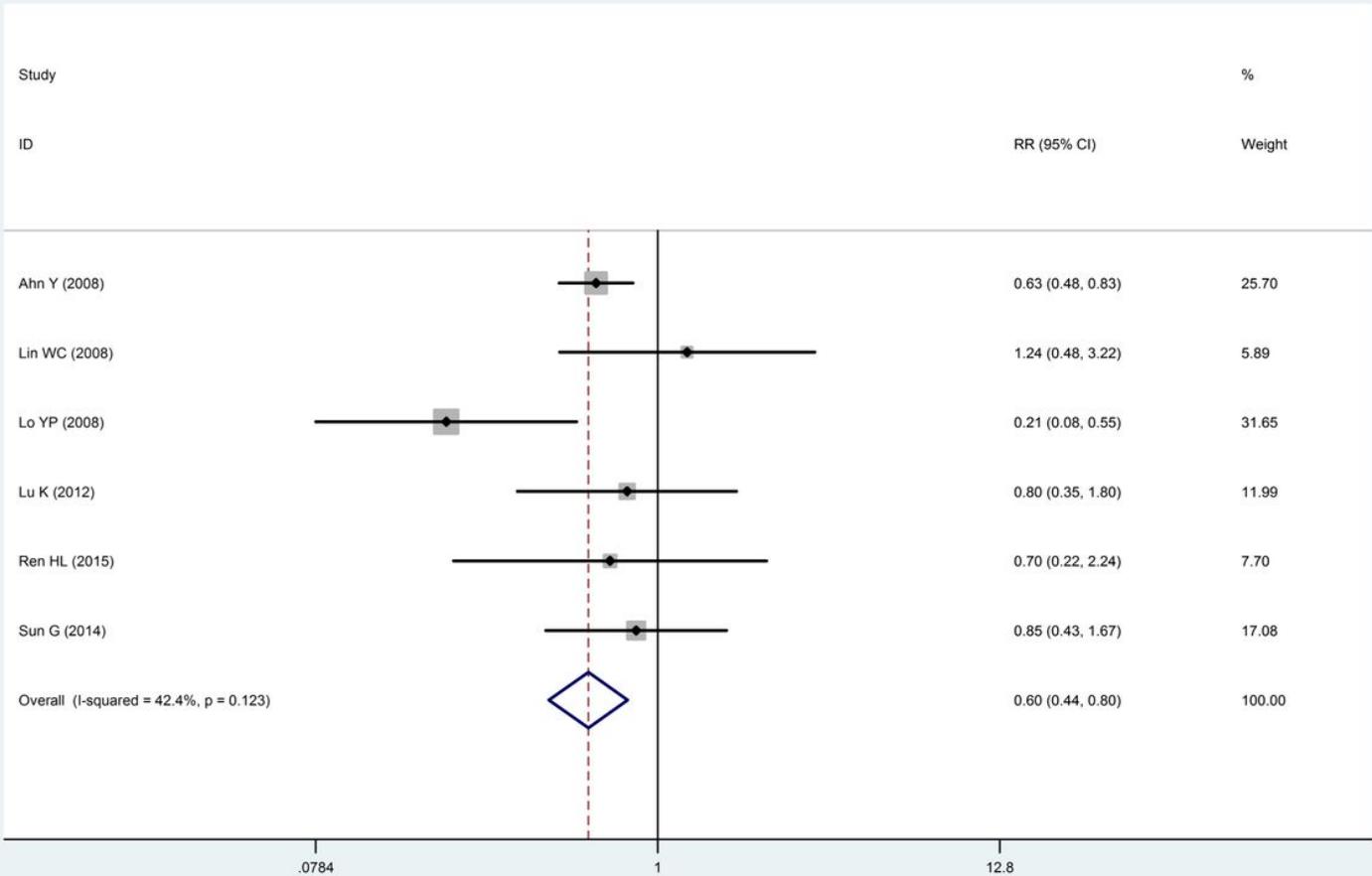


Figure 3

Forest plot diagram showing the cement leakage

