

УДК 616.711-001.5-089.844:616-74](045)

DOI: <http://dx.doi.org/10.15674/0030-59872025391-102>

Risk factors for recurrent vertebral compression fractures after percutaneous vertebroplasty in osteoporotic patients: a systematic review and meta-analysis

A. I. Popov¹, M. V. Moloduk¹, V. O. Kutsenko¹, M. M. Nessonova²

¹Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

²Private higher educational institution «Kharkiv International Medical University». Ukraine

Recurrent vertebral compression fractures (rVCFs) after percutaneous vertebroplasty (PVP) impair quality of life in osteoporotic patients, yet their risk factors remain debated, necessitating a systematic evaluation. Objective. To synthesize clinical data and quantitatively assess the impact of demographic, morphometric, and technical factors on rVCF incidence post-PVP. Methods. A search was conducted in PubMed, Scopus, Medline, and Google Scholar (2010–2024) using MeSH terms: «vertebroplasty», «compression fractures», «osteoporosis», «risk factors», «recurrence». Twenty cohort studies (7,923 patients) were included. Continuous variables were pooled using the Sidik–Jonkman random-effects model (Cohen's d), and categorical variables using the Paule–Mandel model (odds ratio, OR). Heterogeneity was assessed with I^2 and prediction intervals; sensitivity analyses were performed. Evidence certainty was evaluated using GRADE. Results. Significant risk factors for rVCFs included absence of anti-osteoporotic therapy (AOT) (OR = 1.97, I^2 = 40 %), cement leakage (OR = 1.92, I^2 = 68 %), and low bone mineral density (BMD) (d = -0.55, I^2 = 72 %), with moderate GRADE certainty. Female sex (OR = 1.30, I^2 = 39 %) and older age (d = 0.24, I^2 = 62 %) showed weaker associations with low certainty. Cement volume, body mass index, kyphotic angle, its correction, vertebral height restoration, and thoracolumbar junction involvement were not associated with rVCFs. Conclusions. The most significant rVCF risk factors are absence of AOT, cement leakage, and low BMD, nearly doubling the risk. Female sex increases risk by approximately one-third, and older age has a minor effect. These findings highlight the importance of AOT and technical precision in PVP to prevent rVCFs.

Нові компресійні переломи хребців (НКПХ) після пункційної вертебропластики (ПВП) погіршують якість життя пацієнтів з остеопорозом. Чинники ризику залишаються дискусійними, що зумовило необхідність систематичного аналізу. Мета. Узагальнити клінічні дані та кількісно оцінити вплив демографічних, морфометричних і технічних факторів на частоту НКПХ після ПВП. Методи. Проведено пошук у PubMed, Scopus, Medline, Google Scholar (2010–2024 р.) за MeSH-термінами: «vertebroplasty», «compression fractures», «osteoporosis», «risk factors», «recurrence». Включено 20 когортних досліджень (7 923 пацієнти). Кількісні змінні аналізували моделлю Sidik-Jonkman (d Коена), якісні — Paule-Mandel (OR). Гетерогенність оцінювали за I^2 і прогностичними інтервалами, виконано чутливі аналізи. Упевненість доказів оцінено за GRADE. Результати. Виявлено значущі фактори ризику НКПХ: відсутність антиостеопоротичної терапії (AOT) (OR = 1,97; I^2 = 40 %), витік кісткового цементу (OR = 1,92; I^2 = 68 %), низька мінеральна щільність кісткової тканини (МЩКТ) (d = -0,55; I^2 = 72 %) — помірний рівень упевненості за GRADE. Жіноча стать (OR = 1,30; I^2 = 39 %) і старший вік (d = 0,24; I^2 = 62 %) мають слабший вплив із низькою впевненістю. Обсяг цементу, індекс маси тіла, кифотичний кут, його корекція, відновлення висоти хребця та ураження T-L з'єднання не асоціювалися з НКПХ. Висновки. Найвагоміші чинники ризику НКПХ — відсутність AOT, витік цементу та низька МЩКТ, які підвищують ризик удвічі. Жіноча стать збільшує ризик на третину, похилий вік — незначно. Ці дані підкреслюють важливість AOT і технічної точності ПВП для профілактики НКПХ. Ключові слова. Вертебропластика, остеопороз, нові компресійні переломи, метааналіз, чинники ризику.

Keywords. Vertebroplasty, osteoporosis, recurrent compression fractures, meta-analysis, risk factors

Introduction

Vertebral compression fractures (VCFs) are the most common injury resulting from osteoporosis. Studies suggest that their incidence ranges from 30 % to 50 % in individuals over 50 years of age, regardless of gender [1–4]. Population-based research indicates an annual incidence of 10.7 % in women and 5.7 % in men [5]. For those aged 80 and older, the incidence rises to approximately 30 %, while in younger age groups (up to 80), it typically varies between 5 % and 10 % [6].

Vertebral compression fractures (VCFs) can lead to severe pain, spinal deformities, limited mobility, and a significant reduction in quality of life. One of the primary surgical treatments for VCFs is percutaneous vertebroplasty (PVP). First described by H. Deramond and P. Galibert, this technique was originally used to treat vertebral body hemangiomas [7]. Over time, it gained widespread use for treating VCFs caused by osteoporosis, myeloma, or traumatic injuries. PVP has proven to be both safe and effective, especially when compared to conservative treatment options. It provides rapid relief from pain, restores mobility, and facilitates quicker rehabilitation [8, 9].

However, despite the rapid relief of pain and improvement in functional status, some patients may develop complications: new fractures, spinal cord compression, infectious processes, nerve root damage and embolism. The most common and most thoroughly studied complication is new vertebral compression fractures (NVCF) in both adjacent and distant segments. Previous studies have identified a number of factors that influence the risk of NVCF: age, female gender, bone mineral density (BMD), location of the primary fracture, bone cement (BC) distribution, volume of injection and migration, endplate status, primary kyphotic angle (KA), percentage of KA and vertebral height recovery, absence of anti-osteoporosis therapy (AOT), body mass index (BMI), T-L junction [11]. However, the results of observations are often inconclusive or contradictory. This led us to undertake a systematic review aimed at summarising the available evidence regarding risk factors for new vertebral compression fractures following PVP.

Objective: To summarize and analyze the results of clinical trials on risk factors for new vertebral compression fractures after puncture vertebroplasty and to quantify their impact in order to identify factors that significantly increase the likelihood of new vertebral compression fractures in adjacent and distant segments.

Material and Methods

Eligibility Criteria. This systematic review and meta-analysis was registered in PROSPERO (CRD420251068792) and was performed according to the PRISMA guidelines. The PICOS inclusive design was used, in which the population (P) was patients who underwent PVP. The intervention group (I) was individuals with VCFs. Comparisons were made with a group (C) in which NVCFs were detected. The primary outcomes (O) of interest were differences in the presence of NVCF risk factors in these groups. Only comparative studies (S) were considered for inclusion — original articles (prospective, retrospective studies). Publications where vertebroplasty was considered for non-osteoporotic lesions; experimental or preclinical studies (*in vitro*, *in vivo* on animals) that do not contain clinical data on humans; duplicates of the same article in different databases; non-original sources that do not disclose any quantitative or qualitative data on the risk of NCP — were excluded.

A literature search was conducted in PubMed, Scopus, Medline, and Google Scholar from 2010 to 2024. There were no language restrictions.

A combination of MeSH (Medical Subject Headings) and free text terms was used for the search, using the logical operators AND, OR, and NOT. Key terms were Vertebroplasty, Percutaneous Vertebroplasty, Transpedicular Vertebroplasty, Spinal Fractures, Compression Fractures, Osteoporosis, Risk Factors, Recurrent Compression Fractures, Prediction of Compression Spine Fractures.

