Review Article

AO SPINE

Global Spine Journal
2022, Vol. 12(1) 130–141

DOI: 10.1177/2192568220978223
journals.sagepub.com/home/gsj
SAGE

What Are the Risk Factors for Adjacent Vertebral Fracture After Vertebral Augmentation? A Meta-Analysis of Published Studies

Tianyu Zhang, MD[1], Yanhua Wang, MD[1], Peixun Zhang, MD[1,2], Feng Xue, MD[1], Dianying Zhang, MD[1,2,3], and Baoguo Jiang, MD[1,2]

Abstract

Study Design: Meta-analysis.

Objectives: To provide up-to-date evidence-based outcomes for the incidence and risk factors of adjacent vertebral fracture (AVF) after the vertebral augmentation.

Methods: The MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials were searched for studies assessing the risk factors of adjacent vertebral fracture after vertebral augmentation until June 2020. The AVF incidence and factors potentially affecting AVF were extracted and pooled.

Results: A total of 16 studies, encompassing 2549 patients were included in the meta-analysis. The pooled incidence of AVF was 14% after vertebral augmentation. Female, lower T-score, thoracolumbar junction fracture, intravertebral cleft, more injected cement volume, intradiscal cement leakage significantly increased the risk of AVF. Age, body mass index, steroid medication, Cobb angle change, postoperative Cobb angle showed no significant association with AVF.

Conclusions: Identifying the risk factors of AVF can facilitate prevention strategy to avoid the AVF. Female, T-score, thoracolumbar junction fracture, intravertebral cleft, more cement volume, and intradiscal cement leakage increased the risk of AVF.

Keywords

vertebroplasty, kyphoplasty, risk factors, compression fractures, adjacent vertebral fracture

Introduction

Osteoporotic vertebral compression fracture (OVCF) is the commonest osteoporosis fracture[1] affecting 200 million patients worldwide.[2] It causes pain, limited daily activity, kyphosis and brings immense burden to society.

Percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) are widely used in the treatment of OVCF.[3] Through heat effect and stabilization of the injected cement, patients can achieve rapid pain relief.[4] However, the injected cement is harder than normal bone. This causes greater loads transferred to adjacent vertebra and adjacent vertebral fracture (AVF).[5,6]

As a severe complication of vertebral augmentation, AVF draws attention from clinicians.[7,8] Studies have shown that AVF happened in around 7%-29%[9,10] individuals after the vertebral augmentation. Previous meta-analysis[11] has assessed the risk factors for AVF after PVP. However, a few factors were analyzed and the articles included were mostly case-control studies. In recent years, numerous cohort studies have been performed to explore the risk factors of AVF after vertebral augmentation, but controversies still exist.

[1] Department of Traumatic Orthopaedics, Peking University People's Hospital, Beijing, China
[2] Institute of Trauma and Nerve Regeneration, Peking University People's Hospital, Beijing, China
[3] Department of Orthopaedics, Peking University Binhai Hospital, Tianjin, China

Corresponding Authors:
Feng Xue, Dianying Zhang, and Baoguo Jiang, Department of Traumatic Orthopaedics, Peking University People's Hospital, No.11 South Avenue, Xi Zhi Men Xicheng District, Beijing 100044, China.
Emails: drxuefeng@163.com; zdy8016@163.com; jiangbaoguo@vip.sina.com

Due to the lack of reliable and up-to-date evidence-based research, we performed this meta-analysis to detect the incidence and risk factors of the AVF after vertebral augmentation. Because of the similar mechanism of AVF,[10,12] we combined the PKP and PVP for risk factors assessment.

Methods

Search Strategy

This meta-analysis has been registered on the PROSPERO with the registration number of CRD 42 020 196 730. Comprehensive literature research was performed using MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (until June 2020) for searching studies assessing the risk factors of AVF after vertebral augmentation. The language was limited to English and Chinese. The following terms were used for the study object searching: subsequent vertebral fracture, adjacent vertebral collapse, adjacent vertebral fracture, or new vertebral compression fracture. The following terms were used for the intervention searching: augmented vertebrae, vertebral augmentation, kyphoplasty, or vertebroplasty. The relevant bibliographies of searched articles were reviewed to identify any additional study.

Selection Criteria

The inclusion criteria were as follows: (1) cohort study; (2) patient with OVCF; (3) treatment method was PKP or PVP; (4) reporting the risk factors of AVF; (4) data to calculate the odds ratio (OR) or the standardized mean difference (SMD) with 95% confidence interval (CI); (5) minimum 6-month follow-up; (6) published in English or Chinese.

The exclusion criteria were as follows: (1) vertebral compression fracture secondary to the tumor metastasis or infection; (2) included patient with neural symptom; (3) included patient with spinal stenosis. Duplicate publications or studies from the same population were removed.

Data Extraction and Critical Appraisal

Two reviewers (Tianyu Zhang/ Yanhua Wang) independently screened the titles and abstracts of searched articles to identify potential studies. Studies related to the aim of this meta-analysis were included. Then full-text screening was performed to identify studies meeting the inclusion criteria. Disagreements were resolved by a third reviewer (Feng Xue). Finally, the eligible articles were included in this meta-analysis. The study inclusion process was illustrated by a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (Figure 1).

The information extracted from the target articles were: first author's name, publication year, age, gender, cohort size, thoracolumbar (T-L) junction fracture, intravertebral cleft (IVC), body mass index (BMI), bone mineral density (BMD), steroid medication, initially treated fracture >1, preoperative compression rate, cement volume (CV), the ratio of CV and fractured vertebral volume, intradiscal cement leakage, Cobb angle (CA) change, postoperative CA, anti-osteoporosis treatment (AOT).

Two reviewers independently evaluated the quality of included studies according to the Newcastle-Ottawa Scale (NOS) with a 9-point system, which included 3 perspectives: the groups selection (0-4 points); comparability (0-2 points); and ascertainment of either the exposure or outcome (0-3 points). Study more than 6 points was considered as high quality.

Meta-Analysis

We used the STATA 14.0 software (Stata Corporation, College Station, Texas, USA) for meta-analysis. Continuous outcomes were showed in SMD with 95% CI and dichotomous outcomes were presented in OR with 95% CI. Statistical heterogeneity was calculated by the chi-square and I-square tests. Meta-analysis using random-effects model was chosen if the included article was judged to be statistical heterogeneity ($I^2 > 50\%$). Otherwise, the fixed-effects model (Mantel-Haenszel method) was used to estimate the overall outcome. The relationship of AVF incidence and follow-up time was evaluated by Pearson Correlation.

In pooled analysis with statistical heterogeneity, each study was sequentially omitted using the "metaninf" command in STATA to perform sensitivity analysis. The study contributing the highest heterogeneity was analyzed for the reason. The publication bias was evaluated by Begg and Egger test. Subgroup analysis was performed for the incidence of AVF according to the surgery method. P value < 0.05 was considered as statistically significant.

Results

Search Strategy

A total of 1092 citations were searched according to the search strategies. Firstly, 132 duplicates were removed. Secondly, 908 articles were excluded after examining the titles and abstracts. Thirdly, the rest of the 52 articles were assessed for eligibility. After the full tests were reviewed, 35 articles were excluded for the reasons: not target patients, follow-up time less than 6 months, not evaluating the AVF, outcome not present in the required form, not full text, duplicate publication, and other languages. Finally, 16 articles published from 2010 to 2020 were included in the pool study. Figure 1 shows the flow diagram of the selection process.

Study Characteristics and Quality Assessment

These studies included 2 prospective cohort studies and 14 retrospective cohort studies. The characteristics of these studies were presented in Table 1. The assessment factors and conclusions of the studies were in Table 2.