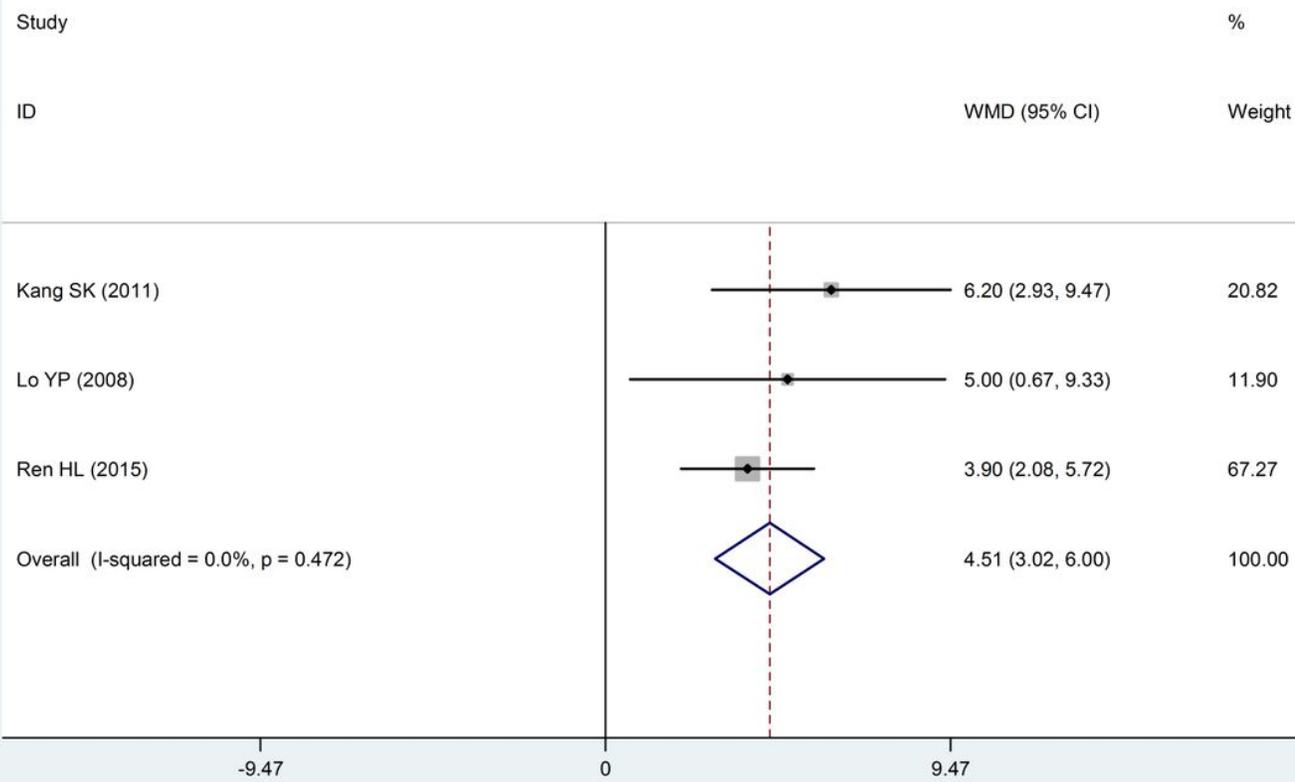


Figure 4

Forest plot diagram showing the kyphosis