The risk of bias in included studies was assessed using the Newcastle–Ottawa (NOS) scale for non-randomized cohorts and cross-sectional studies. Two independent reviewers completed the NOS checklist (domain Selection, Comparability, Outcome; range 0–9); disagreements were resolved by a third expert. The total scores were interpreted as follows: 7–9 — low, 4–6 — moderate, ≤ 3 — high risk of bias. Among the 20 included studies, 10 had low, 9 — moderate, and 1 — high risk of bias.

Findings. Effect size for quantitative measures was estimated based on the standardized mean difference using Cohen's d. In some studies (e. g., [27, 28]), descriptive statistics for quantitative measures were provided as medians and interquartile ranges; in these cases, the mean and standard deviation values needed to calculate Cohen's d were approximated based on the approaches provided in [10]. For qualitative measures, the odds ratio (OR) was used as a measure of effect size.

The pooled effect size (OR) for each potential risk factor was estimated using a random effects model, in which the variance estimate (τ^2) due to different studies was calculated during the analysis of quantitative indicators using the Sidak–Jonkman method due to the high variability of the data and using the Paule–Mandel method using the analysis of qualitative indicators [12].

In addition, point and interval estimates of other indicators of heterogeneity between studies are provided, namely, the I^2 statistic (Higgins & Thompson's I^2 statistic) and the H statistic (Higgins & Thompson's H statistic).

All calculations were performed at a confidence interval of 95 %. For all indicators, the limits of the prediction interval were calculated, which shows the range within which the effect observed in a new study randomly selected from the general population can fall with a probability of 95% [13, 14].

The analysis was mainly performed using the functions of the Meta, Metafor, and Dmetar packages of the R programming language; for some auxiliary calculations, the MS Excel 2021 spreadsheet was used.

The confidence in the combined evidence for each potential factor (age, low BMD, absence of AOT, cement leakage, female gender) was determined using the GRADE approach using the online GRADEpro GDT platform (version 2025.3).

Results

Study Selection

A search of electronic databases yielded 454 articles. Initially, duplicates, case reports, letters, reviews, and non-comparative study designs ($n = 243$) were removed, leaving 211 titles and abstracts for screening. Two independent reviewers then assessed eligibility, excluding 183 publications that did not provide numerical data on group differences in patients with VCFs and NVCFs. This resulted in 28 articles being considered for inclusion. After in-depth review, 11 studies were excluded because they did not meet the eligibility criteria for comparing groups of patients with VCFs and NVCFs. The screening process identified 17 publications for inclusion. Reference lists were also manually reviewed, which resulted in 3 additional studies that met the criteria. Any disagreements between reviewers at any stage were resolved by discussion. In total, 20 comparative studies were included in the meta-analysis, as shown in the PRISMA flowchart (Fig. 1).

Characteristics of included studies

The systematic review included 20 publications published between 2011 and 2024 (Table 1), which

were conducted: 12 in China, 5 in South Korea, 1 each in Japan, Ukraine, and Germany. Most of them were retrospective cohort studies ($n = 19$), and one study was cross-sectional. The total number of patients was 7,923, of whom 1,487 (18.6%) had new vertebral compression fractures (NVCFs). The follow-up period ranged from 5 to 36 months, most often 12. The mean age of the participants ranged from (64.3 ± 11.9) to (74.8 ± 7.8) years, with a predominance of older individuals in all samples, the size of which varied from 60 to 2202 subjects. The proportion of patients with NVCFs ranged from 18.3 to 51.9 % within individual studies. The following possible risk factors for NVCF were considered in the reviewed publications: age; gender (female); BMI; absence of AOT; bone cement leakage; bone cement volume; BMD; CC; T–L junction damage in the case of primary fracture; percentage of KA recovery and vertebral height.

Overall, the included studies differed in design, country of origin, follow-up period, and proportion of new fractures, which allowed for multivariate risk analysis (Tables 2–4).

Risk factor assessment

Age

The effect of patient age on the occurrence of NVCF was investigated in 19 studies included in the meta-analysis. In some studies, older age was associated with an increased risk of NVCF, demonstrating a moderate to large effect, but a significant proportion of them did not show an effect of age (Fig. 2, a).

The estimated pooled effect (0.2891; 95 % CI: 0.1289–0.4494) indicates a statistically significant but small association of age with the risk of NVCF. High heterogeneity ($I^2 = 87.3$ %; $\tau^2 = 0.0950$) resulted in a wide prediction interval that encompassed zero. After excluding 5 publications — statistical outliers, heterogeneity decreased ($I^2 = 24.9$ %; $\tau^2 = 0.0281$), and the pooled effect remained stable (0.2278; 95 % CI: 0.0971–0.3584), indicating a stable but weak relationship (Fig. 2, b).

Body mass index

Eleven studies assessed the relationship between BMI and NVCF. Only S. Cai et al. revealed a significant positive effect, while most of the results had intervals that included zero and indicated the absence of a statistically significant effect. The pooled effect was -0.0670 (95 % CI: -0.2859 ; 0.1519), which also does not confirm the presence of an association. Heterogeneity was high ($I^2 = 78.8$ %; $\tau^2 = 0.1032$; $H = 2.173$).

After excluding the study by S. Cai et al., heterogeneity decreased to $I^2 = 47.6$ % ($\tau^2 = 0.0428$; $H = 1.382$),

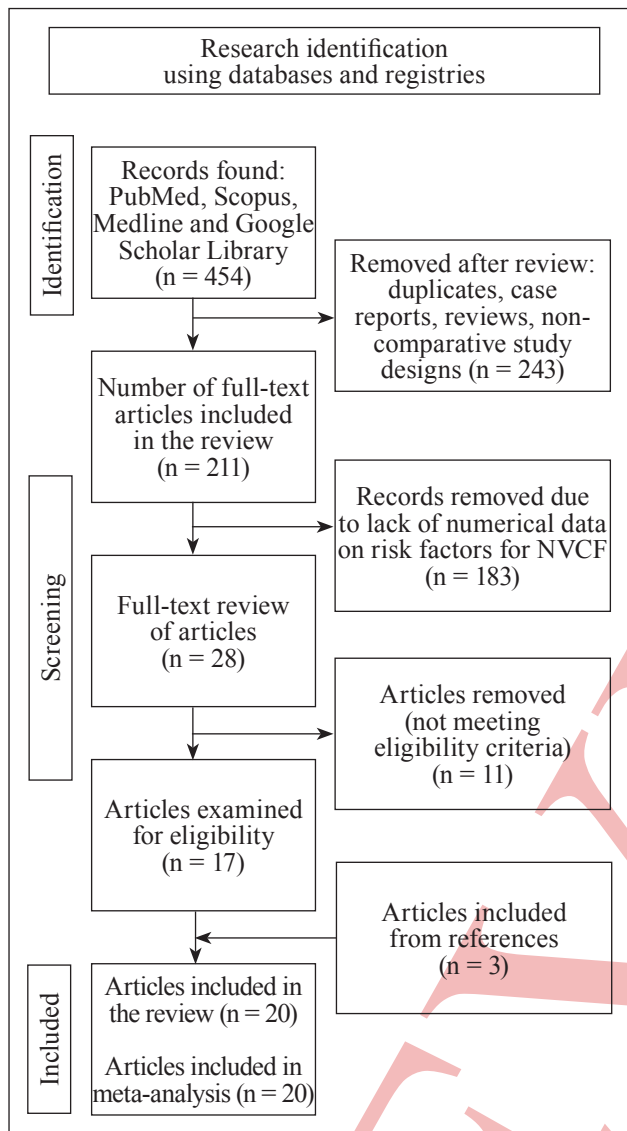


Fig. 1. Flowchart of study selection

but the adjusted effect of -0.1502 (95 % CI: -0.3209 ; 0.0206) remained statistically insignificant (Fig. 3).

