의학석사학위논문

골다공증 성 척추골절에 대한 보조기의 효과: 체계적 문헌고찰과 메타분석

Effect of brace to osteoporotic vertebral fracture: a systematic review and meta-analysis

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Abstract

Effect of brace to osteoporotic vertebral fracture: a systematic review and meta-analysis

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Study design:

A systematic review and meta-analysis

Objects:

The objective is to investigate the effect of brace on osteoporotic vertebral fracture patients through a systematically literature review and meta-analysis.

Summary of Literature Review:

There are 2 systematic reviews published before, neither of them included the latest published article nor comprehensively analyzed outcomes.

Materials and Methods

We searched electrical database with a developed searching strategy. Published randomized control trials were included in meta-analysis. We pooled data with Revman, examined the risk of bias and evaluated the quality of evidence following the guideline and handbook of Cochrane group.

Results:

10 articles were included in the systematic review and 4 of them were included in meta-analysis. Low quality evidence indicates middle term use of Spinomed is better than no use in patients with subacute or chronic osteoporotic vertebral fracture on reduction of pain, correction of kyphosis angle and improvement in quality of life. Very low quality evidence proves use of Spinomed or TLSO-rigid is no better than use of soft brace to patients with acute osteoporotic vertebral fracture.

Conclusions:

It might be applicable to recommend middle term use of Spinomed orthosis to patients with subacute osteoporotic vertebral fracture. This systematic review highlighted the need for high quality RCTs.

Key words:

Spine, osteoporosis, fracture, brace, meta-analysis, rehabilitation

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Introduction

Osteoporosis is a metabolic bone disease causes low bone density, disturbing approximately 200 million people all over the world; osteoporotic fracture is pathological fractures caused by low energy trauma occurring at low bone mineral density sites (1). Among osteoporotic fractures, Osteoporotic vertebral fracture (OVF) is 1 of the most severe ones as a consequence of its high prevalence and huge impact to patients' living (2-4). OVF has a 5-year survival rate of 28%, which is the lowest among all kinds of osteoporotic fracture (5), causes severe pain, activity limitation, restriction of respiratory function and a series of digestive system disease (6, 7). Also, caused by progressive deterioration of vertebral body, the deformity can lower the height, influence the balance, increase the possibility of falling and eventually raise the risk of secondary fracture, which additionally raises economic burden of the patients and the society (1, 6, 7). Therefore, both clinicians and patients should administer OVF earnestly.

Current treatments to OVF include conservative treatments, like medication, orthosis, bed resting and exercise; and operative treatments, like percutaneous vertebroplasty/kyphoplasty and open surgery. Surgeons should recommend conservative treatment if patients' neurological functions remain intact; should propose vertebroplasty/kyphoplasty if the conservative treatment failed to manage pain; should suggest open surgery if the fracture is unstable or accompanying neurological symptoms (7). Generally, surgeons recommend

the orthosis, expecting they can immobilize the fracture site, diminish pain, correct the posture, improve the balance and decrease the risk of falling. But the authentic effect of brace is still uncertain and debatable; the strength of its recommendation remains inconclusive in AAOS guideline (7, 8).

In our study, we try to investigate how the effect of orthosis is and what orthosis are effective through a systematically literature review and meta-analysis.

Method

Data source and searching strategy

Two reviewers developed the searching strategy, followed the method in the guideline of Cochrane Back and Neck (CBN) group and consulted the librarian (9). Key words of the searching strategy include “clinical trial” “osteoporotic fracture” “spine” “orthosis” and “brace”. Detail of the searching strategy was presented in Figure 1.

We searched electronic database as Medline, EMBASE, Central and Web of science since May 30th, 2015, set alerts for every database weekly until March 10th, 2016 and also checked the reference lists of other reviews for relevant articles.

Study selection

One reviewer examined the articles’ potential for full text assessment by screening titles and abstracts, 2 reviewers assessed whether or not the article was qualified to be included in meta-analysis. We solved the disagreements by discussion between 2 reviewers; when not solved, a third reviewer (JH, Lee) was consulted.

To be eligible for systematic review, an article should be an English published clinical trial that recruited participants with at least 1 diagnosed osteoporotic vertebral fracture, either clinical or radiographically, and applied orthosis as or as a part of intervention. We excluded articles which drafted

subjects with traumatic vertebral fracture or pooled participants with and without fracture together and failed to report the cohort separately.

We selected studies, randomized control trials (RCTs) that reported the outcomes we need, from the articles included in systematic review.

Data extraction

Two reviewers independently extracted information from included studies with a standardized table, which includes items like characteristics of participants, types of interventions and outcomes. We clarified the information by contacting authors through e-mail.

Primary outcomes include pain intensity, kyphosis angle and quality of life. We didn't extract data about adverse effects.

Measurement of Risk of bias

Risk of bias is used to describe the internal validity of the study, confirming whether or not the study answers its question correctly. We used the tool recommended in the latest Cochrane Back and Neck Group (CBN) Guideline, which has the same bias categories as those of Cochrane handbook, include selection bias, performance bias, attribution bias, detection bias, reporting bias and other bias, but with more specific items(13 items) and practical criteria (10).

Data synthesis and analysis

We analyzed and synthesized data following the methods in Cochrane handbook. In studies with multiple timeline results, the data from the last visit was extracted; for the cross-over trials, data before the cross-over procedure was extracted; in multi-arm trials, data in groups were combined or separated when needed: the formula for combining groups was shown in Table 6 Formula 1; groups were separated evenly in their number of participants, remaining means and standard deviations unchanged.

The choice between using the value of final visit and the change value from baseline is according to the characteristics of included studies and setting of our summary statics: the final value and the change value from baseline were allowed to pool together if we used the mean difference method as our standard statistic; only one of them should be applied if we used standardized mean difference (SMD) method, also we multiplied -1 to some values to make sure results from different scales could point in the same direction. When needed to estimate the standard deviations (SD) of change value from baseline, we used the Formula 2 in Table 6, assigned 0.5 as the value of correlation (Corr) and ran a sensitivity analysis with the value of 0.4 to testify the reliability of the estimation (11). All formulas were recommended by Cochrane handbook.

Considering the generally existing clinical heterogeneity in literatures about spine, we selected random effect model (10); since the measuring methods are

different among studies, we used SMD as our summary statics. Re-expression of the value of SMD was conducted through rules of thumb for effect sizes (< 0.2 = small effect, 0.2 to 0.8 = moderate effect, > 0.8 = large) (12). We assessed clinical heterogeneity by comparing the characteristics of studies, estimated methodological heterogeneity by measuring the risk of bias and investigated statistical heterogeneity by P value and I^2 value of chi-squared test included in Revman 5.3. The statistical heterogeneity should be considered as existent and statistical significant when P value is not bigger than 0.10 and should be recognized as considerable when I^2 is bigger than 75%. (10, 12).

Other sensitivity analyses, like excluding or including some "dubious" articles, were operated to find out whether or not the result is robust.

Additionally, we conducted subgroup analysis according to different types of orthosis to explore the clinical heterogeneity.

Measurement of Quality of evidence

The quality of evidence can be understood as "external validity", which answers whether or not the study's finding is applicable. We used GRADE approach, which is a system developed by Grading of Recommendations, Assessment, Development and Evaluation Working Group for rating the quality of a body of evidence, appraised them as "high" "moderate" "low" and "very low" level. Different from compiling a guideline, the

quality of evidence reflects how much the reviewers are confident about the truthfulness of the results in a systematic review. The “high” level means “We are very confident that the true effect lies close that of the estimate of the effect”, moderate grade means “We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different”; low grade means “Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect”; and very low grade means “We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect”. The details of GRADE are in “help” column in GRADEpro and Cochrane handbook (12).

The RCTs were deemed as “high quality of evidence” initially; grade would be downgraded according to the severity of deficiency in domains of risk of bias, inconsistency of results, indirectness of evidence, imprecision of results and publication bias.

Risk of bias

Different from its previous version, the latest guideline does not recommend a cut off to stratify the clinical trials into high risk of bias trials or low risk of bias trials, therefore applying the method in Cochrane handbook may be

arduous. Therefore, followed the example in the CBN guideline, we did not downgrade the score when all 6 categories of bias (selective bias, performance bias, detection bias, attribution bias, reporting bias and other bias) are low risk, downgraded 1 score if no more than 3 categories have high or unclear risk of bias and downgraded 2 scores if no less than 4 categories have high or unclear risk of bias (10).

Inconsistency

We downgraded the quality of evidence by 1 score if it exists large statistical heterogeneity ($I^2 > 80\%$), downgraded 2 scores if it exists both large statistical heterogeneity and clinical heterogeneity (12, 13).

Indirectness

We measured indirectness by assessing the possibility of its existence in domains of population, intervention, comparator, comparison and outcome.

Imprecision

We downgraded 1 point if the number of participants is lower than 400 and downgraded 2 if there are very few events and the confidence intervals(CIs) include both appreciable benefit and appreciable harm.

Publication bias

Quality of evidence should be downgraded by 1 level if we detected the existence of publication bias.

We analyzed and synthesized data with Revman 5.3 and reported the tables of quality of evidence and summary of findings with GRADEpro GDT.

Results

We identified 649 relevant citations, acquired 28 full-text articles with 10 of them included in systematic review; 4 of them were qualified to be included in meta-analysis. (Table 1, Table 2). Totally 522 participants were included in systematic review and 281 of them were included in meta-analysis.

Included studies

Six randomized control trials, 2 case-series studies, 1 retrospective study and 1 non-randomized control trial were included in systematic review. Among the RCTs, 4 of them compared Spinomed to other braces or no brace (14-17); one compared rigid orthoses, soft brace and no brace (18); the last one compared exercises with and without posture training support (PTS) (19). Two case series studies evaluated the effect of Spinomed Ⅲ and Knight-Taylor brace, respectively(6, 20). The retrospective study assessed the effect of TLSO–rigid brace (21). The non-randomized control trial assessed three point orthosis and plaster corset (22). All of them were in English; no article was excluded for language restriction.