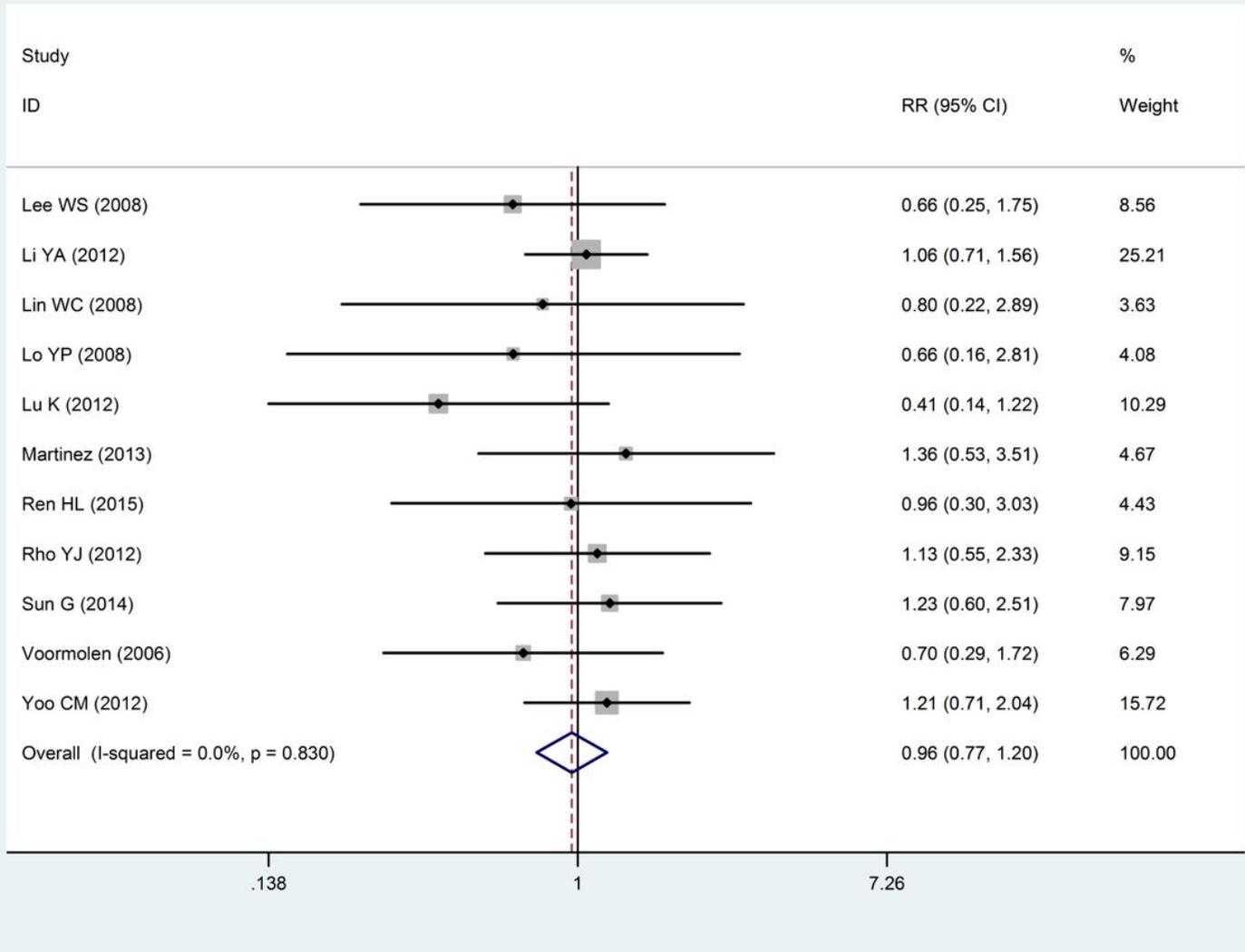


Figure 5

Forest plot diagram showing the gender

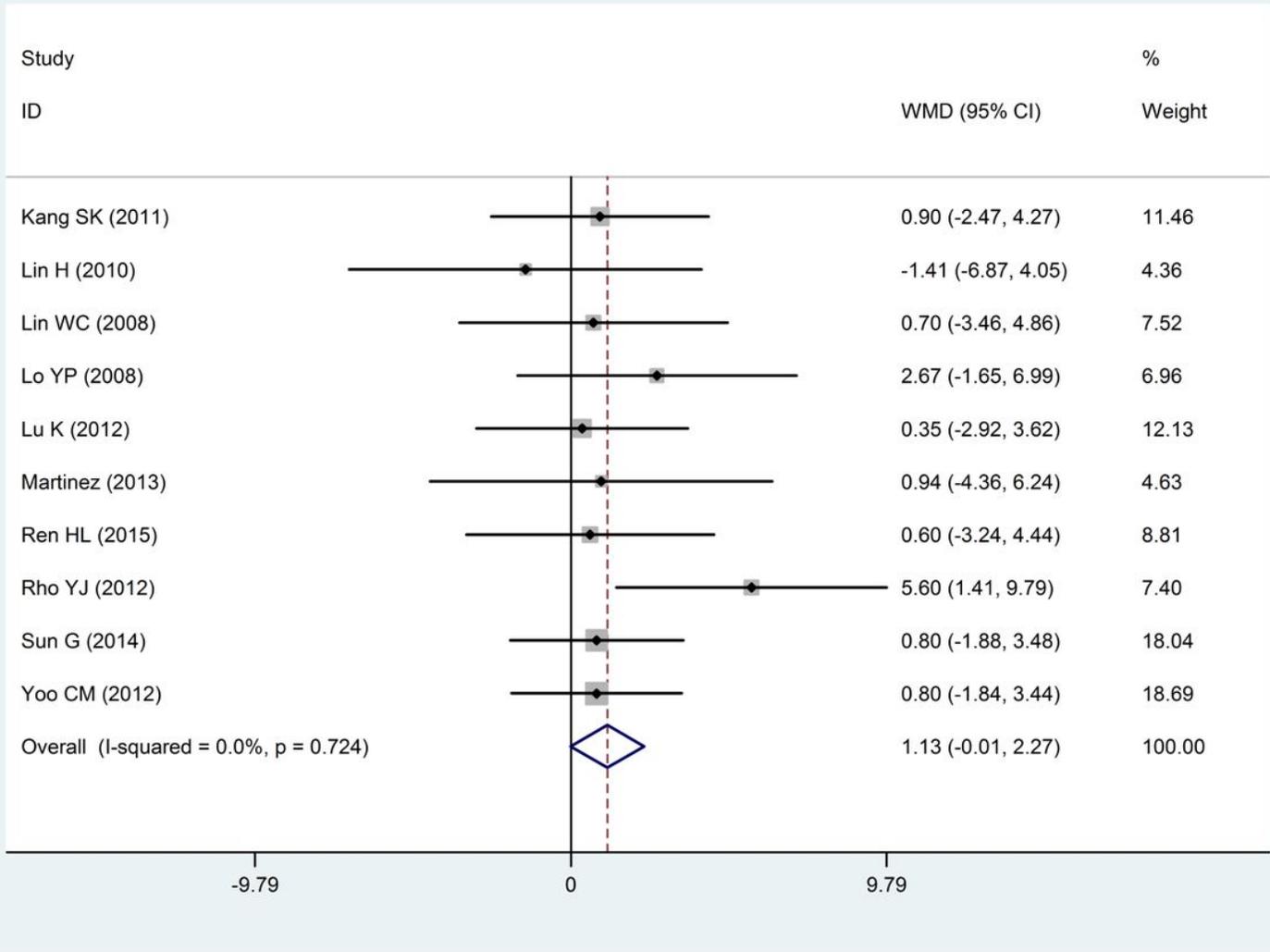