Bone cement volume

Nine studies analyzed the effect of bone cement volume on the risk of NVCF. All standardized mean differences (Cohen's d) indicated no significant effect (Fig. 4). The pooled effect was 0.0321 (95 % CI: -0.0736 ; 0.1379), and the prediction interval (-0.162 ; 0.226) confirmed the absence of an association. The results of the studies were consistent, there was no heterogeneity: $\tau^2 = 0.0042$ (95 % CI: 0.000 – 0.0173), $I^2 = 0.0$ %, $H < 1$.

BMD

A significant association between reduced BMD and the risk of NVCF was found in 13 studies: the pooled effect was -0.6076 (95 % CI: -0.8881 ; -0.3271), which corresponds to a moderate or strong

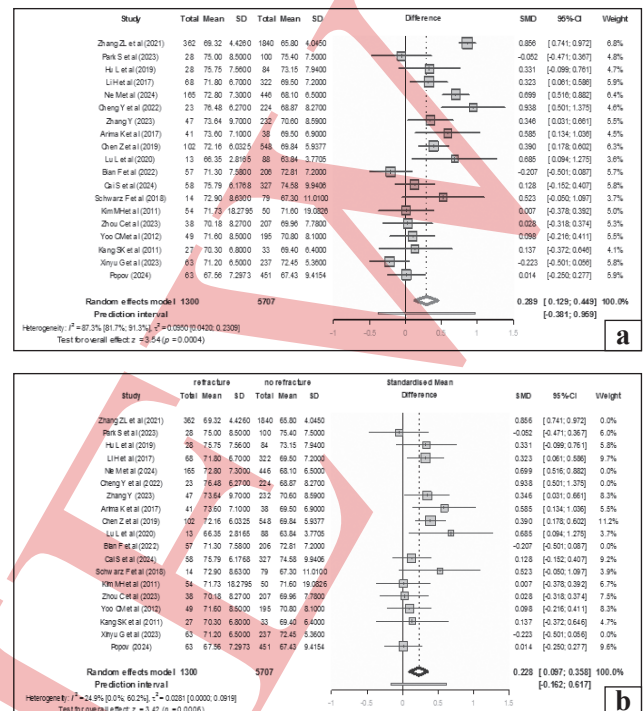


Fig. 2. Forest plot of the association of age of patients with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after exclusion of statistical outliers

effect (Fig. 5, a). At the same time, high heterogeneity ($I^2 = 88.8$ %; $\tau^2 = 0.2289$; $H = 2.982$) is due to the variability of the results between studies.

After excluding statistical outliers, heterogeneity decreased ($I^2 = 72.1$ %; $\tau^2 = 0.0537$; $H = 1.892$), and the adjusted effect size was -0.5515 (95 % CI: -0.7248 ; -0.3783 (Fig. 5, b)) confirming the consistent effect of low BMD on the risk of NVCF. The prediction interval (-1.104 ; 0.001) indicates that similar results should be expected in future studies.

Kyphotic angle

Data regarding the value of KA prior to surgical intervention were identified in only four published studies.

Based on the compilation of their data, we estimated the pooled effect size for this indicator at 0.0805 with 95 % CI: -0.172 ; 0.333 and a prediction interval of -0.6217 to 0.7827 (Fig. 6). The findings suggest that KA does not have a significant effect on the incidence of NVCF.

Statistical data according to Higgins-Thompson $H = 1.3508$ with 95 % CI: $(1.00$; $2.34)$ and $I^2 = 45.195$ % with 95 % CI: $(0.0$; $81.7)$ % indicated moderate heterogeneity, which was also confirmed by the data of the total variance $\tau^2 = 0.0321$ with 95 % CI: $(0.0000$; $0.7587)$, but at the same time no statistical outliers were detected.

Percentage of recovery of the kyphotic angle

Only 2 studies assessed the effect of relative recovery of the KA after surgery on the risk of NVCF.

Table 1

Baseline data of included studies

Author / Year	Country / Design	Total number of patients	Group with NVCF	Group without NVCF	Follow-up months	Age, years	NOS
Zhang Z. L. 2021 [15]	China / RC	2202	362	1840	14.7	69.32 ± 4.43	8
Park S. 2023 [16]	Korea / RC	128	28	100	12.0	73.00 ± 7.00	7
Bian F. 2022 [17]	China / RC	371	81	290	24.0	71.60 ± 8.00	8
Chen Z. 2019 [18]	China / RC	650	102	548	24.0	73.50 ± 7.90	7
Li H. 2017 [19]	China / RC	390	68	322	18.0	70.00 ± 7.00	7
Hu L. 2019 [20]	China / RC	198	28	170	12.0	74.50 ± 7.80	6
Zhou C. 2023 [21]	China / RC	245	38	207	12.0	70.70 ± 7.00	7
Nie M. 2024 [22]	China / RC	611	165	446	36.0	71.80 ± 9.00	8
Cheng Y. 2022 [23]	China / RC	247	23	224	24.0	69.60 ± 8.40	7
Seo D. H. 2014 [24]	Korea / RC	206	29	177	14.0	72.50 ± 6.90	6
Arima K. 2017 [25]	China / RC	556	96	460	12.0	64.30 ± 11.90	6
Lu L. 2020 [26]	China / RC	101	21	80	24.0	68.20 ± 8.40	6
Zhang Y. 2023 [27]	China / RC	279	47	232	18.0	71.10 ± 8.80	8
Cai S. 2024 [28]	China / RC	385	58	327	12.0	70.20 ± 8.10	8
Kim M. H. 2011 [29]	Korea / RC	104	54	50	12.0	71.40 ± 7.50	6
Yoo C. M. 2012 [30]	Korea / RC	244	49	195	12.0	71.40 ± 7.50	6
Kang S. K. 2011 [31]	Korea / RC	60	27	33	12.0	71.00 ± 7.20	6
Guo X. 2023 [32]	China / RC	300	100	200	22.4	71.60 ± 8.60	6
Schwarz F. 2018 [33]	Germany / RC	93	19	74	12.0	68.10 ± 9.40	6
Popov A. 2024 [34]	Ukraine / RC	553	92	461	12.0	69.00 ± 8.00	3

Note. RC is a retrospective cohort.

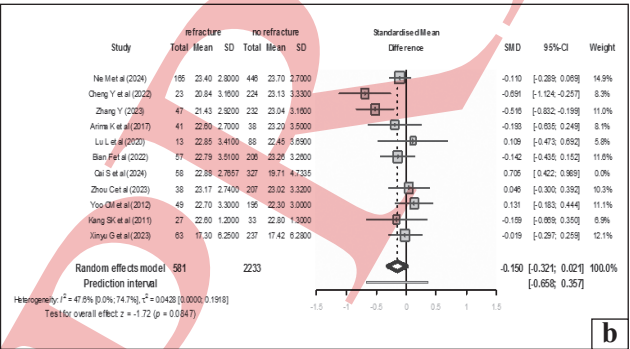
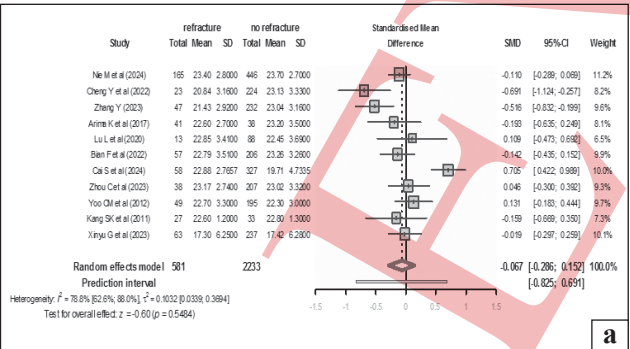


Fig. 3. Forest plot of the association of BMI of patients with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after exclusion of statistical outliers