Description of studies

Spinomed orthosis

Spinomed orthosis are semi-rigid braces which consist of metallic back pad works with a system of belts and Velcro or body suits (6, 15, 16). As introduced in their official website, the Spinomed orthosis have advantages of lightness, active and can stimulate the muscles of patients own; their

indications include OVF, Juvenile osteochondrosis and kyphosis with chronic back pain. Four RCTs and one case series study evaluated the effect of those orthoses, investigating Spinomed brace, Spinomed active brace and Spinomed Ⅲ brace: two RCTs enrolled community-dwelling female participants who had sub-acute vertebral fractures with kyphosis angle more than 60 degrees(15, 16); the other two RCTs recruited hospital source female participants (14, 17); the case series study engaged subjects with persisting back pain for at least 3 months (6). All participants were asked to wear the orthosis for at least 2h/day during walking or training. One study measured for 3 weeks, the others surveyed for 3 to 6 months. One RCT was eliminated from meta-analysis as its incomplete reported results, we connected with the author but failed to get the authorization of acquiring original data (17).

Rigid orthosis

Three-point orthoses, TLSO-rigid and Knight-Taylor brace were categorized as rigid orthosis (23). There are 4 articles about this category, 1 RCT, 1 retrospective study, 1 case series study and 1 non-randomized control trial(18, 20-22).The RCT compared TLSO-rigid to soft brace and no brace, included 60 participants with single level acute OVF. Participants were asked to wear orthosis for eight weeks totally and the final measurements were conducted on the twelfth week after fracture (18). The retrospective study included 55 participants with acute OVF, they were asked to wear TLSO-rigid until the fracture was diagnosed as “settled” and were measured for periods of 2, 3

and 6 months (21). The case series study evaluated the immediate effect of Knight-Taylor brace on 47 participants' balance performance (20). The non-randomized trial included 59 participants and monitored parameters as duration of immobilization, pain intensity, skin changes and other complications (22).

Soft brace

Two studies applied soft brace as an intervention or a contrast, both were mentioned above (14, 18).

Characteristics of included studies were summarized in Table 1 and Table 2.

Risk of bias in included studies

We presented summary of risk of bias in Figure 3. Rationales of the judgement were shown in Table 5.

Most studies had unclear risk of selection bias except 2 articles, which comprehensively described procedures of randomization sequence generalization and allocation concealment (18); 2 trials had high risk of bias in group similarity (17, 19).

All studies had high risk of performance bias in items of blinding to patients and care providers, the other 2 items were rated as low risk in all trials (14-16, 18, 19) except 1, which has insufficiency in controlling the co-intervention and imbalance in compliance between groups (17).

We separately estimated the risk of detection bias in every main outcome. The measurement of kyphosis angle was rated as low risk of bias in all studies because the outcome is objective, which means they were less likely to be influenced by the high risk of bias in performance; the measurement of pain intensity was rated as high risk of bias because pain intensity can be easily influenced by the failure of blinding; the measurement of quality of life was rated as high risk of bias in 5 trials in which used the questionnaires, since they were subjectively measured by patients themselves (14-16, 18, 19). All trials have low risk of bias in timing of outcome assessments.

Four trials have low risk of bias in attribution bias. Li’s and Dionyssiotis’s trials had unclear to high risk of bias in them (14, 17).

Reporting bias should be examined by comparison between protocol and published article but we compared the outcomes in method section with those whose results were reported since no protocol was found (12). Data of control group was not reported adequately by Dionyssiotis et al; therefore it couldn’t be included in meta-analysis. They didn’t report other parameters like kyphosis angle or body sway either, so we considered there was unclear risk of bias in their study(17). Other trials were rated as low risk of bias.

Five trials made clear clarify that funders have no possession of the trials about procedures of planning and/or publishing. (14-18)

Effects of intervention

Results of meta-analysis

Compare between brace and no brace

Totally 3 studies compared brace with no brace, including 219 participants (15, 16, 18).

Pain

Two trials used Miltner's rating scale (15, 16) and one trial used visual analog scale (VAS) (18) to measure the pain intensity. There is low quality evidence (3RCTs, N = 212) that using brace is much better than no use (SMD, -1.10; 95% CIs, -1.61 to -0.59; Heterogeneity: P = 0.07, I^2 = 57%), very low quality evidence (1 RCT, N = 42) that using TLSO-rigid or soft brace is no better than no use to subjects with acute OVF (TLSO-rigid: SMD, -0.57; 95%CIs, -1.48 to 0.34. Soft: SMD, -0.37; 95%CIs, -1.31 to 0.57) and low quality evidence (2 RCTs, N = 170) that middle term use of Spinomed is better than no use to subjects with subacute or chronic OVF (SMD, -1.46; 95% CIs, -1.81 to -1.11). (Figure4, Table 3).

Kyphosis angle

Two trials measured kyphosis angle with three-dimensional photo morphometry (15, 16), one trial used the rate between anterior section and posterior section of vertebral body (18). The outcome of the latter one was multiplied by -1 to keep all results pointing to the same direction. There is low quality evidence (3RCTs, N = 209) that using brace is much better than no use

(SMD, -0.91; 95% CIs, -1.21 to -0.61; Heterogeneity: P = 0.52, I^2 = 0%), very low quality evidence (1 RCT, N = 39) that using TLSO-rigid or soft brace is no better than no use to participants with acute OVF (TLSO-rigid: SMD, -0.72; 95%CIs, -1.69 to 0.26. Soft: SMD, -0.38; 95%CIs, -1.42 to 0.66) and low quality evidence (2 RCTs, N = 170) that middle term use of Spinomed is better than no use to participants with subacute or chronic OVF (SMD, -0.99; 95% CIs, -1.32 to -0.65). (Figure 5, Table 3).

Quality of life

Trials used several different scales to measure this outcome. After comparing with other measurements, we pooled data of Oswestry disability index (ODI) scale in Kim's study and Well-being score in Pfeifer's studies. The data of the latter one was multiplied by -1. There is low quality evidence (3RCTs, N = 212) that using brace is much better than no use (SMD, -1.24; 95% CIs, -2.10 to -0.38; Heterogeneity: P = 0.0004, I^2 = 83%), very low quality evidence (1 RCT, N = 42) that using TLSO-rigid or soft brace is no better than no use to subjects with acute OVF (TLSO-rigid: SMD, -0.49; 95%CIs, -1.39 to 0.41. Soft: SMD, -0.20; 95%CIs, -1.13 to 0.74) and low quality evidence (2 RCTs, N = 170) that middle term use of Spinomed is better than no use to participants with subacute or chronic OVF (SMD, -1.96; 95% CIs, -2.34 to -1.58). (Figure 6, Table 3).

Compare between braces

Totally 2 RCTs were included in this analysis, recruited participants with acute OVFs. They investigated short term (2 weeks) use of Spinomed orthosis and middle term (12 weeks) use of TLSO-rigid, with soft brace as a contrast.

Pain

Li’s study used a “10-point scale” system to measure the pain while Kim et al used VAS. There is very low quality evidence (2 RCTs, N = 79) that using un-soft orthosis is no better than using soft brace (SMD, -0.38; 95%CIs, -0.83 to 0.07; Heterogeneity: P = 0.82, I^2 = 0%) during short to middle term follow up. (Figure 7, Table 4).

Correction of kyphosis

Li et al measured thoracic kyphosis angle from T5 to T12 with sagittal X-ray photo while Kim et al measured with rate between two sections of vertebral body. Data from the latter one was multiplied by -1. There is very low quality evidence (2 RCTs, N = 38) that using un-soft orthosis is no better than using soft brace (SMD, 0.19; 95%CIs, -0.83 to 1.20; P = 0.17, I^2 = 48%) in short to middle duration follow up. (Figure 8, Table 4).

Quality of life

We chose outcome of ODI from Kim’s study and Functional independence measure-motor score (FIM-motor score) from Li’s study. We multiplied -1 to the outcome of FIM-motor score to make sure all outcomes point to the same direction. There is very low quality evidence (2 RCTs, N = 79) that

using un-soft orthosis is no better than using soft brace (SMD, -0.25; 95%CIs, -0.69 to 0.20; P = 0.80, I^2 = 0%) during short to middle period follow up. (Figure9, Table 4).

Results from descriptive review

The results of narrative analysis were summarized in Table 2.

Sensitivity analysis

Sensitivity analysis found the pooled outcome of quality of life had significant change when we excluded 1 of the 2 trials which have some similarity in data (15). The outcome of sensitivity test showed an improvement in quality of life while using brace, but without statistical significant (SMD, -0.91; 95%CIs, -2.08 to 0.26; P = 0.13). (Figure 10).

We also conducted a sensitivity analysis of including/excluding a pilot RCT in our trial (19). Sinaki et al investigated the effect of posture training support (PTS) for 1 month. In their trial the participants with abnormal computerized dynamic posturography benefits most with PTS. However the pilot RCT only included 7 participants, the huge risk of type 2 error is the main reason why we did not included it in our main analysis. No significant difference found in this and other sensitivity analyses.

Publication bias

Publication bias was undetected. But the number of included studies was too few to come to the conclusion of there were no publication bias. (Figure 11-16).

Discussion

We identified 10 trials in this systematic review, with 4 of them included in meta-analysis. We did not synthesize the result in non-randomized trials since our questions of interests can be answered by RCTs. All trials have high risk in performance bias and most of them have unclear risk in selective bias. Our review evaluated the effect of short and middle term use of orthosis on OVF patients and investigated different effects between orthosis. To subjects with subacute or chronic OVF, pooled results provided a low level quality evidence of using Spinomed orthosis for middle term can bring large and significant improvement in pain, kyphosis angle and quality of life; one case series study indicates there is insignificant improvement in pain and short form health survey-36 with the same kind orthosis. To subjects with acute fracture, the effect of brace remains paradoxical: there is a very low quality evidence proves using TLSO-rigid or soft brace is no better than no use; the indirect evidence indicated orthosis might have little effect, through the comparison across studies (14, 18); a retrospective study indicated a significant improvement in quality of life brought by TLSO-rigid but there was no contrast to exclude the interference factors, like self-healing of participants, and the mean kyphosis angle of participants deteriorated from 11.4° to 17.2° (21). K-T brace might provide some benefit in balance but still needs more study to prove it (20). In summarize, only middle to long term use of Spinomed orthosis is effective in pain reduction, kyphosis angle correction and improvement of quality of life to patients with sub-acute or chronic OVF;

there is insufficient evidence proving short term use of any orthosis or middle term use of other orthosis is effective for OVF patients, the quality of evidence ranges from low to very low.