Figure 6

Forest plot diagram showing the age

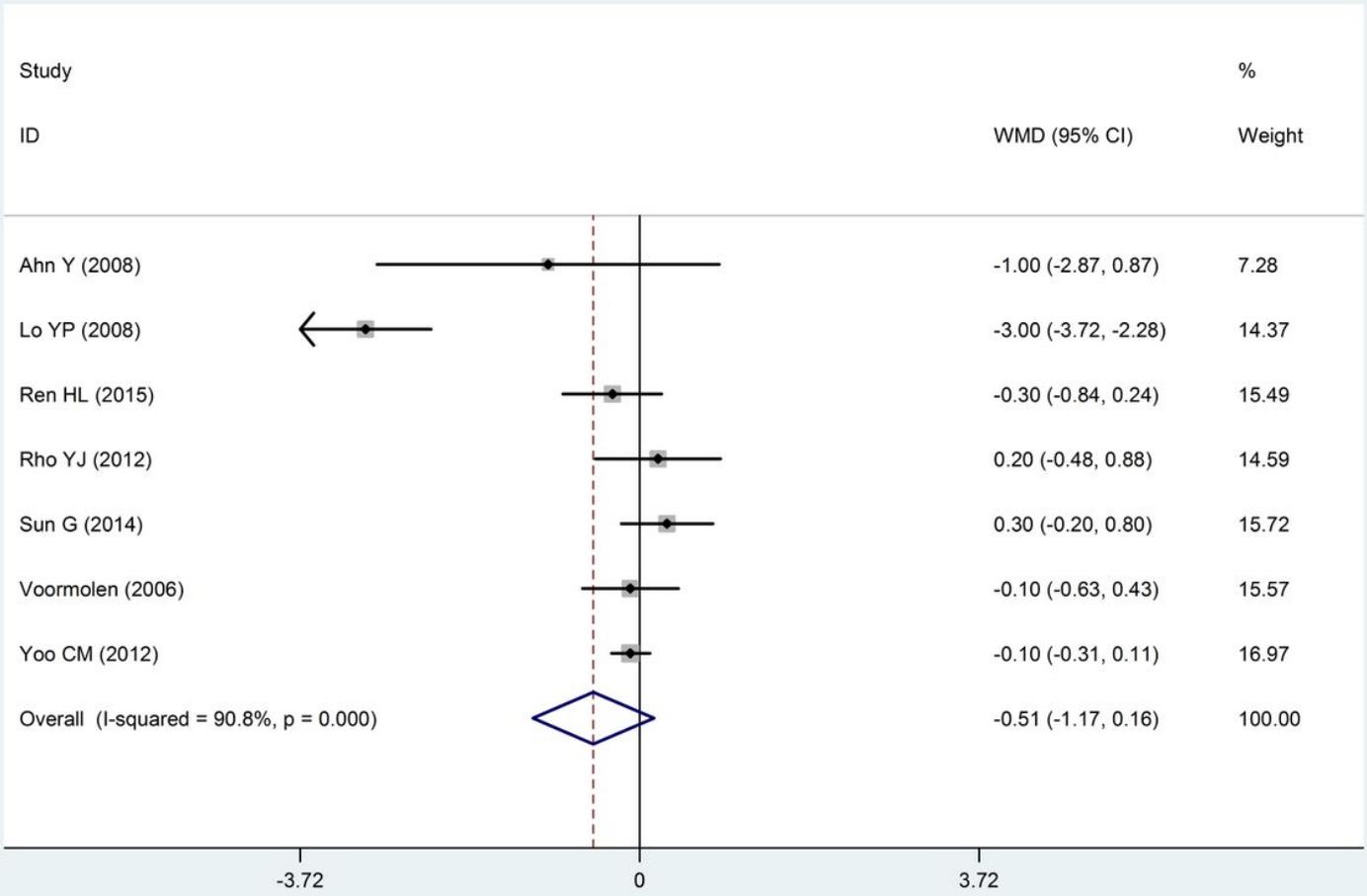