Each study included 46-358 patients, with 2549 patients in total. In these studies, 7 were performed in China (Mainland),[10,13-17] 4 in Korea,[18-21] 1 in Japan,[9] 1 in Turkey,[22] 1 in

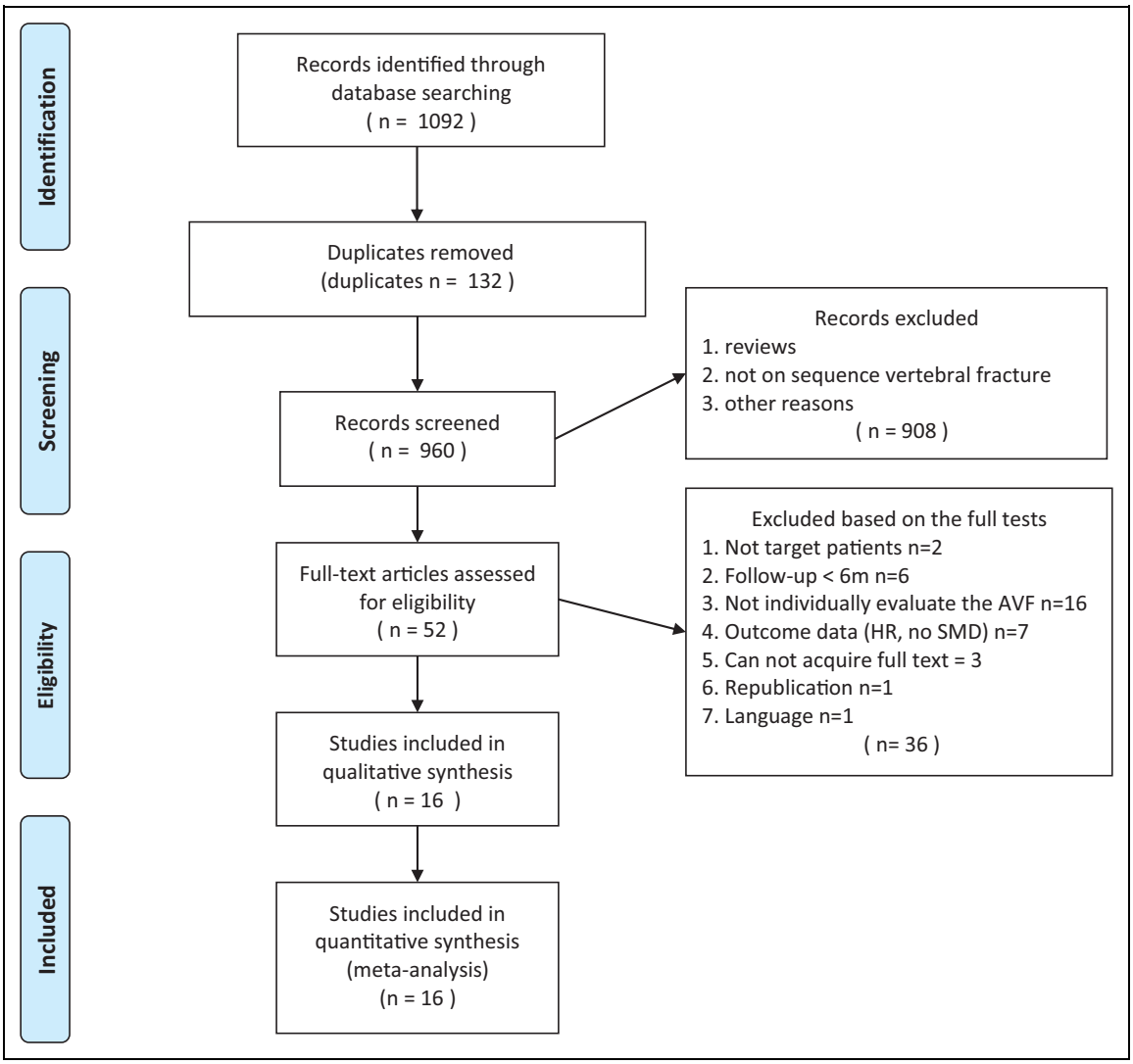

Figure 1. The literature search process was presented in the flow diagram.

Table 1. Baseline Characteristics of Patients in the 16 Included Studies.

Reference	Country	Intervention	Sample size (Case/control)	Mean age	Follow-up	NOS
Chen et al. 2020[13]	China	bPKP	102 (16/86)	71.1	12+	6
Takahashi et al. 2019[9]	Japan	bPKP	109 (32/77)	79.3	6	9
Lee et al. 2019[18]	Korea	PVP	323 (46/277)	74.7	52.8 (9.6)	8
Hu et al. 2019[25]	China	bPVP	112 (84/28)	NK	12	6
Wu et al. 2017[14]	China	uPKP	189 (22/167)	67.8	36 (8)	8
Fu et al. 2017[15]	China	PVP	134 (18/116)	73.18	12+	8
Yang et al. 2016[16]	China	PKP	139 (21/118)	75.9	19.56 (3.92)	7
Lee et al. 2015[19]	Korea	uPVP	198 (15/183)	76.6	48.2 (3.5)	6
Jesse et al. 2015[12]	USA	PKP/PVP	52 (14/38)	68.85	6	6
Wang et al. 2014[10]	China	PKP/PVP	358 (26/332)	70.5	31.2 (10.7)	6
Sun et al. 2014[17]	China	uPVP	175 (21/154)	70.3	12	8
Civelek et al. 2014[22]	Turkey	bPKP	171 (20/151)	68.35	41.04 (21.78)	6
Rho et al. 2012[20]	Korea	PKP/PVP	147 (18/139)	70	35.5	8
Movrin et al. 2012[23]	Slovenia	bPKP	46 (3/43)	67.8	12	9
Lee et al. 2011[21]	Korea	PVP	188 (28/160)	70.9	38.5	7
Chen et al. 2010[24]	China	PVP	106 (86/20)	73	38	7

Abbreviations: PVP, percutaneous vertebroplasty; PKP, percutaneous kyphoplasty; u, unilateral; b, bilateral; NOS, Newcastle-Ottawa Scores; + means at least.

Table 2. Summary of the 16 Studies That Investigated Risk Factors for AVF After the Vertebral Augmentation in the Meta-analysis.

Reference	Study type	Included variables	Variables with significant difference
Chen et al. 2020[13]	RCS	Age, gender, BMD, preoperative compression rate, KA, CA change, diabetes, treatment time, CV, and the intactness of posterior vertebral wall	Diabetes and CA change
Takahashi et al. 2019[9]	PCS	Age, gender, steroid use, smoking status, the use of teriparatide, site of fracture, CV, the presence of old OVF, CA before surgery, and correction CA	Thoracic or T-L fracture, old OVF presence, CA before surgery, and correction CA
Lee et al. 2019[18]	RCS	Age, gender, vertebroplasty technique, T-L junction fracture, BMD, preoperative KA, preoperative sagittal index, preoperative compression ratio, BMI, intradiscal CL, well distributed, CV, leaked intradiscal CV, ratio of CV to vertebral body volume, ratio of leaked intradiscal CV to adjacent disc volume, and N of OVCFs	BMD, preoperative compression ratio, preoperative sagittal index, intradiscal CL, and N of OVCFs
Hu et al. 2019[25]	RCS	Age, gender, body weight, BMD, and CV/bone fracture vertebral volume ratio	Bone cement injection volume, BMD, and gender
Wu et al. 2017[14]	RCS	Age, gender, BMD, the severity of compression fracture, IVC, N of OVCFs, type of bone cement, CV, CL, anesthesia approach, blood pressure variation before and after bone cement filling, restoration rate of vertebral height, AOT	IVC, AOT, intradiscal CL, anesthesia approach and BMD
Fu et al. 2017[15]	RCS	Age, gender, BMD, cement distribution index, volume-cubage index, and CL	BMD, CL, and cement distribution index
Yang et al. 2016[16]	RCS	Age, gender, BMI, smoking history, BMD, bone metabolic markers, N of OVCFs, balloon volume, CL, recovery rate of vertebral height, bone cement leakage intraoperative, and AOT	BMD, balloon volume, CL, recovery rate of vertebral height, and CL
Lee et al. 2015[19]	RCS	Operative time, BMI, smoking history, existence of trauma, BMD, cement location, intradiscal CL, distribution pattern, KA, sagittal index, compression ratio, CV, N of OVCFs, and T-L fracture	N of OVCFs
Jesse et al. 2015[12]	RCS	Age, gender, BMD, BMI, osteoporosis type, and intradiscal CL	Intradiscal CL
Wang et al. 2014[10]	RCS	Age, gender, BMI, steroid medication, duration from onset of symptom to time of surgery, preoperative conservation treatment, BMD, level of treated vertebra, IVC, KA correction, CA (preoperative, postoperative), CA correction, degree of vertebral body compression (preoperative, postoperative), reduction rate, surgical technique (PVP or PKP), cement distribution pattern (compact or trabecular patterns), and CV	Age, BMD, and IVC
Sun et al. 2014[17]	RCS	Age, gender, BMD, bisphosphonate therapy, the changes of spinal geometry, T-L fracture, CV, intradiscal CL, and IVC	BMD and T-L fracture
Civelek et al. 2014[22]	RCS	Age, gender, CV, initial KA, change of the KA, BMD, and height restoration	Gender and preoperative KA
Rho et al. 2012[20]	RCS	Age, gender, BMI, BMD, location of treated vertebra, treatment modality, CV, anterior–posterior ratio of the fractured vertebra, intradiscal CL, and pattern of cement distribution	BMD and intradiscal CL
Movrin et al. 2012[23]	PCS	Age, gender, BMD, KA, CV, and CL	BMD and KA
Lee et al. 2011[21]	RCS	Age, gender, BMD, T-L fracture thoracolumbar fracture, IVC, KA, CA, and CV	T-L fracture thoracolumbar fracture
Chen et al. 2010[24]	RCS	Intradiscal CL	Intradiscal CL