Inefficiency of orthosis in acute period might cause by the inadequate immobilization and the insufficient compliance ratio brought by their discomfort and complications (17, 21). Even the most rigid brace offers limited restriction because the skin and soft tissues lie between the orthosis and skeletal. The orthosis need to be modified to offer the optimal comfort and the best effect. To some patients the orthosis may just play a role of kinesthetic reminder and psychologically remind the patients to move slowly, for example for the obese patients the brace might be less effective considering the deep and malleable soft tissue, in this domain the soft and the rigid brace may have the same effect (24). Skin complication caused by press is the most common adverse events, other complications includes disuse atrophy of para spinal muscles, limited respiration and vexation character of the braces (24).

The great benefit brought by the Spinomed orthosis to patients with sub-acute OVF might attribute to their proper design and unique mechanism. As their official website introduced, the ergonomically design and flexible straps make them easy to put on and offer relatively more comfort to users. Different from the traditional functions of orthosis, the Spinomed orthosis offer more than immobilization: the primary rationale for their effect is the improvement

in the trunk muscle strength, with a concept of biofeedback mechanism. With stronger trunk muscles, the patients may obtain more erect posture, better performance in balance and mobility and more satisfy with their quality of life. Their advantages of outstanding effect and design encouraged the users to continuously wear them, may explain the phenomenon of the great compliance, which was unique and rarely comparing with other equipment especially when using for a longer period (15-17). Also it does not cause atrophy of back muscle which might be one of the reasons why it can be used for a long period. In some aspects it might be more proper to interpret them as rehabilitation therapies than immobilize equipment.

TLSO-rigid might be one of the most commonly used orthosis in spinal trauma, OVF, deformity, neck/low back pain, adolescent spondylolisthesis and postoperative period. It has an optimal effect in restriction of the motion: lateral bending by 94% and flexion extension by 69% in the lumbar spine, lateral bending by 38% and flexion-extension of 49% in thoracic spine (24). It offers the strong immobilization but insufficient evidence proves its efficacy, the incongruity probability caused by the limited number of studies and participants, the low compliance and incorrect usage. Though in the RCT, which investigated TLSO-rigid, only few participants confessed they did not wear orthosis during sitting position, but it does not mean the other participants used the orthosis correctly besides them. The old in Korean might prefer to sit on the ground and in that posture the orthosis might be easily located on the wrong position, also participants might prefer to wear the brace

loosely bothered by the annoyance and strong restriction to abdomen and respiration. Misuse of orthosis can cause considerable performance bias thus it is critical to locate the brace on the correct position and exert proper press, to avoid the high risk of bias it would be better to conduct a RCT in a hospital environment with supervision of the compliance and correct usage, even just for a short period.

Not every type of orthosis is effective in kyphosis angle correction. We noticed the equipment which can extend the upper spine by exerting a backward force to shoulders and a forward force to thoracic region may be helpful in correcting kyphosis posture, including Spinomed brace, Osteomed brace and even posture taping (6, 15-17, 25-27). Also the brace that can elevate the intra-abdominal pressure may reduce the intradiscal pressure in lumbar spine by almost 30%, which might be helpful to stop the deterioration of collapse of vertebral body (24). As mentioned above, a reduced kyphosis angle should benefits OVF patients in many ways like better balance and mobility, but purely correcting the kyphosis angle cannot guarantee the improvement in balance or mobility. In one RCT investigating posture tape, the intervention group has a significant effect in reducing kyphosis angle but no effect on balance (25).

The mechanism of orthosis reducing pain might be both physical and psychological. Using orthosis may relieve the muscles that stretched by the hyper-kyphosis spine and therefore alleviate the pain caused by that.

Psychological factor is one of the main elements of developing chronic back pain (28). Orthosis may improve balance and strength, allowing patients to attend more social activities; with more lively social life patients can have a better mental condition which also helps pain management.

Social life is a complex environment, improvement in single item like kyphosis angle, balance or muscle strength may not help in improving quality of life. There is low quality evidence that using Spinomed orthosis can obtain significant effect, similar conclusion was obtained in a pilot RCT (19). Very low quality evidence indicates that neither short term use of Spinomed orthosis nor middle term use of TLSO-rigid or soft brace is better than control groups. As mentioned above, the middle to long term use of Spinomed orthosis can be interpreted as a rehabilitation e, so it might be rational to propose a hypothesis that it’s the rehabilitation effect of orthosis, instead of immobilization effect, helps in improvement of quality of life, which is consistency with conclusion of other trials and reviews exploring the effect of rehabilitation exercise (29-31). Conversely, the discomfort and complications caused by overly use of rigid brace might decrease the quality of life (28).

Two systematic reviews investigated the subject recently. Newman et al included osteoporosis and osteopenia participants with or without osteoporotic vertebral fracture (23). They conducted a descriptive review without meta-analysis. Rzewuska et al investigated the effect of conservative treatments to OVF patients on pain relief, included interventions as Spinomed orthosis, soft

brace, medication and other conservative treatment (32). Comparing to Newman’s, our study excluded participants without OVF which can bring a more direct conclusion about the fractured patients. Comparing to Rzewuska’s review, we included 1 more article that compared TLSO-rigid group, soft brace group and control group, which allowed us to indirectly investigate the effect of Spinomed brace to patients with acute OVF; we also probed the effect in correcting kyphosis of spine, which is another critical parameter related to the OVF patients. Excluding those differences our conclusions are similar.

Limitations of this review include the lack of included studies and participants, the existence of both clinical and methodological diversity and limitation in methodology. Only 4 trials were included in meta-analysis and 2 of them were from the same author. It has a risk of overestimating the effect of orthosis, which is indicated by the significant change in sensitivity test. Also, the result of the sensitivity analysis was evidence that proved the untrustworthy of the result. The insufficient sample size reduced the power and decreased the level of evidence. The differences in parameters and equipment elevated the heterogeneity and limited the generalizability of the results. Estimation of some data also raised the risk of imprecision of the results, like participants’ censoring during follow up duration made it inconsistency between numbers of participants in the baseline and that of the

final visit. Bias caused by restriction of language can be assumed as ignorable since no study was excluded purely for that reason.

The characteristics of the braces make the high risk in performance bias and the detection bias almost unavoidable, but authors can reduce the risk of selection bias by adequate implementation and elaboration of procedures of randomization sequence generation and allocation concealment, a cross-over randomized control trial, as Pfeifer et al conducted, may also be a proper study design for this kind of interventions (15, 16).

Conclusion

Middle term use of Spinomed orthosis to patients with subacute OVF helps in relieving pain, correcting kyphosis angle and improving quality of life, but our confidence is limited. The general applicability of other interventions to the clinical setting remains questionable. The choice of orthosis should correspond to the need of patients.

This systematic review revealed the need for high quality RCTs which investigate the effect of brace to acute and subacute OVF, with low risk of bias and big sample size, to obtain more dependable evidence.

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Figures

Figure1. Searching strategy

1. randomized controlled trial[pt]
2. controlled clinical trial[pt]
3. randomized controlled trials[mh]
4. random allocation[mh]
5. double-blind method[mh]
6. single blind method[mh]
7. clinical trial[pt]
8. clinical trials[mh])
9. clinical trial"[tw]
10. latin square[tw])
11. placebos[mh]
12. placebo*[tw]
13. random*[tw]
14. research design[mh:noexp]
15. placebos[mh]
16. evaluation studies[mh]
17. follow-up studies[mh]
18. prospective studies[mh]
19. cross-over studies[mh]
20. control*[tw]
21. prospective*[tw]
22. volunteer*[tw]) NOT ((animal[mh] NOT human[mh])

23. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #21
24. Osteoporosis compression fracture
25. osteoporotic fracture
26. #24 OR #25
27. spine
28. spinal
29. vertebral
30. vertebrae
31. #27 OR #28 OR #29 OR #30
32. Brace
33. protective gear
34. protection
35. orthosis
36. orthoses
37. taping
38. # 32 OR #33 OR #34 OR #35 OR #36 OR #37
39. #23 AND #26 AND #31 AND #38