Figure 7

Forest plot diagram showing the cement volume

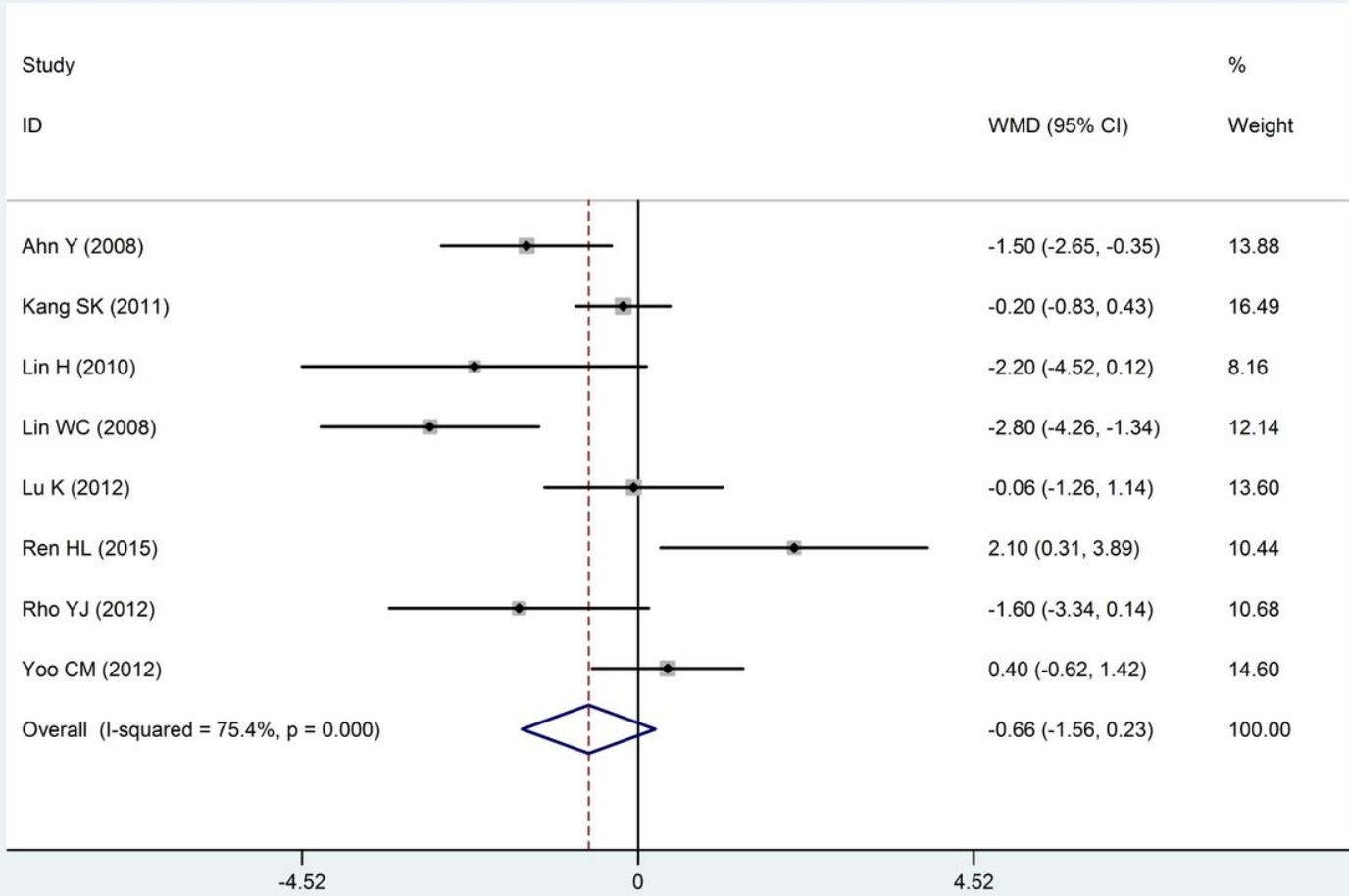