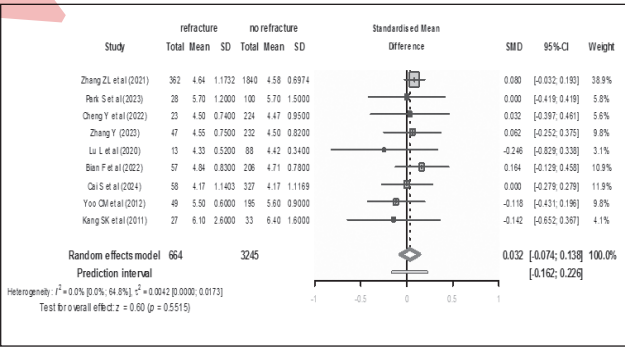


Fig. 4. Forest plot of the association of bone cement volume with new spinal fractures (results of meta-analysis)

One result indicated a moderate effect, the other indicated no effect (Fig. 6). The pooled effect was 0.247 (95 % CI: -0.144; 0.638), which does not allow us to conclude that there is a statistically significant association. The prediction interval (-3.448; 3.942) is almost symmetric, indicating uncertainty in future studies. The data obtained may be limited by the small number of included studies. Heterogeneity was assessed as moderate: $I^2 = 57.0\%$, $\tau^2 = 0.0449$, $H = 1.526$.

Table 2

Investigated risk factors for NVCF

№	Author / Year	Risk factor
1	Zhang Z. L. 2021 [15]	Age, cement volume, cement leakage, BMI, BMD, KA
2	Park S. 2023 [16]	Age, gender, cement volume, cement leakage, AOT, BMI, KA, % KA recovery, T-L junction, % recovery of vertebral height
3	Bian F. 2022 [17]	Age, gender, AOT, BMI, BMD, T-L junction
4	Chen Z. 2019 [18]	Age, gender, cement volume, cement leakage, BMI, T-L junction
5	Li H. 2017 [19]	Age, gender, cement volume, cement leakage, BMI, T-L junction
6	Hu L. 2019 [20]	Age, gender, cement volume, cement leakage, AOT, BMI
7	Zhou C. 2023 [21]	Age, gender, cement volume, cement leakage, BMD, T-L junction, KA, % KA recovery
8	Nie M. 2024 [22]	Age, gender, cement leakage, BMD, % KA recovery
9	Cheng Y. 2022 [23]	Age, gender, cement leakage, BMI, BMD, T-L junction
10	Seo D. H. 2014 [24]	Age, gender, cement volume, cement leakage, BMI, BMD, T-L junction, % KA recovery
11	Arima K. 2017 [25]	Age, cement volume, cement leakage, BMI, BMD, KA
12	Lu L. 2020 [26]	Age, gender, BMI, BMD, KA, % recovery of vertebral height
13	Zhang Y. 2023 [27]	Age, gender, cement leakage, BMD
14	Cai S. 2024 [28]	Age, gender, cement volume, cement leakage
15	Kim M. H. 2011 [29]	Age, cement volume, cement leakage, BMI, BMD, KA
16	Yoo C. M. 2012 [30]	Age, gender, cement volume, cement leakage, AOT, BMI, KA, % KA recovery, T-L junction, % recovery of vertebral height
17	Kang S. K. 2011 [31]	Age, gender, AOT, BMI, BMD, T-L junction
18	Guo X. 2023 [32]	Age, gender, cement volume, cement leakage, BMI, T-L junction
19	Schwarz F. 2018 [33]	Age, gender, cement volume, cement leakage, BMI, T-L junction
20	Popov A. 2024 [34]	Age, gender, cement volume, cement leakage, AOT, BMI

Notes: BMI — body mass index, BMD — bone mineral density, KA — kyphotic angle, AOT — anti-osteoporotic therapy, BC — bone cement.

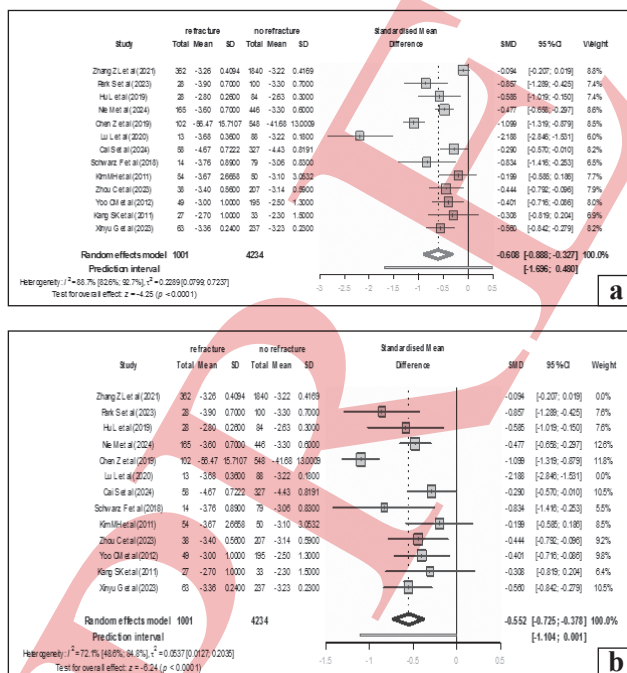


Fig. 5. Forest plot of the association of BMD with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after removal of outliers

Percentage of vertebral height recovery after vertebroplasty

Three studies evaluated vertebral height and its percentage recovery following surgical intervention. The results of these studies showed moderate heterogeneity (Higgins-Thompson $H = 1.1727$ with 95 % CI: 1.00; 3.64; $I^2 = 27.282\%$ with 95 % CI = (0.0; 92.4) %; $\tau^2 = 0.0315$ with 95 % CI: 0.0000; 2.6329), and the pooled effect was 0.2397 with 95 % CI: -0.0755; 0.5549. The data show that spinal height restoration after surgery does not have a measurable impact on NVCF incidence. However, it is important to note that further publications on this topic are needed to draw definitive conclusions. (Fig. 7).

Female gender

4 of 17 publications found a potential association between female gender and the risk of new vertebral compression fractures, one study (G. Xinyu et al.) showed the opposite effect.

In the remaining studies, the odds ratios were not statistically significant (95 % CI included 1), and the pooled effect was 1.20 (95 % CI: 0.91–1.58),

which does not support an association. Heterogeneity was significant: $I^2 = 59.1\%$, $\tau^2 = 0.1785$, $H = 1.56$.

After excluding the outlier (G. Xinyu et al.), the heterogeneity decreased to moderate ($I^2 = 39.3\%$; $\tau^2 = 0.0873$; $H = 1.28$), and the adjusted effect increased to 1.30 (95 % CI: 1.03–1.66), indicating a significant increase in the risk of new vertebral compression fractures in women ($\approx 30\%$). The prediction interval (0.66–2.58) indicates possible variability of the effect in future studies (Fig. 8, 9).

Absence of anti-osteoporosis treatment

Studies on the effect of absence of AOT on the incidence of NVCF showed moderate heterogeneity ($\tau^2 = 0.0395$ with 95 % CI: (0.0000; 0.4898), $H = 1.2862$ with 95 % CI: 1.00; 1.98, $I^2 = 39.553\%$ with 95 % CI: (0.0; 74.6) %). The pooled effect estimate for this risk factor was 1.9695 with 95 % CI: 1.5498; 2.5030 and a prediction interval of 1.1129 to 3.4856 (Fig. 10), which allows us to conclude that the chances of NVCF in the absence of AOT are doubled.