Figure 2. Flow chart

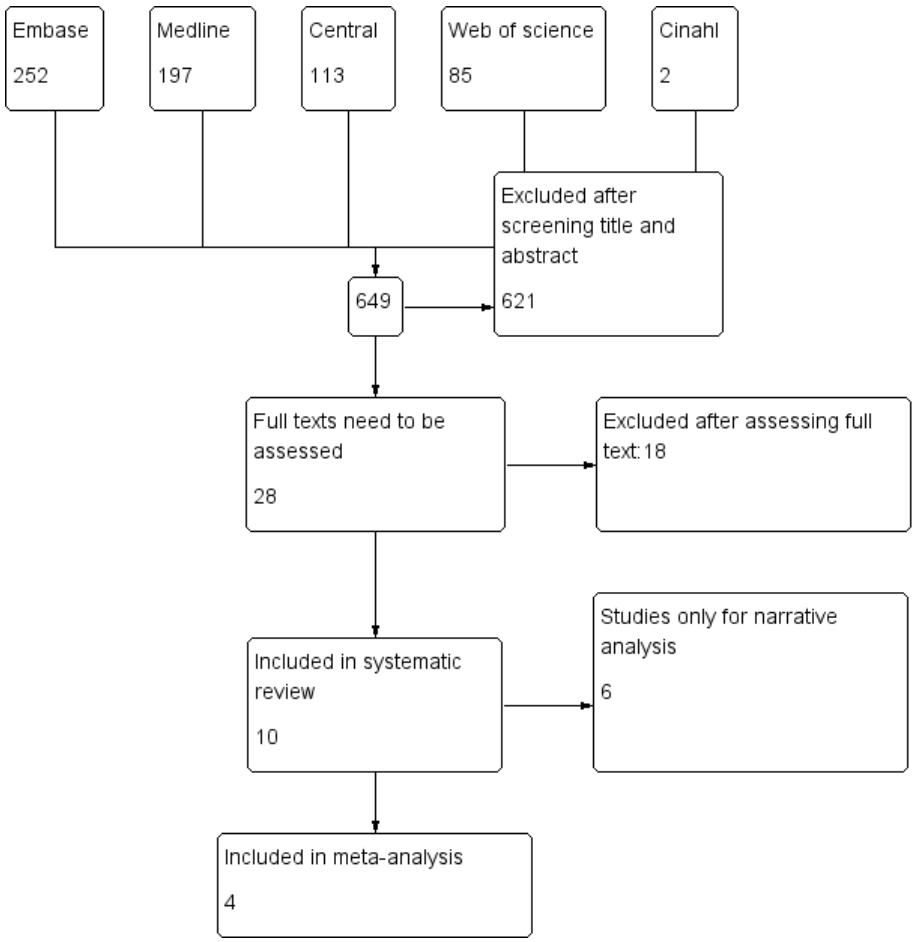


Figure 3. Summary of risk of bias

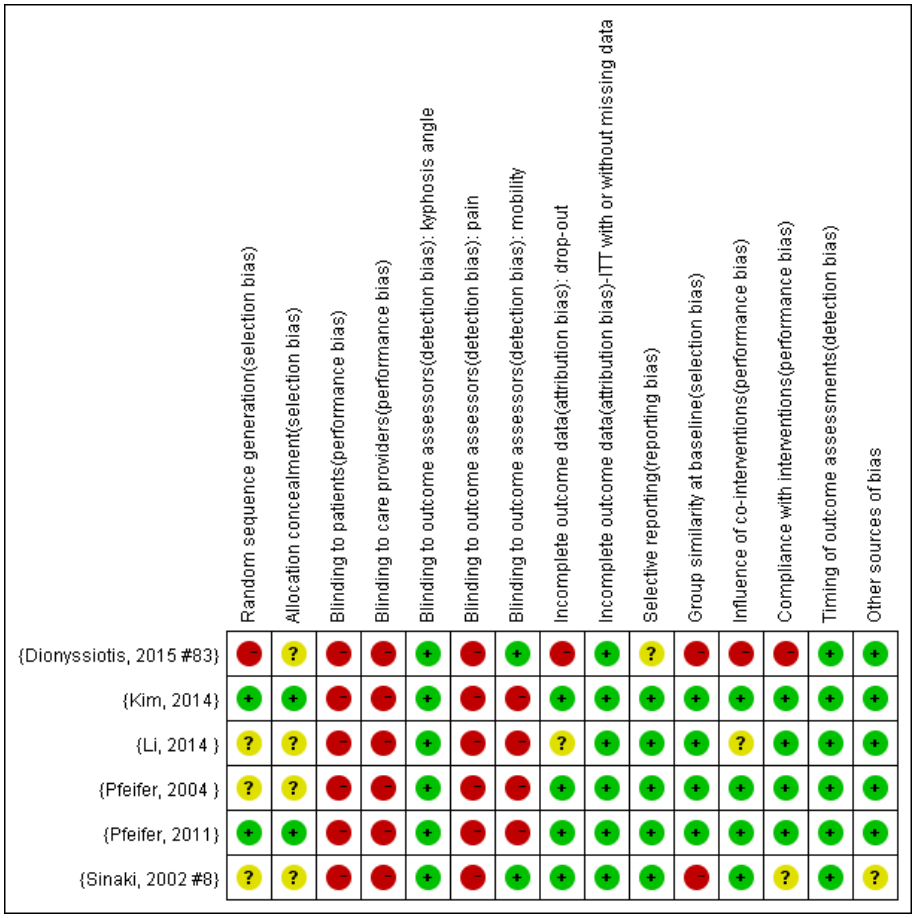


Figure 4. Forest plot. Brace vs no brace on pain reduction.

Pooled data: Using brace is significantly better than no use (SMD -1.02; 95%CIs -1.59 to -0.45; P < 0.05). The effect size is large (SMD > 0.8). Heterogeneity is existent but acceptable (I^2 = 68%, P = 0.03). Subgroup analysis: only Spinomed group has a large and significant effect.

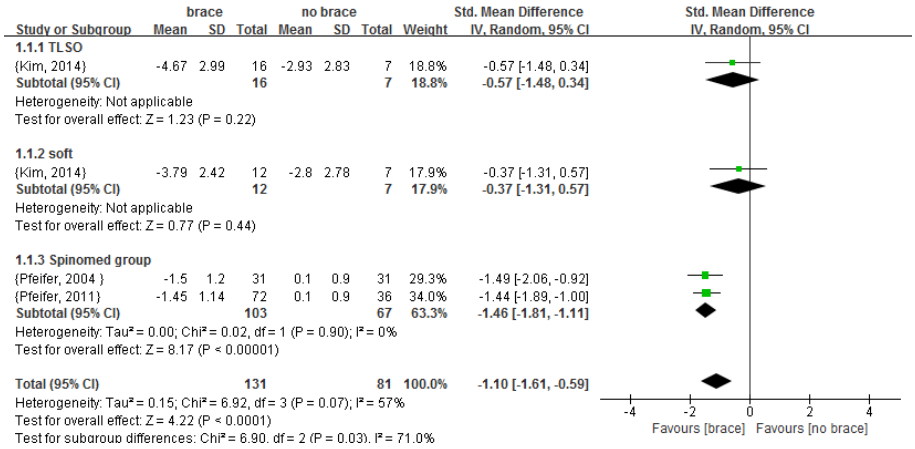


Figure 5. Forest plot. Brace group vs no brace on kyphosis angel correction.

Pooled data: Using brace is significantly better than no use (SMD -0.71; 95%CIs -1.16 to -0.25; P < 0.05). The effect size is moderate (SMD > 0.8). Heterogeneity is existent yet acceptable (I^2 = 53%, P = 0.10). Subgroup analysis: only Spinomed group has a large and significant effect.

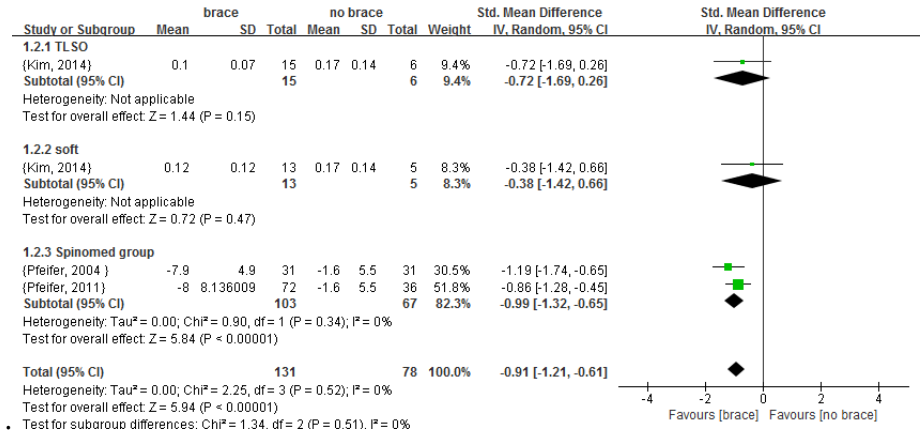


Figure 6. Forest plot. Brace group vs no brace on quality of life.

Pooled data: Using brace is significantly better than no use (SMD -1.16; 95%CIs -2.10 to -0.22; P < 0.05). The effect size is moderate (SMD > 0.8). Heterogeneity is substantial and considerable (I^2 = 87%, P < 0.10). Subgroup analysis: only Spinomed group has a large and significant effect.

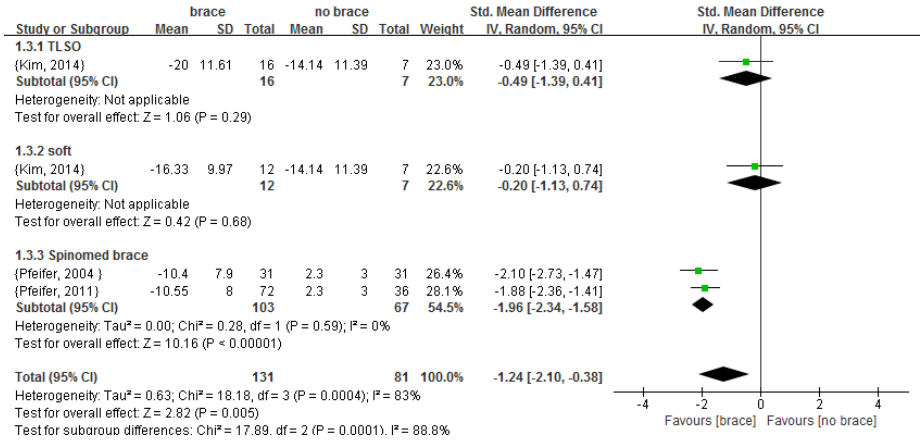


Figure 7. Forest plot. Comparison between braces on pain reduction. Un-soft brace group vs soft brace in pain reduction.

Pooled data: Un-soft brace is not superior to soft brace (SMD -0.35; 95%CIs -0.78 to 0.08; P > 0.05). There is ignorable statistical heterogeneity (I^2 = 0%, P = 0.71) Subgroup analysis: neither TLSO-rigid nor Spinomed brace is better than soft brace.

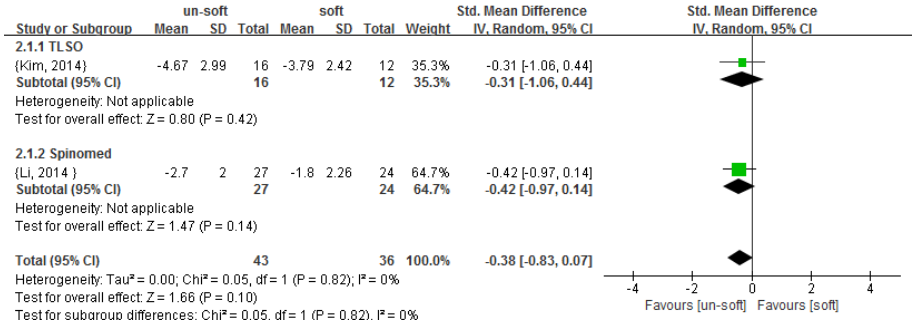


Figure 8. Forest plot. Comparison between braces on kyphosis angle.

Pooled data: Un-soft brace is not superior to soft brace (SMD 0.17; 95%CIs -0.55 to 0.89; P > 0.05). There is ignorable statistical heterogeneity (I^2 = 17%, P = 0.27) Subgroup analysis: Neither TLSO-rigid nor Spinomed brace is better than soft brace.