Figure 8

Forest plot diagram showing the BMI

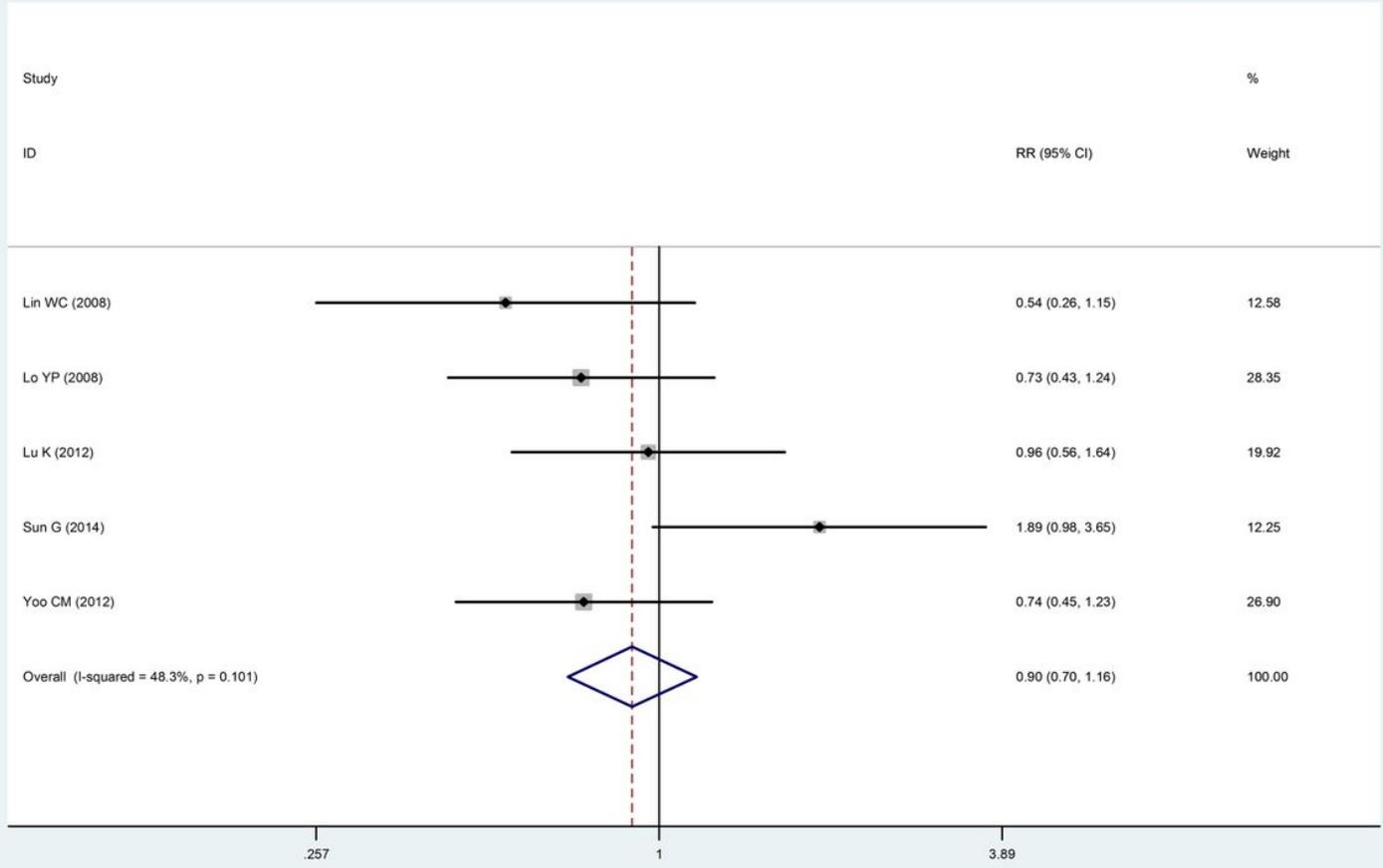


Figure 9