Bone cement leakage

The effect of BC leakage on the risk of NVCF was statistically significant: the pooled effect was 2.13 (95 % CI: 1.33–3.42), indicating an almost two-fold

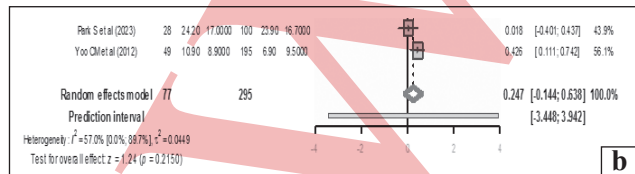
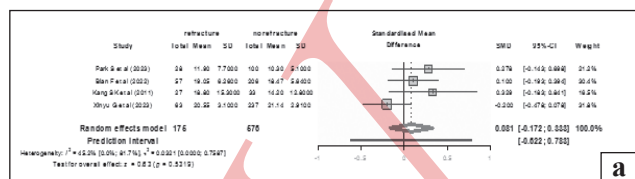


Fig. 6. Forest plot of the association of: a) kyphotic angle with new spinal fractures; b) percentage of kyphotic angle recovery due to surgery for new spinal fractures. Results of meta-analysis

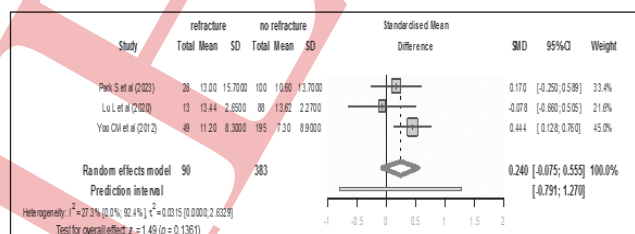


Fig. 7. Forest plot of the percentage of vertebral height recovery after surgery for new spinal fractures (results of meta-analysis)

Results of a meta-analysis on the impact of possible risk factors (quantitative indicators) on the incidence of new spinal fractures

Table 3

Factor	Pooled effect size	Effect	Number of studies	Heterogeneity index		
	Cohen's d (95 % CI)			Higgins & Thompson's H,	* τ^2 (95 % CI)	I^2 (%) (95 % CI)
**Patient's age	0.289 (0.129; 0.449)	weak	19	2.810	0.095 (0.042; 0.231)	87.3 (81.7; 91.3)
Patient's age	0.228 (0.097; 0.358)	weak	14	1.154	0.028 (0.000; 0.092)	24.9 (0.0; 60.2)
**BMI	-0.067 (-0.286; 0.152)	absent	11	2.173	0.103 (0.034; 0.369)	78.8 (62.6; 88.0)
BMI	-0.150 (-0.321; 0.021)	absent	10	1.382	0.043 (0.000; 0.192)	47.6 (0.0; 74.7)
BC volume	0.032 (-0.074; 0.138)	absent	9	0.678	0.004 (0.000; 0.017)	0.0 (0.0; 64.8)
**BMD	-0.608 (-0.888; -0.327)	moderate	13	2.982	0.229 (0.0799; 0.724)	88.8 (82.6; 92.7)
BMD	-0.552 (-0.725; -0.378)	moderate	11	1.892	0.054 (0.013; 0.204)	72.1 (48.6; 84.8)
Kyphotic angle	0.081 (-0.172; 0.333)	absent	4	1.351	0.032 (0.000; 0.759)	45.2 (0.0; 81.7)
% kyphotic angle recovery	0.247 (-0.144; 0.638)	absent	2	1.526	0.045 (N/A)	57.0 (0.0; 89.7)
% vertebral height recovery	0.240 (-0.076; 0.555)	absent	3	1.173	0.032 (0.000; 2.633)	27.3 (0.0; 92.4)

Notes: * — total variance between studies (τ^2) estimated by the Sidak-Jonkman method; ** — data before exclusion of statistical outliers.

increase in odds (Fig. 11). However, heterogeneity was significant ($I^2 = 72.3\%$; $\tau^2 = 0.5846$; $H = 1.90$).

After excluding statistical outliers (L. Lu et al.), the effect remained significant — 1.92 (95 % CI: 1.30–2.82), the prediction interval narrowed (0.53–6.97), and the heterogeneity decreased to $I^2 = 67.8\%$ ($\tau^2 = 0.3129$; $H = 1.76$), but remained moderately high.

T–L junction

The pooled effect estimate for T–L junction injury did not reveal a significant association with NVCF (effect 0.9017; 95 % CI: 0.5132–1.5843; Fig. 12).

The initial heterogeneity was very high ($I^2 = 92.7\%$; $\tau^2 = 1.8336$; $H = 3.69$), with statistical outliers in the studies of H. Li and D. H. Seo et al.

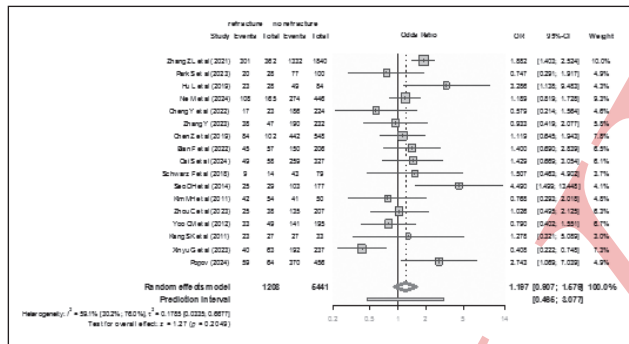


Fig. 8. Forest plot of the association of female gender with new spinal fractures (results of meta-analysis)

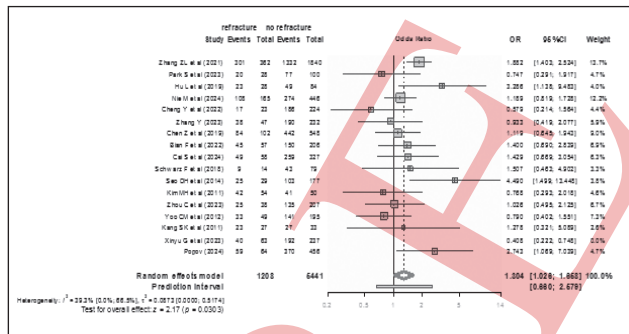


Fig. 9. Forest plot of the association of patient gender with new spinal fractures (results of meta-analysis after excluding statistical outliers)

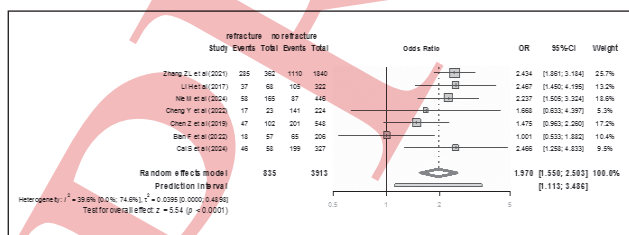


Fig. 10. Forest plot of the association of lack of anti-osteoporotic therapy with new spinal fractures (results of meta-analysis)

After their exclusion, the heterogeneity decreased but remained high ($I^2 = 74.5\%$; $\tau^2 = 0.4795$; $H = 1.98$), and the adjusted effect remained statistically insignificant.

For the indicators whose pooled effect was significant, we additionally assessed the evidence profile using the GRADE approach (Table 5).

Discussion

Comparison of our meta-analysis with previous systematic reviews demonstrates both a consistent convergence of results and fundamental differences that are clinically relevant. First of all, all studies confirm the key role of low BMD in shaping the risk of NVCF after vertebroplasty. In our study, the effect was moderate ($d \approx -0.55$) and remained stable in sensitive analyses, which is consistent with the data of G. Zhai et al. (SMD ≈ -0.41) and partly with the results of S. Dai et al. (WMD ≈ -0.38). Therefore, timely diagnosis and aggressive correction of osteoporosis remain an indispensable link in the prevention of new fractures [35, 36].