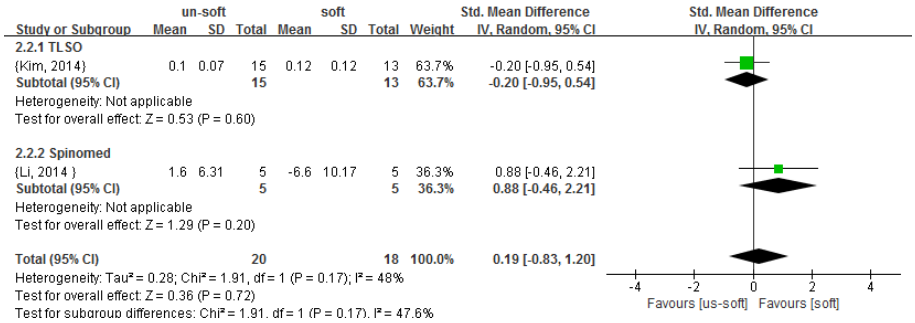


Figure 9. Forest plot. Comparison between studies on quality of life.

Pooled data: Un-soft brace is not superior to soft brace. (SMD -0.27; 95%CIs -0.70 to 0.16; P > 0.05) There is ignorable statistical heterogeneity (I^2 = 0%, P = 0.72) Subgroup analysis: neither TLSO-rigid nor Spinomed brace is better than soft brace.

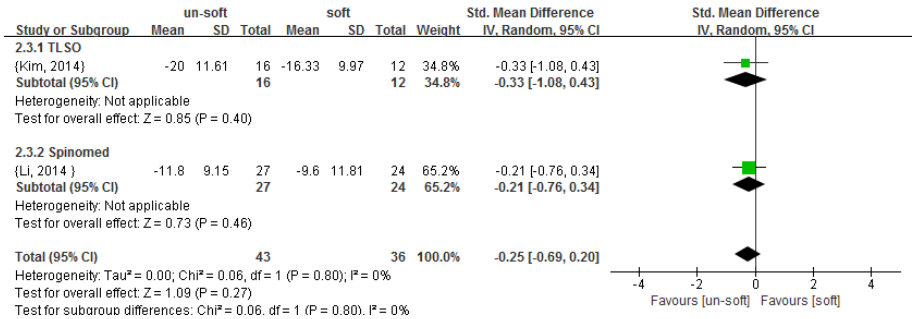


Figure 10. Forest plot. Quality of life.
Sensitivity test excluding one of the two trials reported by one author with some similarity in data. The figure shows sensitivity analysis after excluding one of the two trials which reported by same author with some similarity in data. Pooled data: using brace is not superior to no use (SMD -0.93; 95%CIs, -2.04, 0.18; P > 0.05), different from the main outcome (SMD -1.04; 95%CIs -1.95 to -0.39; P < 0.05).

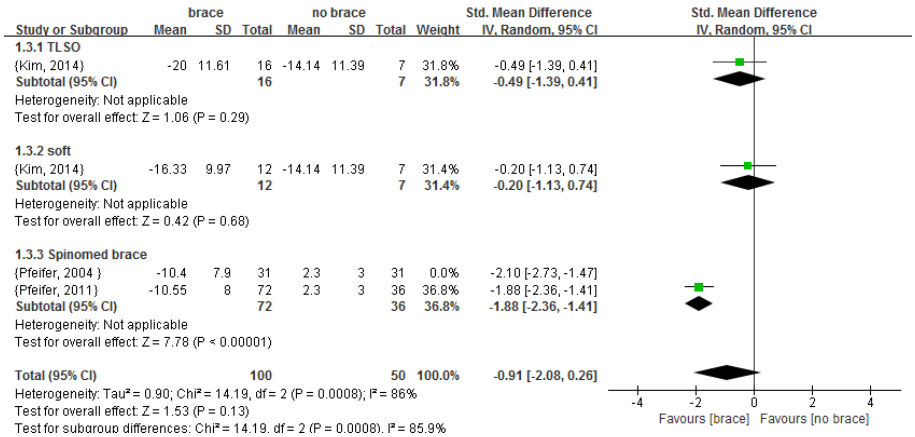


Figure 11. Funnel plot. Comparison: brace vs no brace, Outcome：pain reduction. Publication bias undetected.

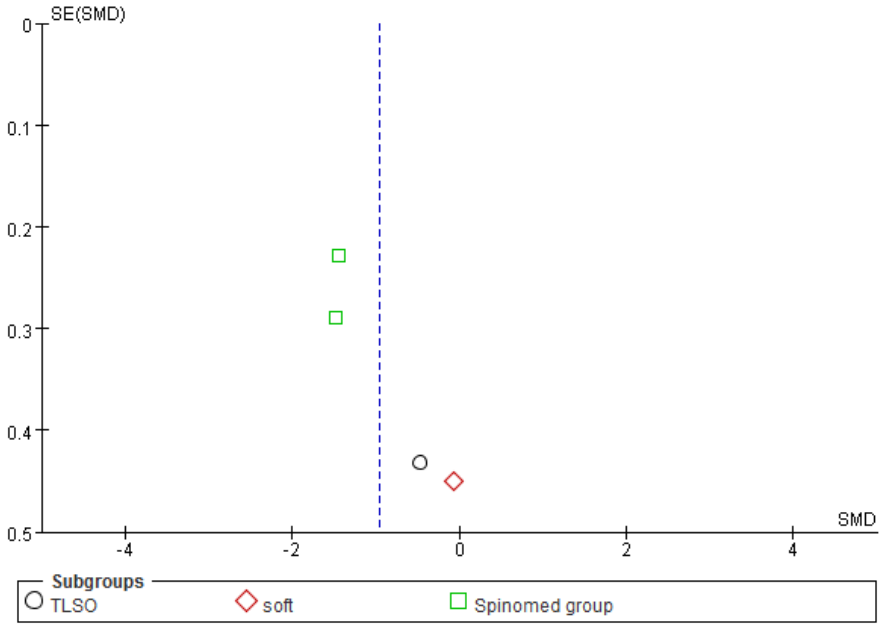


Figure 12. Funnel plot. Comparison: brace vs no brace. Outcome: kyphosis angle.Publication bias undetected.

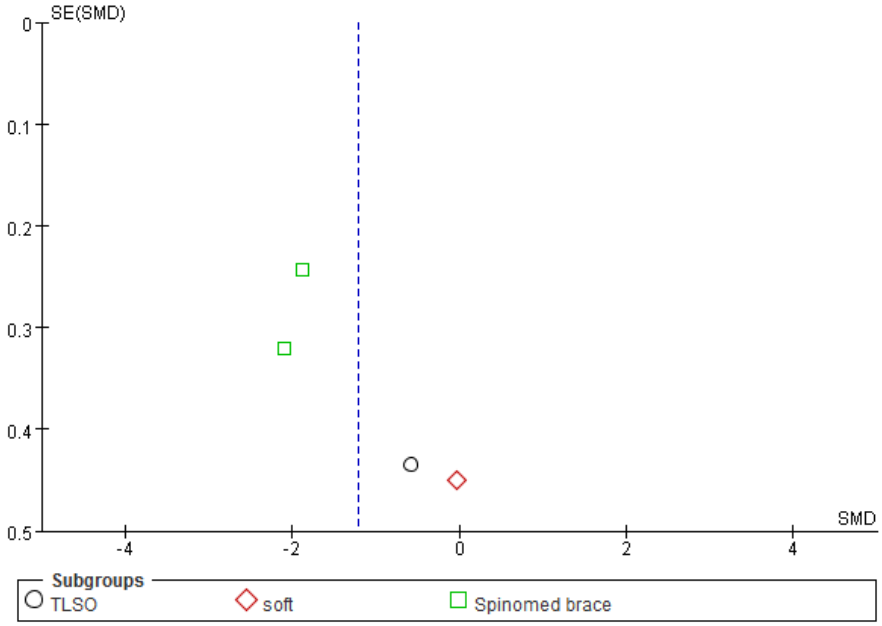


Figure 13. Funnel plot. Comparison: brac vs no brace. Outcome: Quality of life. Publication bias undetected.

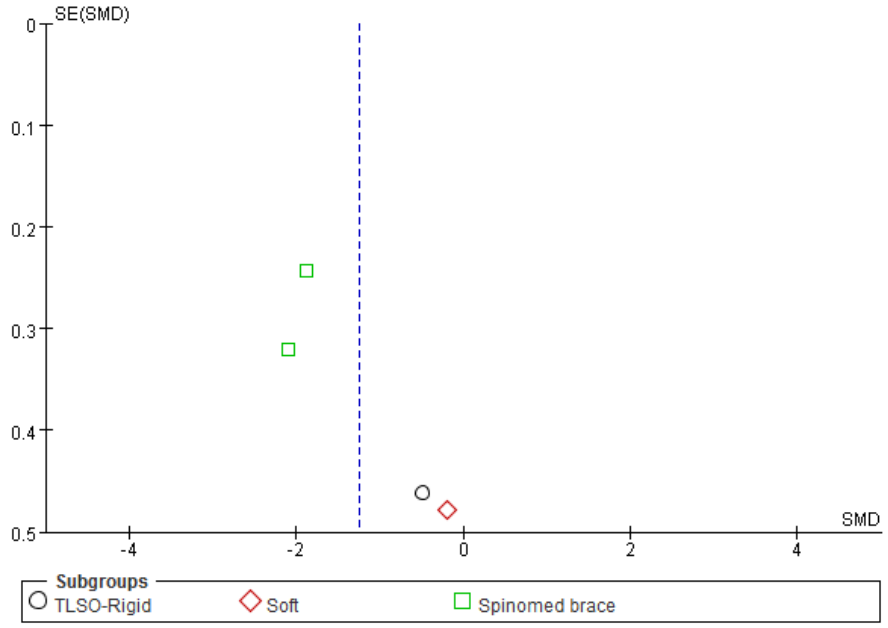


Figure 14. Funnel plot. Comparison: un-soft brace vs soft brace, Outcome: pain reduction.Publication bias undetected.