Abbreviations: PCS, Prospective cohort study; RCS, Retrospective cohort study; N of OVCFs, Number of Osteoporotic Vertebral Compression Fractures; BMD, bone mineral density; IVC, intravertebral cleft; CV, cement volume; CL, cement leakage; BMI, body mass index; T-L, thoracolumbar; KA, kyphotic angle; CA, Cobb angle; AOT, antiosteoporosis treatment.

Slovenia,[23] 1 in American,[12] and 1 in China (Taiwan).[24] Three hundred forty-eight patients occurred AVF in the follow-up period. Six studies assessed risk factors of AVF after PKP, 7 after PVP, and 3 after PKP and PVP.

Age, gender, T-L junction fractures, IVC, BMI, BMD, steroid medication, CV, intradiscal cement leakage, CA change, postoperative CA were finally involved in the risk factors assessment for more than 2 studies providing the outcomes. The initial treated fracture >1,[16,20] preoperative compression rate,[13] the ratio of CV and fracture vertebral volume,[25,26] AOT[14,16] were not conducted in the meta-analysis for lacking sufficient studies.

Articles' qualities were assessed by the Newcastle-Ottawa Scores (NOS) (Table 1). Six studies were regarded as 6 points,[10,12,13,19,22,25] 3 studies were 7 points,[16,21,24] 5 studies were 8 points,[14,15,17,18,20] and 2 studies were 9 points.[9,23] Publication bias was assessed by the gender data and no statistical publication bias was found (Egger test, $P = 0.279$; Begg, $P = 0.246$).

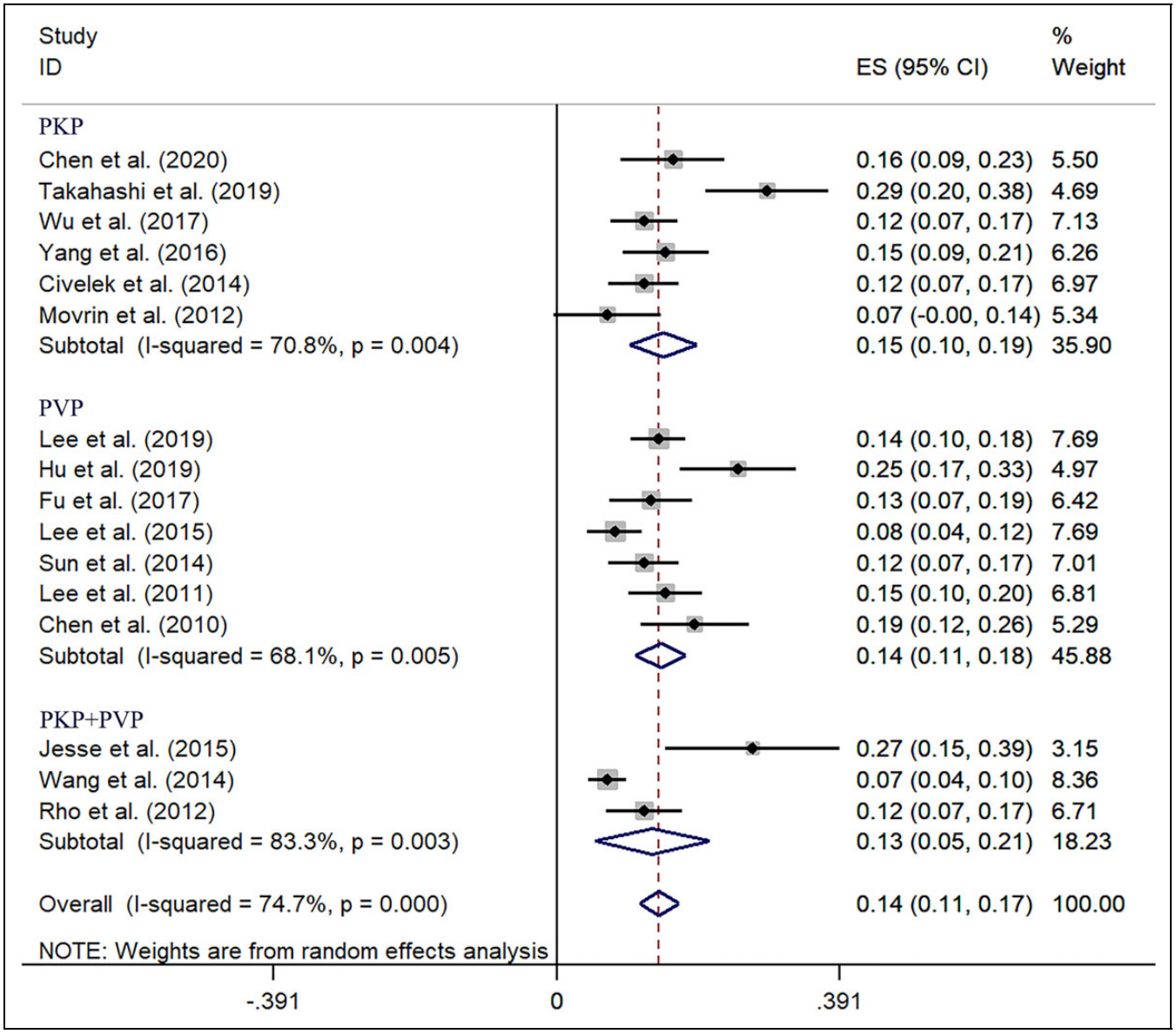

Figure 2. Forest plots illustrated the incidence of AVF after the vertebral augmentation. Subgroup analysis was performed according to the surgery methods.

Incidence of AVF

The pooled incidence of AVF after vertebral augmentation was 14% in the 2549 patients. In subgroup analysis, the incidence of AVF was 14.3% after PVP[15,17,19,21,24-26] and 14.7% after PKP[9,13,14,16,22,23] (Figure 2). There was heterogeneity between the studies (P = 0.000; I^2 = 74.7%). The incidence of AVF was not correlated with the follow-up time (Pearson Correlation Coefficient = 0.483).

Pooled Analysis of Preoperative Risk Factors

Age data was reported in 10 studies.[9,10,12-16,18,21,22] Meta-analysis using random-effects model showed that age did not significantly influence the risk of AVF (SMD = 0.068; 95%CI, −0.136 to 0.273; P = 0.512). A heterogeneous test indicated a moderate heterogeneity among the studies (P = 0.034; I^2 = 50.4%).

Gender data was pooled from 13 studies.[9,10,12-18,21-23,25] The meta-analysis using fixed-effects model revealed that female gender was the risk factor for the AVF (OR = 1.472; 95% CI, 1.47-4.08; P = 0.022) (Figure 3), with no significant heterogeneity between the studies (P = 0.935; I^2 = 0%).

Fracture level data was pooled from 5 studies using fixed-effects model. T-L junction fracture[9,10,17,18,20] significantly increased the risk of AVF (OR = 1.027; 95% CI, 0.493-1.561; P = 0.000) (Figure 4). No significant heterogeneity was found between the studies (P = 0.823; I^2 = 0%).