Bone cement leakage was also a notable factor. In our analysis, it almost doubled the risk of fracture (OR ≈ 1.92), which is practically identical to the meta-analysis by Dai et al. [36] (OR ≈ 2.05) and supports the conclusions of a previous review by Mao et al. [37]. A recent study by Wu et al. detailed the anatomical prerequisites for cement leakage, namely

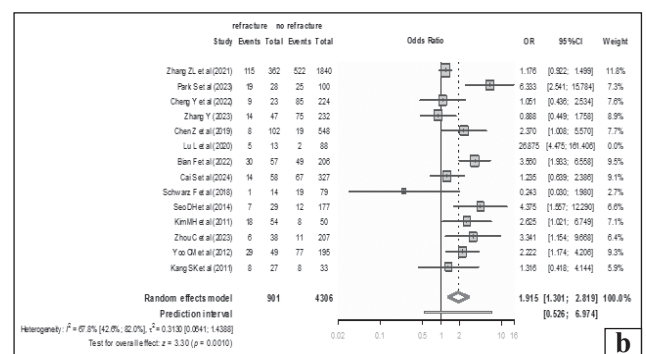
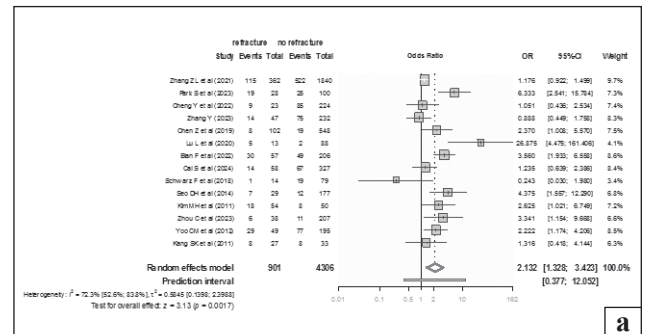


Fig. 11. Forest plot of the association of bone cement leakage with new spinal fractures: a) results of meta-analysis; b) results of meta-analysis after removing statistical outliers

Table 4

**Results of a meta-analysis on the impact of possible risk factors (qualitative indicators)
on the incidence of new spinal fractures**

Factor	Pooled effect size	Number of studies	Heterogeneity index		
	OR (95 % CI)		Higgins & Thompson's H _s	* τ^2 (95 %-CI)	I ² (%) (95 %-CI)
**Female gender	1.966 (0.9066; 1.5792)	17	1.5640	0.1785 (0.0335; 0.6677)	59.12 (30.2; 76.0)
Female gender	1.3041 (1.0256; 1.6583)	16	1.2840	0.0873 (0.000; 0.5174)	39.1 (0.0; 66.5)
Lack of osteoporotic treatment	1.9695 (1.5498; 2.5030)	7	1.2860	0.0395 (0.000; 0.4898)	39.55 (0.0; 74.6)
**Bone cement leakage	2.1318 (1.3276; 3.4233)	14	1.8990	0.5846 (0.1398; 2.3988)	72.275 (52.6; 83.8)
Bone cement leakage	1.9152 (1.3013; 2.8186)	13	1.7630	0.3129 (0.0641; 1.4388)	67.82 (42.6; 82.0)
**Damage to the T–L junction	0.9069 (0.3765; 2.1847)	10	3.6898	1.8336 (0.7846; 6.4829)	92.66 (88.6; 95.3)
Damage to the T–L junction	0.9017 (0.5132; 1.5843)	8	1.9807	0.4796 (0.1153; 1.5843)	74.51 (48.5; 87.4)

Notes: * — total variance between studies (τ^2) estimated by the Paule–Mandel method; ** — data before exclusion of statistical outliers.

Table 5

**GRADE profile of risk factors for new vertebral compression fractures
after puncture vertebroplasty**

Factor	Number of studies/patients	Pooled effect (95 % CI)	I ² , %	Confidence level
Absence of AOT	7 / 4 748	OR = 1.97 (1.55;2.50)	40	⊕⊕⊕ Moderate
Bone cement leakage	13 / 5 106	OR = 1.92 (1.30;2.82)	68	⊕⊕⊕ Moderate
Low BMD	11 / 2 932	Cohen's d = 0.55 (0.38;0.73)	72	⊕⊕⊕ Moderate
Advanced age	14 / 3 384	Cohen's d = 0.29 (0.13;0.45)	25	⊕⊕ Low
Female gender	16 / 6 349	OR = 1.30 (1.03;1.66)	39	⊕⊕ Low

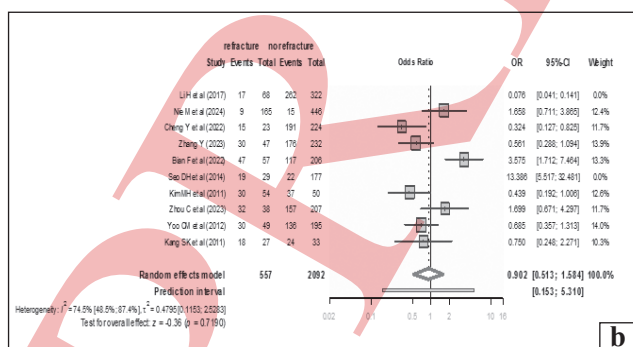
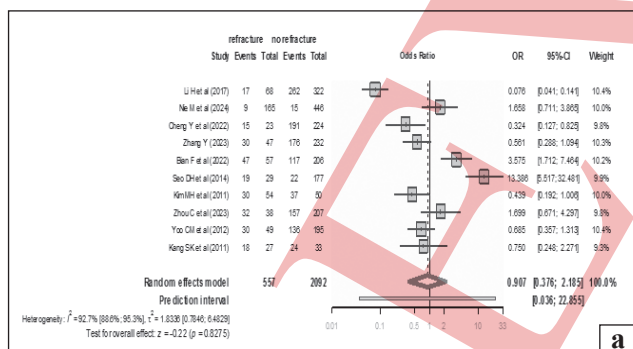


Fig. 12. Forest plot of the association of T–L junction damage in a primary fracture with new vertebral fractures: a) meta-analysis results; b) meta-analysis results after removing statistical outliers

cortical disruption and vacuum gap, emphasizing the importance of neutralizing these factors during intervention [38].

A notable contribution of our work is the quantitative analysis of the consequences of not receiving anti-osteoporotic therapy. Our findings reveal that the absence of drug therapy nearly doubles the risk of new fractures, whereas most prior reviews have merely described this association without statistical validation [36, 37]. This underscores the importance of AOT as a central component of secondary prevention strategies.

Regarding demographic variables, female gender was associated with an almost 30 % increased risk, which was consistent with the estimates of S. Dai, although statistical significance was not reached in the review by G. Zhai. Age showed a small but reproducible effect: in our pooled effects, the weighted average difference was about 2–3 years, which is practically the same as the results of S. Dai, while the review by G. Zhai, limited to the sample up to 2017, did not find a signal effect.

Interestingly, neither cement volume nor body mass index showed a significant association with

the incidence of new fractures in our study or in previous reviews. This finding suggests that efforts to adjust these parameters in an attempt to reduce risk are not supported by evidence.

Methodologically, our study is distinguished by a wider involvement of almost 7000 patients from different regions and the use of modern statistical approaches (Sidik–Jonkman, Paule–Mandel, predictive intervals, GRADE), while most of the predecessors used the classic DerSimonian–Laird model without grading the certainty of evidence. This provides higher external validity and practical applicability of our findings.

Limitations

First, the vast majority of the studies we included had a retrospective cohort design (19 out of 20), which limits the evidence of the conclusions due to the potential risk of systematic errors. Second, there was significant heterogeneity between studies for factors such as age, BMD, and cement leakage ($I^2 > 70\%$), suggesting variability in methodologies, population characteristics, and interpretation of results across studies. Although sensitive analyses were performed to exclude outliers, residual heterogeneity remained. Third, some potentially important risk factors had insufficient numbers of included studies (% vertebral height recovery, % KA recovery, KA), limiting the validity of conclusions about them.