Forest plot diagram showing the thoracolumbar spine

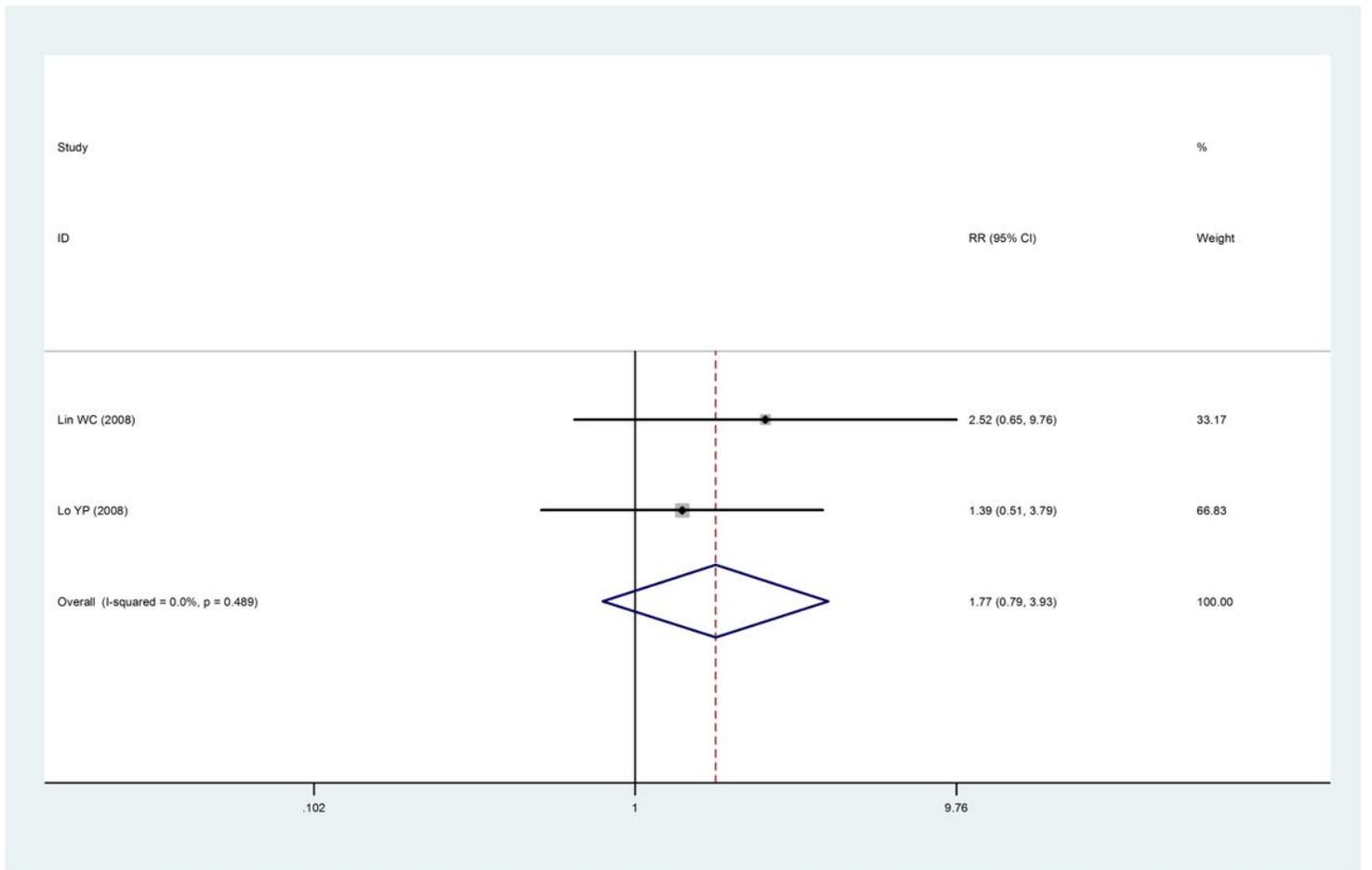


Figure 10

Forest plot diagram showing the cement injection approach

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