IVC data was included in 3 studies.[10,14,17] Pooling these studies with random-effects model showed that IVC could

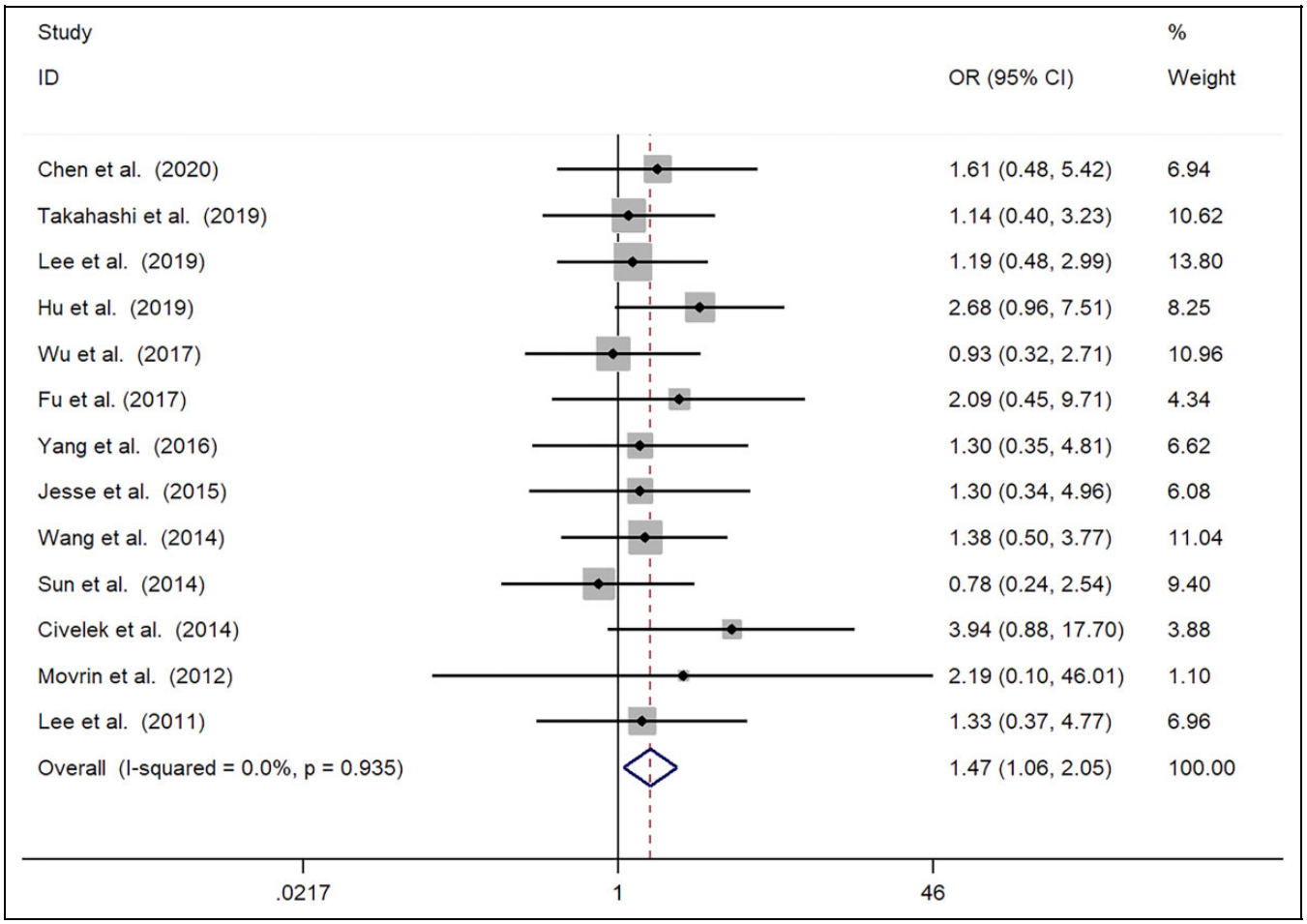

Figure 3. Forest plots of meta-analysis for gender data.

induce the AVF after the vertebral augmentation (OR = 4.456; 95% CI, 1.072-18.529; P = 0.040) (Figure 5), with statistical heterogeneity (P = 0.004; I^2 = 82.2%).

T-score data was provided by 9 studies.[10,12,14-16,18,21,22,25] Patients with lower T-score were statistical more likely to develop AVF (SMD = −0.589; 95%CI, −0.812 to −0.366; P = 0.000) under the random-effects model of meta-analysis (Figure 6). Moderate statistical heterogeneity existed between the studies (P = 0.019; I^2 = 56.3%).

BMI of the patients was explored by 6 studies.[9,10,12,16,18,22] The pooled studies using the fixed-effects model indicated that BMI had no significant difference between the AVF group and non-AVF group (SMD = −0.028; 95%CI, −0.199 to 0.143; P = 0.346). There was little heterogeneity (P = 0.346; I^2 = 10.9%).

Steroid medication data was reported by 3 studies.[9,10,17] The pooled studies using the fixed-effects model showed no significant difference between the AVF and non-AVF group (OR = 1.915; 95% CI, 0.800-4.585; P = 0.769). There was no statistical heterogeneity (P = 0.769; I^2 = 0.0%).

Pooled Analysis of Operative Risk Factors

Cement volume data was reported in 8 studies.[9,10,13-16,18,22] Pooling studies using the random-effects model revealed that more cement volume injected resulted in higher risk of AVF after vertebral augmentation (SMD = 1.010; 95%CI, 0.250-0.768; P = 0.000) (Figure 7). There was statistical heterogeneity between the studies (P = 0.000; I^2 = 95.5%).

Intradiscal cement leakage data was presented in 7 studies.[10,12,14,17,18,20,24] Pooling these studies using the fixed-effects model showed that the intradiscal cement leakage could increase the rate of AVF (OR = 1.457; 95% CI, 0.644-2.271; P = 0.000) (Figure 8), with a moderate heterogeneity (P = 0.211; I^2 = 28.5%).

CA change was reported by 3 studies.[9,10,13] Pooling these studies using the random-effect model showed that the CA change had no significant difference between the AVF group and non-AVF group (SMD = 1.410; 95%CI, −0.270 to 3.090; P = 0.100). Statistical heterogeneity was found in these studies (P = 0.000; I^2 = 97.2%).