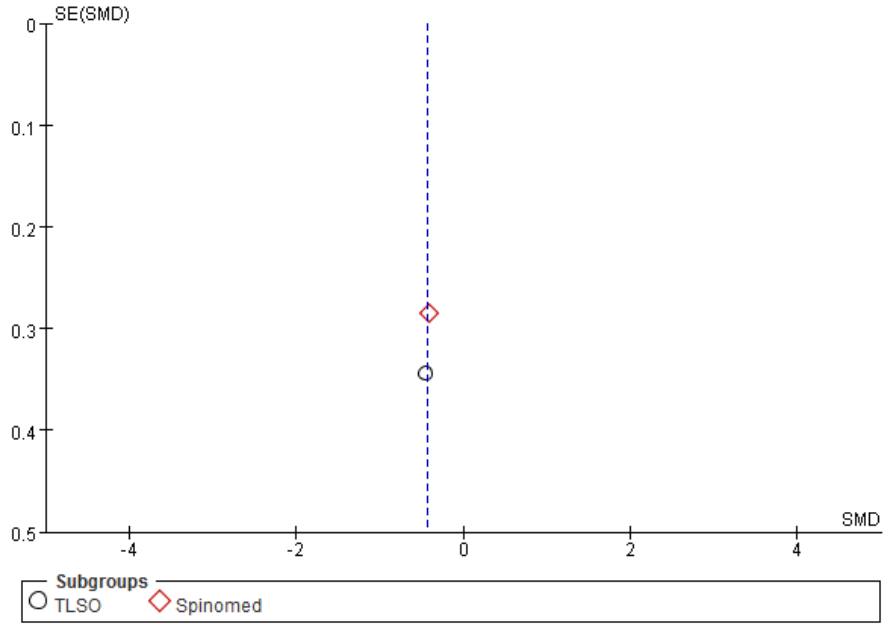


Figure 15. Funnel plot. Comparison: un-soft brace vs soft brace. Outcome: kyphosis angle.Publication bias undetected.

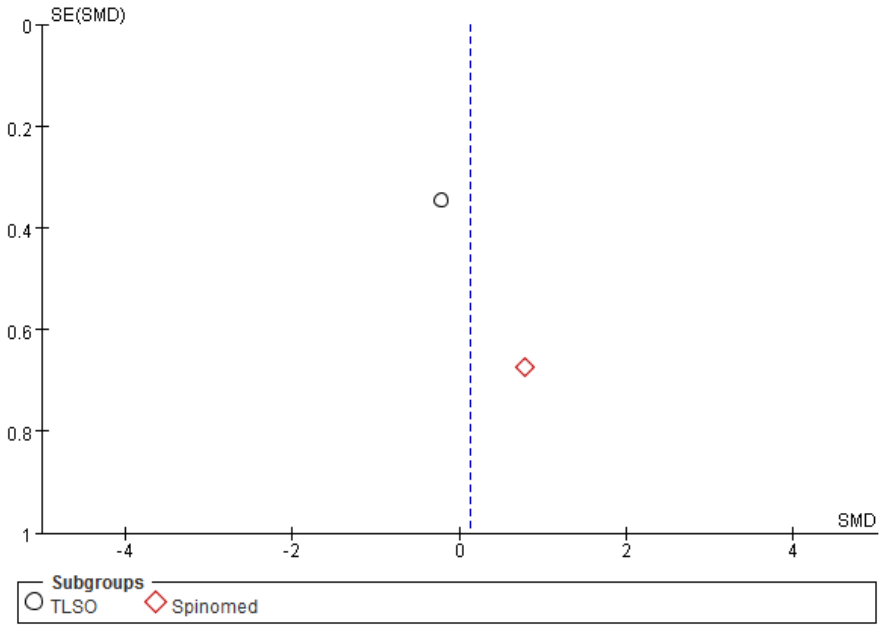
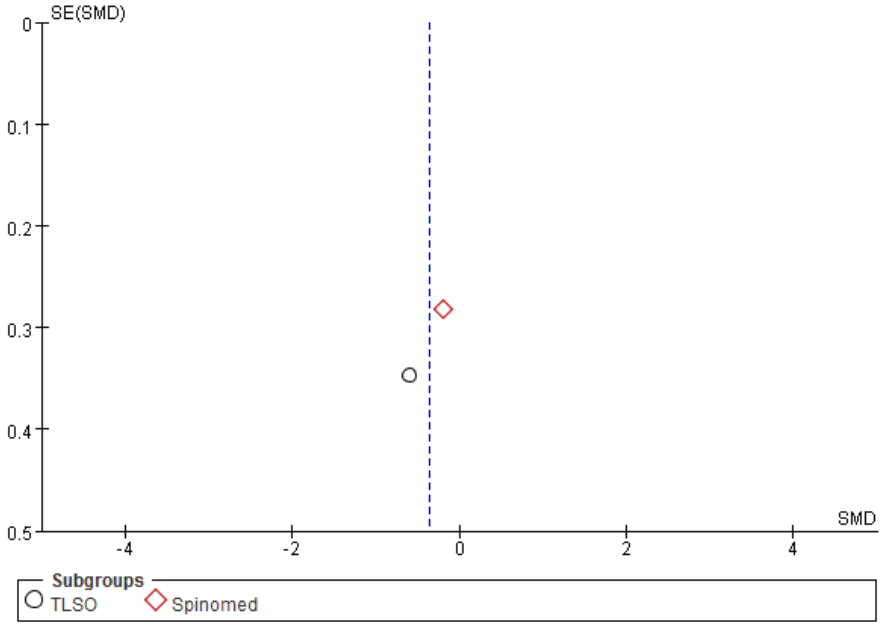


Figure 16. Funnel plot. Comparison: un-soft brace vs soft brace. Outcome：quality of life.Publication bias undetected.



Tables

Table 1. Characteristics of studies included in MA

Study ID	Study design	Participants number	Phase of fracture	Participants source	Intervention	Follow up duration
Kim et al., 2014	RCT	60	Acute	Hospital	Soft brace: 8 wk Rigid brace: 8 wk Control group: no brace	12 wk
Li et al., 2014	RCT	51	Acute	Hospital	Group 1: TLSO, the1st week; SpinoMed, the 2nd and the 3rd week Group 2: TLSO, the 1st week; Soft brace, the 2nd and the 3rd week	3 wk
Pfeifer et al., 2011*	RCT	108	Subacute	Community	Group 1: Spinomed orthosis, 12 mon Group 2: Spinomed active orthosis, 12 mon Group 3: no brace	12 mon
Pfeifer et al., 2004*	RCT	62	Subacute	Community	Group 1: Spinomed, 12 mon Group 2: no brace	12 mon

*This trial was designed as a cross-over study. We extracted the data before cross-over procedure, on the 6th month.

Table 2. Characteristics of studies included in study but excluded from MA

Study ID	Study type	Participants number	Phase of fracture	Participants source	Interventions	Follow up duration	Conclusion
Dionyssiots et al.，2015*	RCT	50	Subacute	Hospital	Group 1: Semi-rigid orthosis Group 2: Elastic orthosis Group 3: Control group	6 mon	Wearing Spinomed orthosis decreased back pain significantly and increased trunk muscle strength significantly.
Sinaki and Lynn, 2002	Pilot RCT	7	NA	Hospital	Group 1: PTS + Exercise Group 2: Exercise	1 mon	Subjects who had abnormal balance had the most significant improvement in balance.
Valentin et al., 2014	Case series study	13	NA	NA	Spinomed III	3 mon	The improvement in the back extensor strength was significant; but not in pain or physical function.
Talic et al., 2012	N-RCT	59	NA	Hospital	Group 1: Three-point orthosis Group 2: Plaster corset	1-4 mon	Plaster corset offered stability; but patients with orthoses were more mobile. Duration of immobilization was significantly longer in orthosis group.
Murata et al., 2012	Retrospective study	55	Acute	Hospital	Plastic TLSO orthosis	6 mon	TLSO promoted the healing of OVF. Mean kyphosis angle deteriorated from 11.4° to 17.2°.
Liaw et al., 2009	Case series study	47	NA	Hospital	Knight-Taylor orthosis	Immediately	Knight-Taylor brace improved in static and dynamic motor balance but decreased the directional control.

MA, meta-analysis; RCT, randomized controlled trial; PTS, posture training support; NA, not available; TLSO, thoracolumbar sacral orthosis; N-RCT, non-randomized controlled trial.

*The data reported in this article was insufficient to be included in meta-analysis.

Table 3. Summary of findings (SOF) table of brace vs. no brace

Outcomes	Anticipated absolute effects (95% CI)	No. of participants (studies)	Overall quality of evidence (GRADE)
Pain reduction-pooled data	SMD 1.1 fewer (1.61 fewer to 0.59 fewer)	212 (3 studies)	⊕⊕◯◯ LOW[*,†]
Pain reduction-TLSO	SMD 0.57 fewer (1.48 fewer to 0.34 more)	23 (1 study)	⊕◯◯◯ VERY LOW[‡,§]
Pain reduction-soft brace	SMD 0.37 fewer (1.31 fewer to 0.57 more)	19 (1 study)	⊕◯◯◯ VERY LOW[‡,§]
Pain reduction-Spinomed group	SMD 1.46 fewer (1.81 fewer to 1.11 fewer)	170 (2 studies)	⊕⊕◯◯ LOW[‖,†]
Kyphosis angle-pooled data	SMD 0.91 fewer (1.21 fewer to 0.61 fewer)	209 (3 studies)	⊕⊕◯◯ LOW[¶,†]
Kyphosis angle-TLSO	SMD 0.72 fewer (1.69 fewer to 0.26 more)	21 (1 study)	⊕◯◯◯ VERY LOW[**,§]
Kyphosis angle-soft brace	SMD 0.38 fewer (1.42 fewer to 0.66 more)	18 (1 study)	⊕◯◯◯ VERY LOW[**,§]
Kyphosis angle-Spinomed group	SMD 0.99 fewer (1.32 fewer to 0.65 fewer)	170 (2 studies)	⊕⊕◯◯ LOW[†,††]
Quality of life-pooled data	SMD 1.24 fewer (2.1 fewer to 0.38 fewer)	212 (3 studies)	⊕◯◯◯ VERY LOW[*,†,††]
Quality of life-TLSO	SMD 0.49 fewer (1.39 fewer to 0.41 more)	23 (1 study)	⊕◯◯◯ VERY LOW[‡,§]
Quality of life-soft brace	SMD 0.2 fewer (1.13 fewer to 0.07 more)	19 (1 study)	⊕◯◯◯ VERY LOW[‡,§]
Quality of life-Spinomed brace	SMD 1.96 fewer (2.34 fewer to 1.58 fewer)	170 (2 studies)	⊕⊕◯◯ LOW[‖,†]

CIs, confidence intervals; SMD, standardized mean difference; RCT, randomized controlled trial; TLSO, thoracolumbar sacral orthosis.