It should be noted that the majority of studies used for the analysis (91 % of cases (18 of 20 cases)) considered the Asian population. This is significant given that race is necessarily taken into account when assessing BMD, as representatives of this population have a lower risk of osteoporosis compared with Caucasians.

Conclusions

A systematic review and meta-analysis of 20 studies identified the most significant predictors of new vertebral compression fractures following percutaneous vertebroplasty: the absence of anti-osteoporotic therapy, bone cement leakage, and low bone mineral density. The first two factors were found to approximately double the risk of new fractures, with the quality of evidence assessed by GRADE as moderate. Female gender increases the likelihood by approximately one-third, and older age has a statistically significant but small effect; for these, the level of confidence remains low. In contrast, cement volume, amount and correction of kyphosis, restoration of vertebral height, body mass index, body weight and T–L junction involvement did not show a significant association with new fractures.

Conflict of interest. The authors declare that there is no conflict of interest.

Prospects for further research. The prospect of future research will be the creation of a unified system of treatment, prevention and prognosis of NVCF after PVP, as well as its implementation in the treatment protocols of such patients in hospitals in Ukraine.

Information on funding. The study was conducted within the framework of the implementation of scientific and research work of the State Institution “Professor M.I. Sytenko Institute of Spine and Joint Pathology of the NAMS of Ukraine” “To develop prediction and improve the treatment of new compression fractures of the thoracic and lumbar vertebrae in patients with diffuse osteoporosis after vertebroplasty” (state registration number 0123U1042019).

Contribution of the authors. Popov A. I. — development of the research concept, participation in data collection, analysis of the results; Molodyuk M. V. — data collection, analysis of the results, drafting the article; Kutsenko V. O. — development of the research concept, participation in data collection; Nessonova M. M. — statistical processing of digital data and description of indicators. All authors participated in drafting the article and approved the final manuscript.

References

1. Yu, F., & Xia, W. (2019). The epidemiology of osteoporosis, associated fragility fractures, and management gap in China. *Archives of osteoporosis*, 14(1), 32. <https://doi.org/10.1007/s11657-018-0549-y>
2. Noriega, D., Marcia, S., Theumann, N., Blondel, B., Simon, A., Hassel, F., Maestretti, G., Petit, A., Weidle, P. A., Mandly, A. G., Kaya, J., Touta, A., Fuentes, S., & Pflugmacher, R. (2019). A prospective, international, randomized, noninferiority study comparing an implantable titanium vertebral augmentation device versus balloon kyphoplasty in the reduction of vertebral compression fractures (SAKOS study). *The spine journal*, 19(11), 1782–1795. <https://doi.org/10.1016/j.spinee.2019.07.009>
3. Ballane, G., Cauley, J. A., Luckey, M. M., & El-Hajj Fuleihan, G. (2017). Worldwide prevalence and incidence of osteoporotic vertebral fractures. *Osteoporosis international*, 28(5), 1531–1542. <https://doi.org/10.1007/s00198-017-3909-3>
4. O'Neill, T. W., Felsenberg, D., Varlow, J., Cooper, C., Kanis, J. A., & Silman, A. J. (1996). The prevalence of vertebral deformity in European men and women: The European vertebral osteoporosis study. *Journal of bone and mineral research*, 11(7), 1010–1018. <https://doi.org/10.1002/jbmr.5650110719>
5. Alexandru, D., & So, W. (2012). Evaluation and management of vertebral compression fractures. *The permanente journal*, 16, 46–51. <https://doi.org/10.7812/TPP/12-037>
6. Beall, D. (2018). Review of vertebral augmentation: An updated meta-analysis of the effectiveness. *International Journal of spine surgery*, 12, 295–321. <https://doi.org/10.14444/5036>
7. Galibert P, Deramond H, Rosat P, & Le Gars D. (1987). Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty. *Neurochirurgie*; 33, 166–168. [in French]
8. Fusco, A. (2019). Benefits and harms of percutaneous vertebroplasty for the treatment of osteoporotic vertebral compression fracture: A Cochrane review summary with commentary. *American journal of physical medicine & rehabilitation*, 98(12), 1151–1152. <https://doi.org/10.1097/PHM.0000000000001274>
9. Zhang, Y., Shi, L., Tang, P., & Zhang, L. (2017). Comparison of the efficacy between two micro-operative therapies of old patients with osteoporotic vertebral compression fracture: A network meta-analysis. *Journal of cellular biochemistry*, 118(10), 3205–3212. <https://doi.org/10.1002/jcb.25966>
10. Wan, X., Wang, W., Liu, J., & Tong, T. (2014). Estimating