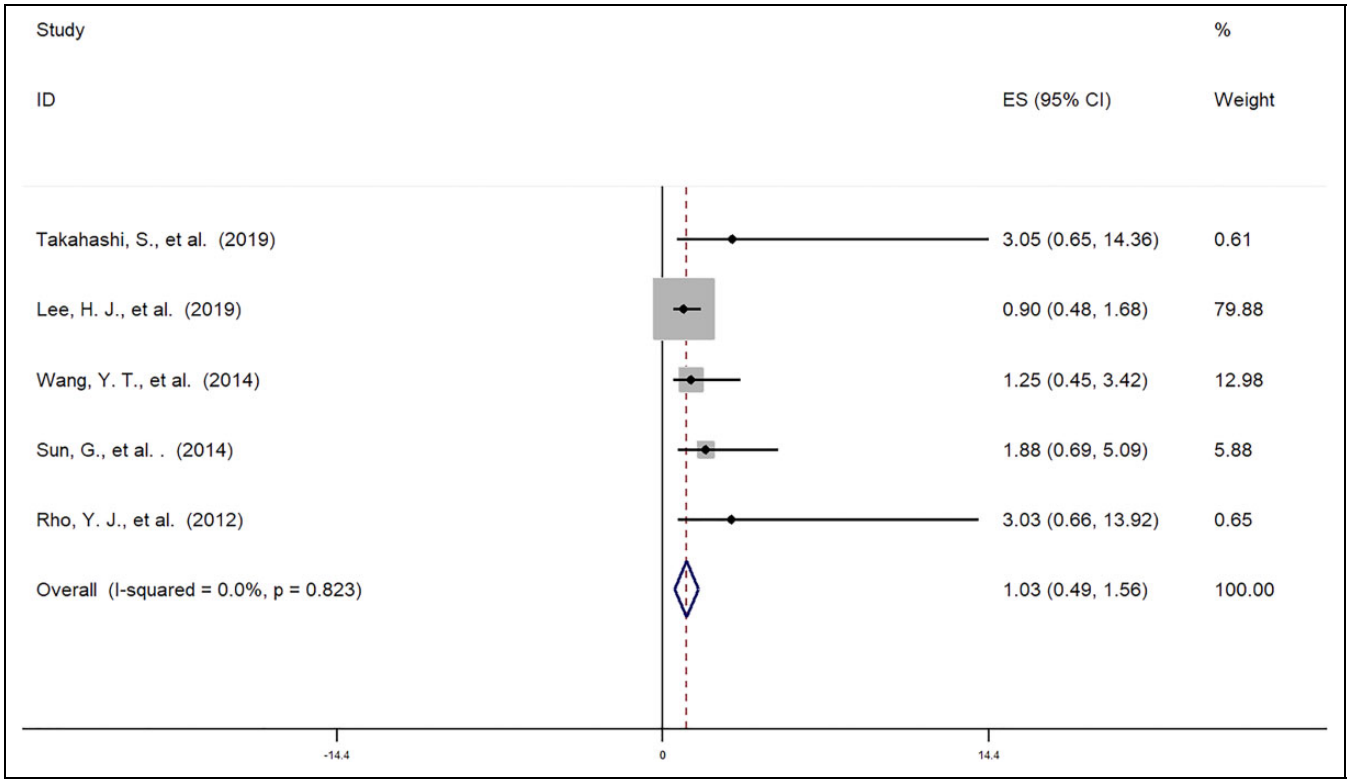

Figure 4. Forest plots of meta-analysis for T-L junction fractures data.

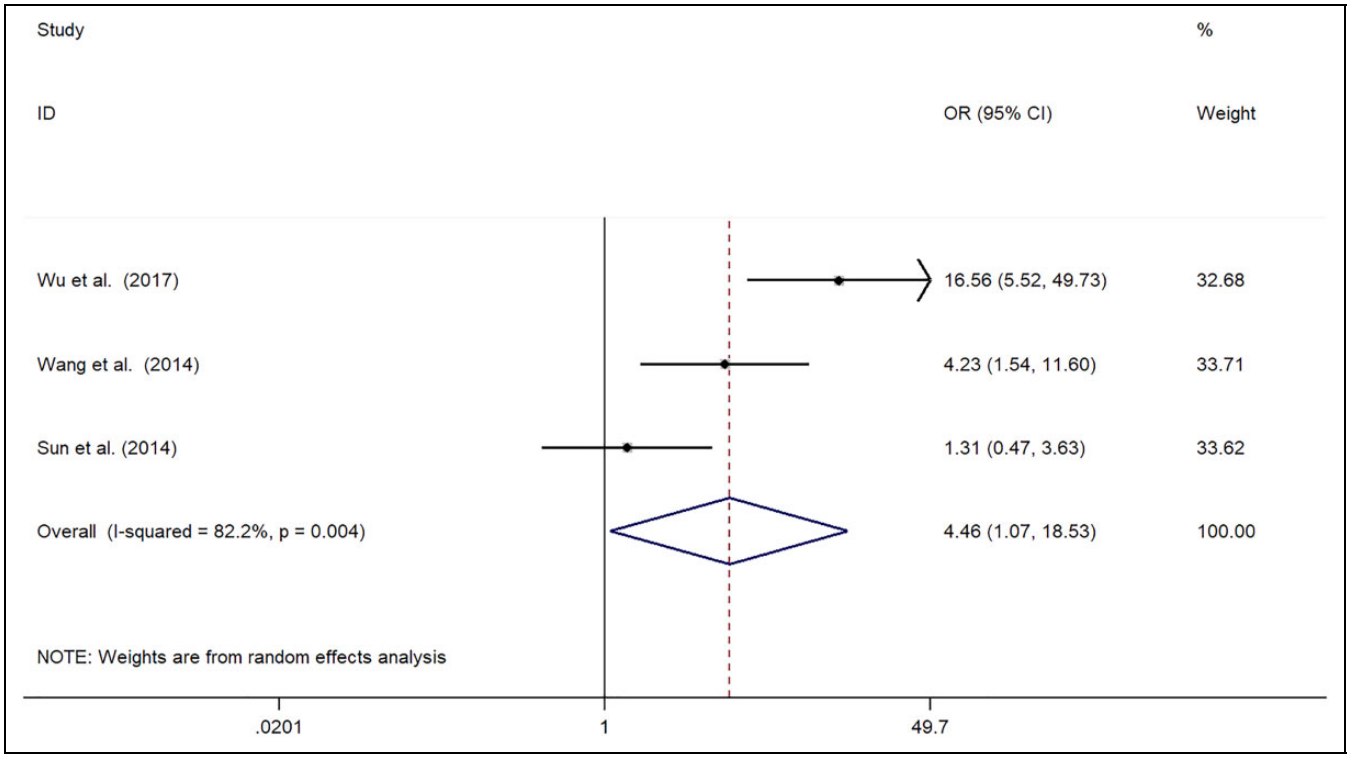

Figure 5. Forest plots of meta-analysis for IVC data.

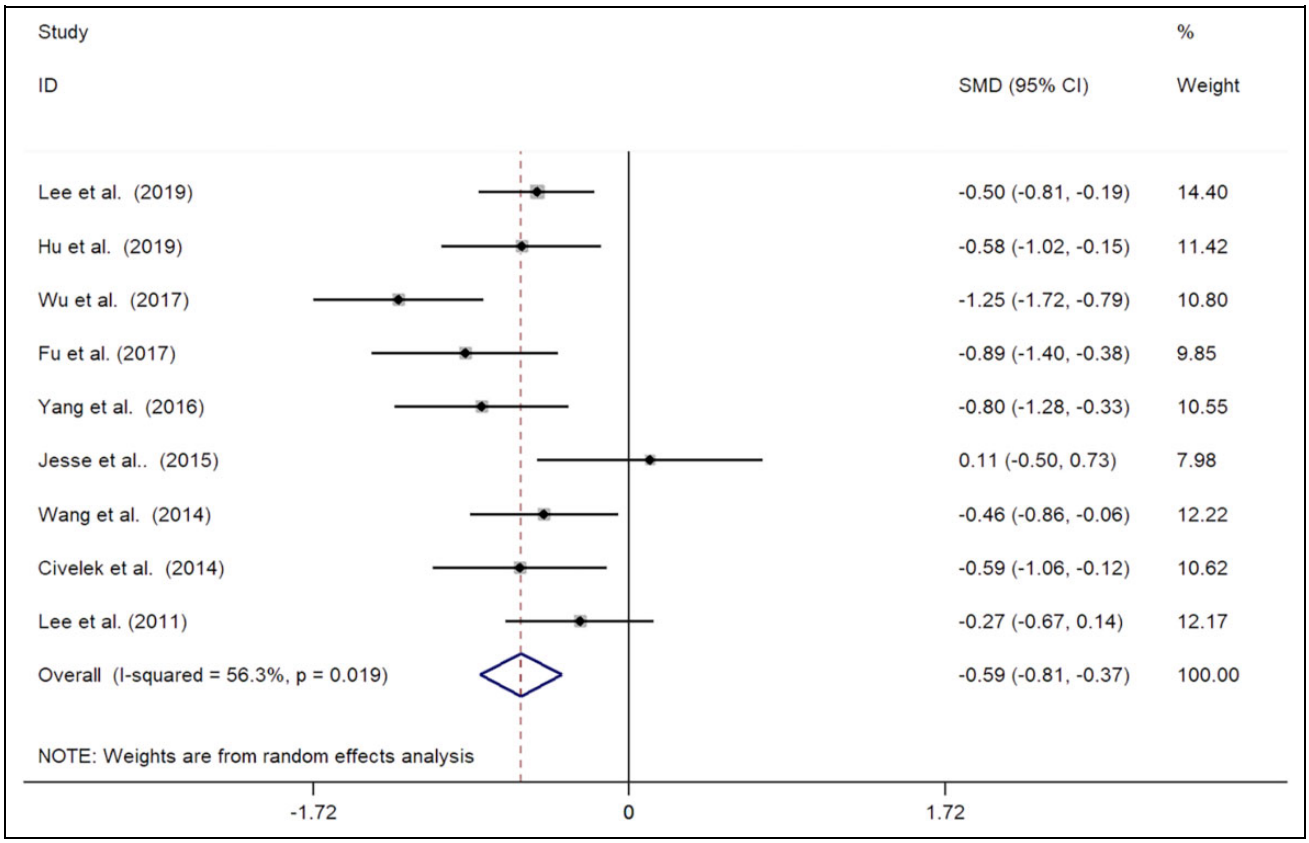

Figure 6. Forest plots of meta-analysis for T-score data.