[*]Serious study limitation: three trials were included, with high risk of performance bias and detection bias;

[†]Serious imprecision: sample size was smaller than 400;

[‡]Serious study limitation: one trial was included, with high risk of detection bias and performance bias;

[§]Very serious imprecision: sample size was too small and CIs was wide;

[‖] Serious study limitation: two trials were included, with high risk of performance bias and detection bias;

[¶]Serious study limitation: three trials were included, with high risk of performance bias;

[**]Serious study limitation: one trial was included, with high risk of performance bias;

[††]Serious study limitation: two trials were included, with high risk of performance bias;

[‡‡]Very serious inconsistency: the statistical heterogeneity was large (I^2 > 80%) and the clinical heterogeneity existed.

Table 4. Summary of findings (SOF) table of un-soft brace vs. soft brace

Outcomes	Anticipated absolute effects (95% CIs)	No. of participants (studies)	Overall quality of evidence (GRADE)
Pain reduction-pooled data	SMD 0.38 fewer (0.83 fewer to 0.07 more)	79 (2 studies)	⊕◯◯◯ VERY LOW[*,†,‡]
Pain reduction-TLSO	SMD 0.31 fewer (1.06 fewer to 0.44 more)	28 (1 study)	⊕◯◯◯ VERY LOW[§, ‖]
Pain reduction-Spinomed orthosis	SMD 0.42 fewer (0.97 fewer to 0.14 more)	51 (1 study)	⊕⊕◯◯ LOW[¶,‡]
Kyphosis angle-pooled data	SMD 0.19 fewer (0.83 fewer to 1.2 more)	38 (2 studies)	⊕◯◯◯ VERY LOW[**,†, ‖]
Kyphosis angle-TLSO	SMD 0.2 fewer (0.95 fewer to 0.54 more)	28 (1 study)	⊕◯◯◯ VERY LOW[††, ‖]
Kyphosis angle-Spinomed orthosis	SMD 0.88 more (0.46 fewer to 2.21 more)	10 (1 study)	⊕◯◯◯ VERY LOW[‡‡, ‖]
Quality of life-pooled data	SMD 0.25 fewer (0.69 fewer to 0.02 more)	79 (2 studies)	⊕◯◯◯ VERY LOW[*,†,‡]
Quality of life-TLSO	SMD 0.33 fewer (1.08 fewer to 0.43 more)	28 (1 study)	⊕◯◯◯ VERY LOW[§, ‖]
Quality of life-Spinomed brace	SMD 0.21 fewer (0.76 fewer to 0.34 more)	51 (1 study)	⊕⊕◯◯ LOW[¶,‡]

CIs, confidence intervals; SMD, standardized mean difference; RCT, randomized controlled trial; TLSO, thoracolumbar sacral orthosis.

[*]Serious study limitation: two trials were included, with high risk of performance bias and detection bias;

[†]Serious inconsistency: measurement time was different between studies;

[‡]Serious imprecision: sample size was smaller than 400;

[§]Serious study limitation: one study was included, with high risk of performance bias and detection bias;

|| Very serious imprecision: sample size was too small and CIs was wide;

¶Serious study limitation: one study was included, with high risk of performance and detection bias;

**Serious study limitation: two trials were included, with high risk of performing bias;

††Serious study limitation: one study was included, with high risk of performance bias;

‡‡Serious study limitation: one study was included, with high risk of performance bias and unclear risk of selection bias.

Table 5. Rationales for the judgement of the risk of bias

Study ID: Kim, 2014	Level	Quote
Random sequence generation (Selection bias)	Low risk of bias	"This randomization was performed using a computer-generated randomization list, which was concealed from the first author (H.-J.K.) before the randomized allocation." Criteria quote: A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with 2 groups), rolling a dice (for studies with 2 or more groups), drawing of balls of different colors, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, preordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and preordered list of treatment assignments.
Allocation concealment (Selection bias)	Low risk of bias	"This randomization was performed using a computer-generated randomization list, which was concealed from the first author (H.-J.K.) before the randomized allocation." Criteria quote: Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.
Blinding to patients (Performance bias)	High risk of bias	The character of intervention. Criteria quote: Index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.
Blinding to care provider (Performance bias)	High risk of bias	The character of intervention. Criteria quote: Index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful.
Blinding to outcome assessors (Detection bias) - kyphosis angle	Low risk of bias	The outcome measurement was objective, which means it was less likely to be influenced by the failure of blinding. Criteria quote: for outcome criteria that do not suppose a contact with participants (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome.
Blinding to outcome assessors (Detection bias) - pain	High risk of bias	The outcome measurement was subjective and was easily influenced by the failure of blinding. Criteria quote: for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored ''yes''.
Blinding to outcome assessors (Detection bias) - quality of life	High risk of bias	The outcome measurement was subjective and was easily influenced by the failure of blinding. Criteria quote: for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the

		blinding procedure is adequate for outcome assessors if participant blinding is scored ‘‘yes’’.
Incomplete outcome data (Attribution bias): drop-out	Low risk of bias	The lost ratio is 13.3%. Criteria quote: The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a ‘‘yes’’ is scored.
Incomplete outcome data (Attribution bias) - ITT* or modified ITT	Low risk of bias	“All data were evaluated with use of intention-to treat analysis.” Criteria quote: All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of noncompliance and co-interventions.
Selective reporting (Reporting bias)†	Low risk of bias	Undetected. Criteria quote: The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified.
Group similarity at baseline (Selection bias)	Low risk of bias	“The baseline characteristics of the participants were similar among the three groups.” Criteria quote: Groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s).
Influence of co-interventions (Performance bias)	Low risk of bias	“There was no significant difference in opioids use among the three groups at twelve weeks.” Criteria quote: If there were no co interventions or they were similar between the index and control groups.
Compliance with interventions (Performance bias)	Low risk of bias	“On the basis of self-reported compliance, one patient in the soft-brace group and one patient in the rigid-brace group admitted to not wearing the brace in the sitting position during the twelve-week follow-up period; however, these patients wore the rigid or soft brace in the standing or walking positions.” Criteria quote: The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered for several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (e.g., surgery), this item is irrelevant.
Timing of outcome assessments (Detection bias)	Low risk of bias	“At the twelve-week assessment, complete data were available for forty-nine (81.7%) of the sixty participants.” Criteria quote: Timing of outcome assessment should be identical for all intervention groups and for all primary outcome measures.

Other sources of bias	Low risk of bias	"The funds were used to pay for salaries and conference expenses. The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript." Criteria quote: 1, When the outcome measures were not valid. There should be evidence from a previous or present scientific study that the primary outcome can be considered valid in the context of the present. 2, Industry-sponsored trials. The conflict of interest (COI) statement should explicitly state that the researchers have had full possession of the trial process from planning to report without funders with potential COI having any possibility to interfere in the process. If, for example, the statistical analyses have been done by a funder with a potential COI, usually ''unsure'' is scored.

ITT, intention to treat.

*Three principles of "intention to treat": 1, Keep participants in the intervention groups to which they were randomized, regardless of the intervention they actually received. 2, Measure outcome data on all participants. 3, Include all randomized participants in the analysis. The first one is widely acceptable, the second one is impossible, the third one is contentious. — in our review our criteria for ITT is the trial which fulfill the first principle, which means no matter with or without missing data.

†Reporting bias should be examined by comparison between protocol and published article but no protocol was found, so we compared the outcomes in method section with those whose results were reported.

Study ID: Li, 2014	Risk of bias	Quote
Random sequence generation (Selection bias)	Unclear risk of bias	Not mentioned.
Allocation concealment (Selection bias)	Unclear risk of bias	Not mentioned.
Blinding to patients (Performance bias)	High risk of bias	The character of intervention.
Blinding to care providers (Performance bias)	High risk of bias	The character of intervention.
Blinding to outcome assessors (Detection bias) - kyphosis angle	Low risk of bias	The outcome measurement was objective, which means it was less likely to be influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - pain	High risk of bias	The outcome measurement was subjective and easily influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - quality of life	High risk of bias	The outcome measurement was subjective and easily influenced by the failure of blinding.

Incomplete outcome data (Attribution bias): drop-out	Unclear risk of bias	Kyphosis outcome only reported in 10 subjects.
Incomplete outcome data (Attribution bias) - ITT* or modified ITT	Low risk of bias	Outcomes of participants were reported as their allocation.
Selective reporting (Reporting bias)	Low risk of bias	Undetected.
Group similarity at baseline (Selection bias)	Low risk of bias	"The levels of vertebral fracture were different among patients." But the difference was deemed tolerable by reviewer.
Influence of co-interventions (Performance bias)	Unclear risk of bias	Participants were worn TLSO for 1st week and wore soft and Spinomed for the 2nd and the 3rd weeks. Did not mention the compliance of interventions.
Compliance with interventions (Performance bias)	Low risk of bias	"This study had evaluated the efficacy of SpinoMed® orthosis by a prospective and randomized control trial, with the subjects' compliance monitored by clinicians in hospital."
Timing of outcome assessments (Detection bias)	Low risk of bias	3 weeks (1 week TLSO, 2 weeks Spinomed orthosis or soft brace).
Other sources of bias	Low risk of bias	"This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors."

ITT, intention to treat; TLSO, thoracolumbar sacral orthosis.

Study ID: Pfeifer, 2004	**Risk of bias**	**Quote**
Random sequence generation (Selection bias)	Unclear risk of bias	Not mentioned.
Allocation concealment (Selection bias)	Unclear risk of bias	Not mentioned.
Blinding to patients (Performance bias)	High risk of bias	The character of intervention.
Blinding to care providers (Performance bias)	High risk of bias	The character of intervention.
Blinding to outcome assessors (Detection bias) - kyphosis angle	Low risk of bias	The outcome measurement was objective, which means it was less likely to be influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - pain	High risk of bias	The outcome measurement was subjective and was easily influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - quality of life	High risk of bias	The outcome measurement (questionnaire) was subjective and easily influenced by the failure of blinding.
Incomplete outcome data (Attribution bias): drop-out	Low risk of bias	No lost data on the 6th month.
Incomplete outcome data (Attribution bias) - ITT* or modified ITT	Low risk of bias	The baseline data and change value from baseline on the 6th months was reported according to participants' initial allocation.