- the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Medical research methodology*, 14(1). <https://doi.org/10.1186/1471-2288-14-135>
11. Harrer, M., Cuijpers, P., Furukawa, T. A., & Ebert, D. D. (2021). Pooling effect sizes. *Doing Meta-Analysis with R*, 93–138. <https://doi.org/10.1201/9781003107347-6>
 12. Harrer, M., Cuijpers, P., Furukawa, T. A., & Ebert, D. D. (2021). Between-study heterogeneity. *Doing Meta-Analysis with R*, 139–172. <https://doi.org/10.1201/9781003107347-7>
 13. Borenstein, M., Hedges, L. V., Higgins, J. P., & Rothstein, H. R. (2021). Introduction to meta-analysis. <https://doi.org/10.1002/9781119558378>
 14. Spineli, L. M., & Pandis, N. (2020). Prediction interval in random effects meta analysis. *American journal of orthodontics and dentofacial orthopedics*, 157(4), 586–588. <https://doi.org/10.1016/j.ajodo.2019.12.011>
 15. Zhang, Z.-L., Yang, J.-S., Hao, D.-J., Liu, T.-J., & Jing, Q.-M. (2021). Risk factors for new vertebral fracture after percutaneous vertebroplasty for osteoporotic vertebral compression fractures. *Clinical interventions in aging*, 16, 1193–1200. <https://doi.org/10.2147/CIA.S312623>
 16. Park, S., Choi, S. S., Kim, H., Byun, S. Y., & Lee, C. H. (2023). Risk factors for new vertebral compression fracture after vertebroplasty and efficacy of osteoporosis treatment: A STROBE-compliant retrospective study. *Medicine*, 102(47), e35042. <https://doi.org/10.1097/MD.00000000000035042>
 17. Bian, F., Bian, G., Zhao, L., Huang, S., Fang, J., & An, Y. (2022). Risk factors for recollapse of new vertebral compression fractures after percutaneous kyphoplasty in geriatric patients: Establishment of a nomogram. *BMC Musculoskeletal disorders*, 23, 458. <https://doi.org/10.1186/s12891-022-05409-3>
 18. Chen, Z., Wu, Y., Ning, S., Ma, T., & Wu, Z. (2019). Risk factors of secondary vertebral compression fracture after percutaneous vertebroplasty or kyphoplasty: A retrospective study of 650 patients. *Medical science monitor*, 25, 9255–9261. <https://doi.org/10.12659/MSM.915312>
 19. Li, H., Yang, D.-L., Ma, L., Wang, H., Ding, W.-Y., & Yang, S.-D. (2017). Risk factors associated with adjacent vertebral compression fracture following percutaneous vertebroplasty after menopause: A retrospective study. *Medical science monitor*, 23, 5271–5276. <https://doi.org/10.12659/MSM.907364>
 20. Hu, L., Sun, H., Wang, H., Cai, J., Tao, Y., Feng, X., & Wang, Y. (2019). Cement injection and postoperative vertebral fractures during vertebroplasty. *Journal of orthopaedic surgery and research*, 14, 228. <https://doi.org/10.1186/s13018-019-1273-z>
 21. Zhou, C., Huang, S., Liao, Y., Chen, H., Zhang, Y., Li, H., Zhu, Z., & Wang, Y. (2023). Correlation analysis of larger side bone cement volume/vertebral body volume ratio with adjacent vertebral compression fractures during vertebroplasty. *Frontiers in Endocrinology*, 14, 1072087. <https://doi.org/10.3389/fendo.2023.1072087>
 22. Nie, M., Chen, Z., Shi, L., Cao, H., & Xu, L. (2024). Prediction of new vertebral compression fracture within 3 years after percutaneous vertebroplasty for osteoporotic vertebral compression fracture: Establishment and validation of a nomogram prediction model. *PLOS ONE*, 19(5), e0303385. <https://doi.org/10.1371/journal.pone.0303385>
 23. Cheng, Y., Cheng, X., & Wu, H. (2022). Risk factors of new vertebral compression fracture after percutaneous vertebroplasty or percutaneous kyphoplasty. *Frontiers in endocrinology*, 13, 964578. <https://doi.org/10.3389/fendo.2022.964578>
 24. Seo, D.-H., Oh, S.-H., Yoon, K. W., Ko, J. H., Kim, Y. J., & Lee, J. Y. (2014). Risk factors of new adjacent compression fracture after percutaneous vertebroplasty: Effectiveness of bisphosphonate in osteoporotic or osteopenic elderly patients. *Korean journal of neurotrauma*, 10(2), 86–91. <https://doi.org/10.13004/kjnt.2014.10.2.86>
 25. Arima, K., Abe, Y., Nishimura, T., Okabe, T., Tomita, Y., Mizukami, S., Kanagae, M., & Aoyagi, K. (2017). Association of vertebral compression fractures with physical performance measures among community-dwelling Japanese women aged 40 years and older. *BMC musculoskeletal disorders*, 18, 188. <https://doi.org/10.1186/s12891-017-1531-3>
 26. Lu, L., Liu, Y., Nazierhan, S., Sun, Z., Aikeremu, D., Alimasi, W., Xu, K., Niyazi, W., & Wang, H. (2020). Expression changes of IL-17 in zoledronic acid combined with PVP technology in the treatment of postmenopausal osteoporotic vertebral compression fracture and its predictive value of relapse. *Journal of musculoskeletal & neuronal interactions*, 20(4), 563–569.
 27. Zhang, Y., Sun, J. J., Zhang, Z., Huang, F., Lv, J., & Zhu, Q. (2023). Risk factors for new vertebral compression fracture after percutaneous vertebral augmentation: A retrospective study. *Medical science monitor*, 29, e940134. <https://doi.org/10.12659/MSM.940134>
 28. Cai, S., Liu, W., Cai, X., Xu, C., Hu, Z., Quan, X., Deng, Y., Yao, H., Chen, B., Li, W., Yin, C., & Xu, Q. (2024). Predicting osteoporotic fractures post-vertebroplasty: A machine learning approach with a web-based calculator. *BMC surgery*, 24, 142. <https://doi.org/10.1186/s12893-024-02427-x>
 29. Kim, M.-H., Lee, A. S., Min, S.-H., & Yoon, S.-H. (2011). Risk factors of new compression fractures in adjacent vertebrae after percutaneous vertebroplasty. *Asian spine journal*, 5(3), 180–187. <https://doi.org/10.4184/asj.2011.5.3.180>
 30. Yoo, C. M., Park, K. B., Hwang, S. H., Kang, D. H., Jung, J. M., & Park, I. S. (2012). The analysis of patterns and risk factors of newly developed vertebral compression fractures after percutaneous vertebroplasty. *Journal of Korean neuro-surgical society*, 52(4), 339–345. <https://doi.org/10.3340/jkns.2012.52.4.339>
 31. Kang, S.-K., Lee, C.-W., Park, N.-K., Kang, T.-W., Lim, J.-W., Cha, K.-Y., & Kim, J.-H. (2011). Predictive risk factors for refracture after percutaneous vertebroplasty. *Annals of rehabilitation medicine*, 35(6), 844–851. <https://doi.org/10.5535/arm.2011.35.6.844>
 32. Guo, X., Zhu, N., Zhang, H., & Dingjun, H. (2023). Vertebral refracture after percutaneous vertebroplasty for osteoporotic vertebral compression fractures with and without brace wearing: A retrospective study of 300 patients. *Frontiers in surgery*, 9, 1056729. <https://doi.org/10.3389/fsurg.2023.1056729>
 33. Schwarz, F., Burckhart, M., Lawson McLean, A., Kalff, R., & Waschke, A. (2018). Risk factors for adjacent fractures after cement-augmented thoracolumbar pedicle screw instrumentation. *International journal of spine surgery*, 12(5), 565–570. <https://doi.org/10.14444/5069>
 34. Popov, A., & Moloduk, M. (2024). Analysis of the results of percutaneous vertebroplasty of compression fractures of bodies of chest and lumbar vertebrae on the background of osteoporosis. *Orthopaedics traumatology and prosthetics*, (1), 13–18. <https://doi.org/10.15674/0030-59872024113-18>
 35. Zhai, G., Li, A., Liu, B., Lv, D., Zhang, J., Sheng, W., Yang, G., & Gao, Y. (2021). A meta-analysis of the secondary fractures for osteoporotic vertebral compression fractures after percutaneous vertebroplasty. *Medicine*, 100(16), e25396. <https://doi.org/10.1097/MD.00000000000025396>
 36. Dai, C., Liang, G., Zhang, Y., Dong, Y., & Zhou, X. (2022). Risk factors of vertebral re-fracture after PVP or PKP for osteoporotic vertebral compression fractures, especially in Eastern Asia: A systematic review and meta-analysis. *Journal of orthopaedic surgery and research*, 17, 161. <https://doi.org/10.1186/s13018-022-03038-z>
 37. Mao, W., Dong, F., Huang, G., He, P., Chen, H., Qin, S., & Li, A. (2021). Risk factors for secondary fractures to percutaneous vertebroplasty for osteoporotic vertebral compression fractures: A systematic review. *Journal of orthopaedic surgery and research*, 16, 644. <https://doi.org/10.1186/s13018-021-02722-w>

38. Wu, Y., Zhou, Z., Lu, G., Ye, L., Lao, A., Ouyang, S., Song, Z., & Zhang, Z. (2025). Risk factors for cement leakage after percutaneous vertebral augmentation for osteoporotic verteb-

ral compression fractures: A meta-analysis. *International journal of surgery*, 111, 1231–1243. <https://doi.org/10.1097/JS9.0000000000001895>

The article has been sent to the editors 06.06.2025	Received after review 18.06.2025	Accepted for printing 03.07.2025
--	-------------------------------------	-------------------------------------

RISK FACTORS FOR RECURRENT VERTEBRAL COMPRESSION FRACTURES AFTER PERCUTANEOUS VERTEBROPLASTY IN OSTEOPOROTIC PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. I. Popov ¹, M. V. Moloduk ¹, V. O. Kutsenko ¹, M. M. Nessonova ²

¹ Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine, Kharkiv

² Private higher educational institution «Kharkiv International Medical University». Ukraine

✉ Andrii Popov, MD, DSci in Orthopaedics and Traumatology: aipopovdoc@gmail.com; <https://orcid.org/0000-0002-9006-7721>

✉ Mykyta Moloduk, MD: NikitaMoloduk@gmail.com; <https://orcid.org/0009-0005-0058-424X>

✉ Volodymyr Kutsenko, MD, DSci in Orthopaedics and Traumatology: kutsvlad1956@gmail.com; <https://orcid.org/0000-0001-7924-6553>

✉ Maryna Nessonova, PhD in Technology: m.nessonova@khimu.edu.ua; <https://orcid.org/0000-0001-7729-317X>