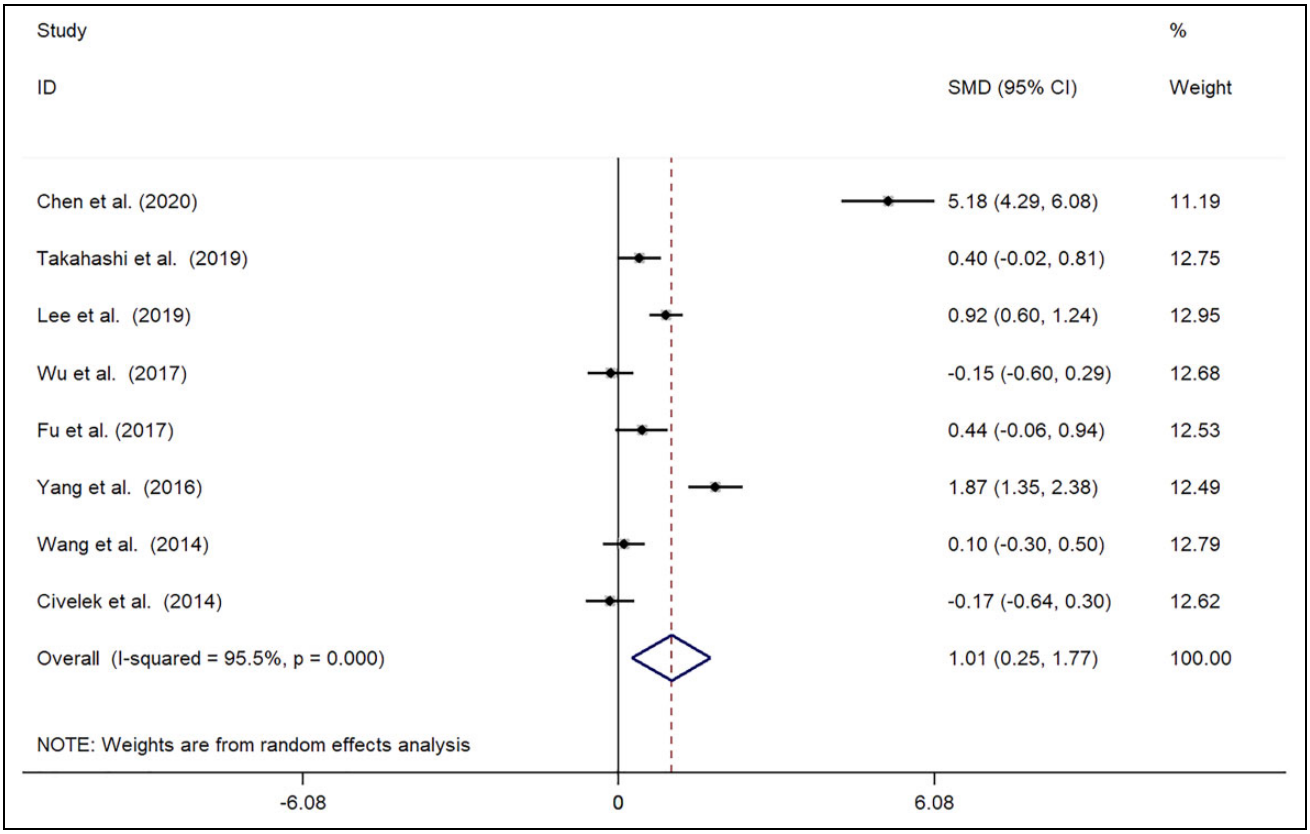

Figure 7. Forest plots of meta-analysis for cement volume data.

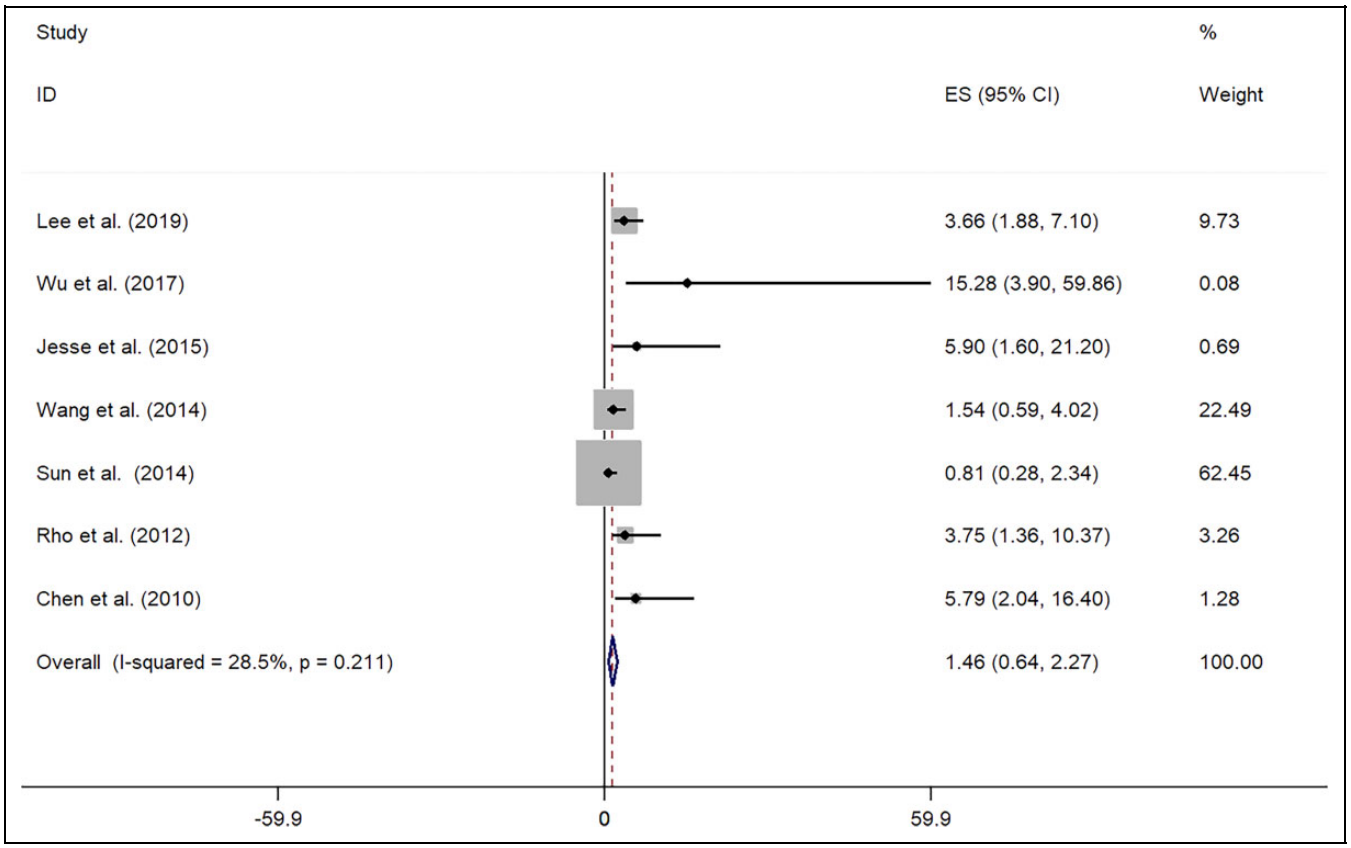

Figure 8. Forest plots of meta-analysis for intradiscal cement leakage data.