Selective reporting (Reporting bias)	Unclear risk of bias	Seemed to have identical data with the article published on 2011.
Group similarity at baseline (Selection bias)	Low risk of bias	"Both groups were comparable concerning age, height, weight, number of vertebral fractures, loss of height since the age of 25, number of non-vertebral fractures, and falls within the previous 2 yrs. In addition, concomitant diseases and concomitant medications were distributed similarly. Specifically, the use of analgesics was sporadic in both groups."
Influence of co-interventions (Performance bias)	Low risk of bias	"Specifically, the use of analgesics was sporadic in both groups. Five women in group A took analgesics two or three times a weeks, whereas three women in group B used analgesics two or three times a week."
Compliance with interventions (Performance bias)	Low risk of bias	"The overall compliance of the study participants was excellent: all 62 study subjects completed at least 6 mos of intervention each, and another 28 subjects continued for a 12-mo period."
Timing of outcome assessments (Detection bias)	Low risk of bias	6 months.
Other sources of bias	Low risk of bias	"Medi-Bayreuth had no control over the decision to approve or submit the manuscript for publication."

ITT, intention to treat.

Study ID: Pfeifer, 2011	**Risk of bias**	**Quote**
Random sequence generation (Selection bias)	Low risk of bias	"The randomization of study subjects was performed externally by a statistical consultant bureau."
Allocation concealment (Selection bias)	Low risk of bias	"The randomization of study subjects was performed externally by a statistical consultant bureau."
Blinding to patients (Performance bias)	High risk of bias	The character of intervention.
Blinding to care providers (Performance bias)	High risk of bias	The character of intervention.
Blinding to outcome assessors (Detection bias) - kyphosis angle	Low risk of bias	The outcome measurement was objective, which means it was less likely to be influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - pain	High risk of bias	The outcome measurement was subjective and easily influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - quality of life	High risk of bias	The outcome measurement (questionnaire) was subjective and easily influenced by the failure of blinding.
Incomplete outcome data (Attribution bias): drop-out	Low risk of bias	Data remains intact.
Incomplete outcome data (Attribution bias) - ITT* or modified ITT	Low risk of bias	"All study subjects, who were initially randomized and received an orthosis, had been included into the analysis (intention-to-treat analysis)."

Selective reporting (Reporting bias)	Unclear risk of bias	Seemed to have identical data with article reported on 2004.
Group similarity at baseline (Selection bias)	Low risk of bias	Concomitant diseases and concomitant medications were distributed similarly.
Influence of co-interventions (Performance bias)	Low risk of bias	"Specifically, the use of analgesics was sporadic in all groups. Only five women in group A (14%) took analgesics on a daily basis, three women in group B (8%) used analgesics, and five (14%) women in group C took medications for pain relief."
Compliance with interventions (Performance bias)	Low risk of bias	"The overall compliance of the study participants was excellent: 105 study subjects completed at least 6 mos of intervention each, and another 100 subjects continued over a 12-mo period."
Timing of outcome assessments (Detection bias)	Low risk of bias	6 months.
Other sources of bias	Low risk of bias	"Financial disclosure statements have been obtained, and no conflicts of interest have been reported by the authors or by any individuals in control of the content of this article."

ITT, intention to treat.

Study ID: Dionyssiotis, 2015	**Risk of bias**	**Quote**
Random sequence generation (Selection bias)	High risk of bias	"As controls, women who denied wearing the prescribed orthosis were enrolled."
Allocation concealment (Selection bias)	Unclear risk of bias	Not mentioned.
Blinding to patients (Performance bias)	High risk of bias	The character of intervention.
Blinding to care providers (Performance bias)	High risk of bias	The character of intervention.
Blinding to outcome assessors (Detection bias) - kyphosis angle	Low risk of bias	The outcome measurement was objective, which means it was less likely to be influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - pain	High risk of bias	The outcome measurement was subjective and easily influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - quality of life	Low risk of bias	The computer measuring system minimized the influence caused by failure of blinding.
Incomplete outcome data (Attribution bias): drop-out	High risk of bias	Only reported part of participants' data.
Incomplete outcome data (Attribution bias) - ITT* or modified ITT	Low risk of bias	Outcomes of participants were reported as their allocation.
Selective reporting (Reporting bias)	Unclear risk of bias	No protocol found but result was significantly insufficiently reported according to their study design. Quote: "Our purpose was to repeat a clinical trial using similar methods but various orthoses in order to determine generalizability."
Group similarity at	High	"Women of group A (Spinomed) were significantly older,

baseline (Selection bias)	risk of bias	and at the beginning of the study, they felt more pain compared with the control group."
Influence of co-interventions (Performance bias)	High risk of bias	"The effect of some drugs on back pain was not analyzed as controls also took drugs."
Compliance with interventions (Performance bias)	High risk of bias	"The compliance was highest for Spinomed (90%) followed by Osteomed and Spinomed active (50%), while Spine-X showed the lowest compliance of 30%."
Timing of outcome assessments (Detection bias)	Low risk of bias	6 months.
Other sources of bias	Low risk of bias	"This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors."

ITT, intention to treat.

Study ID: Sinaki, 2002	**Risk of bias**	**Quote**
Random sequence generation (Selection bias)	Unclear risk of bias	Not mentioned.
Allocation concealment (Selection bias)	Unclear risk of bias	Not mentioned.
Blinding to patients (Performance bias)	High risk of bias	The character of intervention.
Blinding to care providers (Performance bias)	High risk of bias	The character of intervention.
Blinding to outcome assessors (Detection bias) - kyphosis angle	Low risk of bias	The outcome measurement was objective, which means it was less likely to be influenced by the failure of blinding.
blinding to outcome assessors (Detection bias) - pain	High risk of bias	The outcome measurement was subjective and easily influenced by the failure of blinding.
Blinding to outcome assessors (Detection bias) - quality of life	Low risk of bias	In this study, the clinician performing CDP was blind to the study group assignment of the subjects.
Incomplete outcome data (Attribution bias): drop-out	Low risk of bias	No lost.
Incomplete outcome data (Attribution bias) - ITT* or modified ITT	Low risk of bias	Outcomes of participants were reported as their allocation.
Selective reporting (Reporting bias)	Low risk of bias	Undetected.
Group similarity at baseline (Selection bias)	High risk of bias	There was significant difference in important parameters between groups at the baseline.
Influence of co-interventions (Performance bias)	Low risk of bias	All participants had the exercise.
Compliance with interventions (Performance bias)	Unclear risk of bias	Not mentioned.

Timing of outcome assessments (Detection bias)	Low risk of bias	4 weeks.
Other sources of bias	Unclear risk of bias	Participation in this study was strictly voluntary, and no remuneration was offered or provided to participants.

ITT, intention to treat; PDP, proprioceptive dynamic posture; CDP, computerized dynamic posturography.

Table 6. Formula for handling data.

Formula 1, Formula for combining groups.

	Group 1 (e.g. males)	Group 2 (e.g. females)	Combined groups
Sample size	N_1	N_2	$N_1 + N_2$
Mean	M_1	M_2	$\frac{N_1M_1 + N_2M_2}{N_1 + N_2}$
SD	SD_1	SD_2	$\sqrt{\frac{(N_1 - 1)SD_1^2 + (N_2 - 1)SD_2^2 + \frac{N_1N_2}{N_1 + N_2}(M_1^2 + M_2^2 - 2M_1M_2)}{N_1 + N_2 - 1}}$

Formula 2, Formula used for estimation of the standard deviations of change value from baseline.

$$\text{SDchange} = \sqrt{SDbaseline^2 + SDfinal^2 - (2 \times Corr \times SD\text{baseline} \times \text{SDfinal})}$$

논문초록

골다공증성 척추골절에 대한 보조기의 효과: 체계적 문헌고찰과 메타분석

연구목적

골다공증성 척추골절 환자에게 체계적으로 문헌고찰과 메타 분석을 통해 보조기의 효과를 조사하는 것이다.

선행연구문헌 요약

골다공증성 척추골절에서 보조기의 효능에 대해 이견이 있다. 과거에도 보조기의 효능성에 대한 체계적인 문헌고찰이 있었지만 포함된 문헌이 적고 최근에 발표된 무작위 배정 전향적 연구가 포함되어 있지 않았으며 메타분석은 없었다. 기존에 발표된 문헌고찰에는 3개 전향적 연구가 포함되었고, Spinomed 보조기가 통증 또는 장애의 회복에 효과가 있었다는 보고가 있다.

대상 및 방법

골다공증성 척추골절과 보조기와 연관된 검색어로 Medline, Embase, Pubmed Central과 Web of science 등 Database를 두 명의 독립된 저자가 검색하였으며 무작위배정 전향적 연구만 포함 하였다. 검색결과는 다른 체계적 문헌고찰고도 비교하였고, program 은 Revman을 이용 하였고, Random effect model 을 사용하였다. Risk of bias는 Cochrane Back Group에서 추천한 도구를 착용하였고, 신뢰도를 확인하기 위하여 sensitivity test 도 실행하였다. 평가지표로는 보조기에 의한 통증경감, 후만각 교정, 기능향상을 포함하였다.

결과

최종적으로 4개 연구를 분석하였으며, 경성 보조기군이 보조기를 착용하지 않은 군에 비해 통증경감, 후만각 교정 및 기능개선에 효과가 있었다. 그러나 중등도 기간의 보조기착용은 경성보조기나 연성보조기지 각각이 통증이나 후만각 교정에 효과가 없었다. 반경성보조기도 장기 착용시 통증, 후만각교정, 기능개선에 효과가 있다. 또한, 후만각이 심한 골절환자에서 Spinomed 보조기의 장기착용은 역시 통증, 후만각교정 및 기능개선에 효과가 있었다. 근거의 수준은 후만각 교정에 대해서는 중등도였고 통증이나 기능개선에 대해서는 낮은 수준이었다.

결론

골다공증성 척추골절 환자에게 보조기 중기 착용은 통증 감소, 후만각 교정 및 기능개선에 효과가 있다. 그러나, 근거의 수준을 고려할 때 추후 추가적인 전향적 무작위배정 연구가 필요하다.

주요어 :

척추, 골다공증, 골절, 보조기, 메타분석 , 재활치료

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