Pooled Analysis of Postoperative Risk Factors

Postoperative CA was reported by 3 studies.[9,13,22] Random-effects model was chosen for meta-analysis as the significant heterogeneity between the studies ($P = 0.000$; $I^2 = 97.6\%$). The postoperative CA was not significantly associated with the AVF (SMD = −0.651; 95%CI, −2.530 to 1.228; $P = 0.497$).

Discussion

Numerous studies were performed to investigate the risk factors of AVF after vertebral augmentation in recent years. However, there is a lack of up-to-date meta-analysis for these studies. We provided reliable and evidenced-based outcomes for clinicians to identify patients with a high risk of AVF.

The Incidence of AVF

The incidence of AVF ranged from 7%-29%, with a pooled incidence of 14%. Different incidences of AVF among studies were due to different criteria and study types. There is no significant difference in the incidence of AVF between the PKP and PVP. Incidence did not increase with prolonged follow-up time, because AVF mostly occurred in 1-2 months after the vertebral augmentation.[27,28] Follow-up more than 6 months was enough for evaluating AVF.

Risk Factors for AVF

In this pooled study, female, T-L junction fracture, IVC, lower T-score, more CV, and cement intradiscal leakage significantly increased the risk of AVF. Age, BMI, steroid medication, CA change, and postoperative CA were not significantly related to AVF. In a previous meta-analysis, Zhang et al.[11] concluded that lower T-score, lower BMI, and intradiscal cement leakage could significantly increase the risk of AVF after PVP surgery. Age, gender, IVC, surgical approach, T-L vertebral fracture, and CL were not significantly associated with AVF. However, the studies' quality included in Zhang's meta-analysis was relative lower.

The female gender was very likely to be a risk factor of AVF. Firstly, the vertebral fracture is more likely to happen in female for disease susceptibility. Secondly, female patients always have smaller vertebra volume than male. The conventional volume of cement is relatively excess for female, which leads to a harder augmented vertebra than male. Hence, female has a significantly higher incidence of AVF.

Our pooled study showed that patients with lower T-score have higher risk of AVF, which was consistent with Zhang's study.[11] T-score is a standard index for osteoporosis evaluation. The severer osteoporosis of the vertebra can withstand less stress and load. Therefore, anti-osteoporosis treatment is needed for patient to reduce the risk of AVF.

Thoracolumbar junction fracture is a risk factor of AVF. As the transition zone from the rigid thoracic to the lumbar, the T-L area has maximum flexion and extension range.[29] This makes this region the commonest fracture site.

IVC was associated with AVF. In the vertebra with a cleft, the cement is easier to form compact distribution,[29,30] which is more unstable than trabecular distribution. This leads to inhomogeneous stress conduction to adjacent vertebrae. Moreover, IVC is regarded as the imaging sign of vertebral osteonecrosis,[31,32] which indicates poor blood supply of vertebrae. Both 2 factors lead to a high risk of AVF.

More cement induced AVF. The cement injection makes the vertebra 12 times stiffer and 35 times stronger than untreated vertebra.[5] Cement augmentation creates a "pillarlike" effect, which results in reduced inward bulge of the augmented vertebra endplates and increased inward bulge of the adjacent vertebra endplates.[6] This conducts more load on adjacent vertebra. Finite element analysis reveals that 30% of the vertebral volume is an appropriate cement volume for restoration of the bone hardness. The volume of cement injected exceeding 30% increases the stress of adjacent vertebra.[33] More cement makes vertebra stiffer, which increases the "pillarlike" effect. Finally, more cement results in the AVF.

Our current study showed that intradiscal cement leakage increases the risk of AVF. Intradiscal cement leakage results in severer "pillarlike" effect on adjacent vertebra.[5] What is more, intradiscal cement changes the internal environment of disc leading to the stiffness of disc.[34,35] Both finally cause AVF. The same conclusion was reached in a previous pool study.[11] Therefore, strategies are needed to reduce the cement leakage, such as continuous X-ray fluoroscopy during the cement injection and accurate puncture to avoid endplate damage.[10]

Besides the factors we contained in our studies, smoking history,[19] diabetic status,[13] preoperative sagittal index,[18] initial treated fracture >1,[19] anesthesia approach,[14] and AOT[14] were also reported as risk factors for AVF.

Sensitivity Analysis

To identify the reasons for heterogeneity, we carried out sensitivity analysis by the "metaninf" function in STATA. In the meta-analysis of incidence data, Takahashi et al.[9] contributed the highest heterogeneity because the judgment standard of AVF in its trial was the imaging findings. Therefore, more cases were diagnosed as AVF. In the meta-analysis of age data, Chen et al.[13] produced the most heterogeneity among the studies. Further analysis revealed that the SD in his trial was narrower compared to other studies. As for pooled results of IVC data, Sun et al.[17] generated the maximum heterogeneity. In his study, X-ray, MRI and the cement filling pattern were all involved for IVC judgment, which increased the diagnosis of IVC. In the analysis of T-score data, Wu et al.[14] and Jesse et al.[12] produced the maximum heterogeneity. However, both studies did not significantly impact the results. In the pool study of CA change data, Chen's study[13] produced the max heterogeneity. The SD of CV data in Chen's study is narrower than other studies. The same problem happened in the pool study of postoperative CA. Though Chen's study brought relatively large heterogeneity, the random-effect was chosen to eliminate the influence of Chen's data on the results.

Strengths and Limitations

We improve the inclusion criteria of the studies by restricting the minimum follow-up time to ensure including most AVF patients. We excluded the case-control studies for its low methodological quality. Study with the max heterogeneity was investigated for its potential causes.

Limitations of this study include the variability in criteria used to collect and define the presence of AVF. There is heterogeneity in several pool results. The studies with heterogeneity were found by the "metainf" function in STATA and the random-effect model was used to reduce the influence of bias to make the result trustworthy.

Conclusions

AVF occurs in 14% of the patients after the vertebral augmentation. Female, lower T-score, T-L junction fractures, IVC, more cement volume, and cement intradiscal leakage are the risk factors for the AVF. The assessment for the risk factors of AVF helps the clinicians to predict the high-risk AVF patients better and make optimal treatment choices.

Authors' Note

TYZ and FX conceived the study. TYZ and YHW performed data collection, data extraction, statistical analysis, and manuscript drafting. PXZ revised the manuscript. FX, DYZ and BGJ take responsibility for this study. All authors have read and approved the final manuscript. All data in this article is all the published data.

Acknowledgments

Tian-yu Zhang would like to thank Yue Liao for English language editing as well as silent support for life and work.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Beijing Municipal Science and Technology Project [grant number D161100002816001]; Ministry of Education Key Laboratory of trauma treatment and nerve regeneration [grant number BMU2019XY007-01].

ORCID iD

Tianyu Zhang, MD https://orcid.org/0000-0002-2968-0084

References

1. Ström O, Borgström F, Kanis JA, et al. Osteoporosis: burden, health care provision and opportunities in the EU: a report

prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos*. 2011;6(1-2): 59-155. doi:10.1007/s11657-011-0060-1
2. Dong R, Chen L, Tang T, et al. Pain reduction following vertebroplasty and kyphoplasty. *Int Orthop*. 2013;37(1):83-87. doi:10.1007/s00264-012-1709-0
3. Lemke DM. Vertebroplasty and kyphoplasty for treatment of painful osteoporotic compression fractures. *J Am Acad Nurse Pract*. Jul 2005;17(7):268-276. doi:10.1111/j.1745-7599.2005.0045.x
4. Hulme PA, Krebs J, Ferguson SJ, Berlemann U. Vertebroplasty and kyphoplasty: a systematic review of 69 clinical studies. *Spine*. 2006;31(17):1983-2001. doi:10.1097/01.brs.0000229254.89952.6b
5. Baroud G, Vant C, Wilcox R. Long-term effects of vertebroplasty: adjacent vertebral fractures. *J Long-Term Effects Med Implants*. 2006;16(4):265-280. doi:10.1615/jlongtermeffmedimplants.v16.i4.10
6. Baroud G, Heini P, Nemes J, Bohner M, Ferguson S, Steffen T. Biomechanical explanation of adjacent fractures following vertebroplasty. *Radiology*. 2003;229(2):606-607. Author reply 607-8. doi:10.1148/radiol.2292030378
7. Zhang H, Xu C, Zhang T, Gao Z, Zhang T. Does percutaneous vertebroplasty or balloon kyphoplasty for osteoporotic vertebral compression fractures increase the incidence of new vertebral fractures? A meta-analysis. *Pain Phys*. 2017;20(1):E13-e28.
8. Fan B, Wei Z, Zhou X, et al. Does vertebral augmentation lead to an increasing incidence of adjacent vertebral failure? A systematic review and meta-analysis. *Int J Surg (London, England)*. 2016; 36(Pt A):369-376. doi:10.1016/j.ijsu.2016.11.082
9. Takahashi S, Hoshino M, Yasuda H, et al. Development of a scoring system for predicting adjacent vertebral fracture after balloon kyphoplasty. *Spine J*. 2019;19(7):1194-1201. doi:10.1016/j.spinee.2019.02.013
10. Wang YT, Wu XT, Chen H, Wang C, Mao ZB. Adjacent-level symptomatic fracture after percutaneous vertebral augmentation of osteoporotic vertebral compression fracture: a retrospective analysis. *J Orthop Sci*. 2014;19(6):868-876. doi:10.1007/s00776-014-0610-7
11. Zhang Z, Fan J, Ding Q, Wu M, Yin G. Risk factors for new osteoporotic vertebral compression fractures after vertebroplasty: a systematic review and meta-analysis. *J Spinal Disord Tech*. 2013;26(4): E150-E157. doi:10.1097/BSD.0b013e31827412a5
12. Jesse MK, Petersen B, Glueck D, Kriedler S. Effect of the location of endplate cement extravasation on adjacent level fracture in osteoporotic patients undergoing vertebroplasty and kyphoplasty. *Pain Phys*. 2015;18(5):E805-E814.
13. Chen C, Fan P, Xie X, Wang Y. Risk factors for cement leakage and adjacent vertebral fractures in kyphoplasty for osteoporotic vertebral fractures. *Clin Spine Surg*. 2020;33(6):E251-E255. doi:10.1097/bsd.0000000000000928
14. Wu J, Guan Y, Fan S.Analysis of risk factors of secondary adjacent vertebral fracture after percutaneous kyphoplasty. *Biomed Res (India)*. 2017;28(5):1956-1961.
15. Fu ZZ, Chen ZX, Qin Y, et al. Low cement distribution index is a risk factor for refracture of the adjacent segments after percutaneous vertebroplasty. *Nan Fang Yi Ke Da Xue Xue*. 2017;37(7):947-951.
16. Yang S, Liu Y, Yang H, Zou J. Risk factors and correlation of secondary adjacent vertebral compression fracture in percutaneous kyphoplasty. *Int J Surg (London, England)*. 2016;36(Pt A):138-142. doi:10.1016/j.ijsu.2016.10.030
17. Sun G, Tang H, Li M, Liu X, Jin P, Li L. Analysis of risk factors of subsequent fractures after vertebroplasty. *Eur Spine J*. 2014; 23(6):1339-1345. doi:10.1007/s00586-013-3110-0
18. Lee HJ, Park J, Lee IW, Yi JS, Kim T. Clinical, radiographic, and morphometric risk factors for adjacent and remote vertebral compression fractures over a minimum follow-up of 4 years after percutaneous vertebroplasty for osteoporotic vertebral compression fractures: novel three-dimensional voxel-based morphometric analysis. *World Neurosurg*. 2019;125:e146-e157. doi:10.1016/j.wneu.2019.01.020
19. Lee DG, Park CK, Park CJ, Lee DC, Hwang JH. Analysis of risk factors causing new symptomatic vertebral compression fractures after percutaneous vertebroplasty for painful osteoporotic vertebral compression fractures: a 4-year follow-up. *J Spinal Disord Tech*. 2015;28(10):E578-E583. doi:10.1097/bsd.0000000000000043
20. Rho YJ, Choe WJ, Chun YI. Risk factors predicting the new symptomatic vertebral compression fractures after percutaneous vertebroplasty or kyphoplasty. *Eur Spine J*. 2012;21(5):905-911. doi:10.1007/s00586-011-2099-5
21. Lee KA, Hong SJ, Lee S, Cha IH, Kim BH, Kang EY. Analysis of adjacent fracture after percutaneous vertebroplasty: does intradiscal cement leakage really increase the risk of adjacent vertebral fracture? *Skeletal Radiol*. 2011;40(12):1537-1542. doi:10.1007/s00256-011-1139-x
22. Civelek E, Cansever T, Yilmaz C, et al. The retrospective analysis of the effect of balloon kyphoplasty to the adjacent-segment fracture in 171 patients. *J Spinal Disord Techn*. 2014;27(2):98-104. doi:10.1097/bsd.0b013e31824e9b98
23. Movrin I. Adjacent level fracture after osteoporotic vertebral compression fracture: a nonrandomized prospective study comparing balloon kyphoplasty with conservative therapy. *Wiener klinische Wochenschrift*. 2012;124(9-10):304-311. doi:10.1007/s00508-012-0167-4
24. Chen WJ, Kao YH, Yang SC, Yu SW, Tu YK, Chung KC. Impact of cement leakage into disks on the development of adjacent vertebral compression fractures. *J Spinal Disord Tech*. 2010; 23(1):35-39. doi:10.1097/BSD.0b013e3181981843
25. Hu L, Sun H, Wang H, et al. Cement injection and postoperative vertebral fractures during vertebroplasty. *J Orthop Surg Res*. 2019;14(1):228. doi:10.1186/s13018-019-1273-z
26. Lee BG, Choi JH, Kim DY, Choi WR, Lee SG, Kang CN. Risk factors for newly developed osteoporotic vertebral compression fractures following treatment for osteoporotic vertebral compression fractures. *Spine J*. 2019;19(2):301-305. doi:10.1016/j.spinee.2018.06.347
27. Li H, Yang DL, Ma L, Wang H, Ding WY, Yang SD. Risk factors associated with adjacent vertebral compression fracture following percutaneous vertebroplasty after menopause: a retrospective

study. *Med Sci Monit*. 2017;23:5271-5276. doi:10.12659/msm.907364

28. Fribourg D, Tang C, Sra P, Delamarter R, Bae H. Incidence of subsequent vertebral fracture after kyphoplasty. *Spine*. 2004; 29(20):2270-2276. Discussion 2277. doi:10.1097/01.brs.0000142469.41565.2a
29. Heo DH, Chin DK, Yoon YS, Kuh SU. Recollapse of previous vertebral compression fracture after percutaneous vertebroplasty. *Osteoporosis Int*. 2009;20(3):473-480. doi:10.1007/s00198-008-0682-3
30. Yu W, Jiang X, Liang D, et al. Intravertebral vacuum cleft and its varied locations within osteoporotic vertebral compression fractures: effect on therapeutic efficacy. *Pain Phys*. 2017;20(6): E979-e986.
31. Lin CL, Lin RM, Huang KY, Yan JJ, Yan YS. MRI fluid sign is reliable in correlation with osteonecrosis after vertebral fractures: a histopathologic study. *Eur Spine J*. 2013;22(7):1617-1623. doi: 10.1007/s00586-012-2618-z
32. Libicher M, Appelt A, Baier I, et al. The intravertebral vacuum phenomen as specific sign of osteonecrosis in vertebral compression fractures: results from a radiological and histological study. *Eur Radiol*. 2007;17(9):2248-2252.
33. Kim JM, Shin DA, Byun DH, Kim HS, Kim S, Kim HI. Effect of bone cement volume and stiffness on occurrences of adjacent vertebral fractures after vertebroplasty. *J Korean Neurosurgl Soc*. 2012;52(5):435-440. doi:10.3340/jkns.2012.52.5.435
34. Takahara K, Kamimura M, Moriya H, et al. Risk factors of adjacent vertebral collapse after percutaneous vertebroplasty for osteoporotic vertebral fracture in postmenopausal women. *BMC Musculoskeletal Disord*. 2016;17(1):1261-1262. doi:10.1186/s12891-016-0887-0
35. Baroud G, Nemes J, Heini P, Steffen T. Load shift of the intervertebral disc after a vertebroplasty: a finite-element study. *Eur Spine J*. 2003;12(4):421-426. doi:10.1007/s00586-002-0512-9