Int J Clin Exp Med 2017;10(7):9864-9870
www.ijcem.com /ISSN:1940-5901/IJCEM0052379

Review Article

Influence of exercise intervention on pain, quality of life and functional mobility in patients with osteoporotic vertebral fractures: a systematic review and meta-analysis

Tao Liu*, Lei Sheng*, Zhengu Huang

Department of Orthopaedics, The People's Hospital of Dazu District Chongqing, Chongqing 400016, P. R. China.
**Equal contributors.*

Received March 7, 2017; Accepted May 31, 2017; Epub July 15, 2017; Published July 30, 2017

Abstract: Background: Exercise intervention might be beneficial to the patients with osteoporotic vertebral fractures. However, the results remained controversial. We conducted a systematic review and meta-analysis to explore the effect of exercise intervention on pain, quality of life and functional mobility of patients with osteoporotic vertebral fractures. Methods: PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases were systematically searched. Randomized controlled trials (RCTs) assessing the effect of exercise intervention on osteoporotic vertebral fractures were included. Two investigators independently searched articles, extracted data, and assessed the quality of included studies. The primary outcome was pain scores Meta-analysis was performed using random-effect model. Results: Six RCTs involving 425 patients were included in the meta-analysis. Overall, compared with control intervention, exercise intervention was found to significantly reduce the pain scores (Std. mean difference =-0.95; 95% CI=-1.37 to -0.53; P<0.0001) and improve the quality of life (Std. mean difference =-1.09; 95% CI=-1.86 to -0.31; P=0.006), but demonstrated no influence on timed up and go (Std. mean difference =-0.36; 95% CI=-0.96 to 0.24; P=0.24), physical function (Std. mean difference =-0.32; 95% CI=-0.72 to 0.08; P=0.12). Conclusions: Compared to control intervention, exercise intervention was found to significantly reduce the pain scores and improve the quality of life, but had no influence on timed up and go and physical function.

Keywords: Exercise intervention, pain, quality of life, functional mobility, osteoporotic vertebral fractures

Introduction

Osteoporosis could result in reduced strength and increased risk for fractures because of low bone mineral density and microarchitectural deterioration of bone [1-3]. Vertebral fractures became ubiquitous in osteoporosis patients and they may happen during normal daily activities including stair climbing and bending forward etc. Previous studies reported that the prevalence of morphometric vertebral fractures for patients (≥50 years old) ranged from 7.2% to 12% in men and 7% to 16% in women [4-6]. Osteoporotic vertebral fractures led to back pain, subsequent fractures, low quality of life, disability, kyphosis and high mortality. The back pain was mainly caused by the fractures and secondary changes in the intervertebral joints and the neighboring muscular ligament complex [7-10].

There were pharmacological and non-pharmacological treatment for these osteoporotic vertebral fractures. Anti-osteoporotic medications could decrease fracture risk through improving bone mineral density and influencing bone remodeling [11-13]. Non-pharmacological treatment included physical exercise to improve muscle strength and functional mobility, quality of life and to reduce pain [5, 14, 15]. Exercise was generally straightforward, and widely accepted. Specially designed exercises was recommended for patients with osteoporotic vertebral fractures in order to improve spinal stability and posture [16-18]. Exercise intervention was reported to alleviate pain, improve the quality of patients' life and functional mobility of patients with osteoporotic vertebral fractures [5, 19, 20].

In contrast to this promising finding, however, some relevant RCTs showed that exercise intervention had no influence on pain control and the quality of life for osteoporotic vertebral fractures [5, 21]. Considering these inconsistent effects, we therefore conducted a systematic review and meta-analysis of RCTs to evaluate the effectiveness of exercise intervention on pain, quality of life and functional mobility of patients with osteoporotic vertebral fractures.

Materials and methods

This systematic review and meta-analysis were conducted according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement [22] and the *Cochrane Handbook for Systematic Reviews of Interventions* [23]. All analyses were based on previous published studies, thus no ethical approval and patient consent were required.

Literature search and selection criteria

PubMed, EMbase, Web of science, EBSCO, and the Cochrane library were systematically searched from inception to March 2017, with the following keywords: exercise or physical activity, and osteoporotic vertebral fracture. No limitation was enhanced. To include additional eligible studies, the reference lists of retrieved studies and relevant reviews were also hand-searched and the process above was performed repeatedly until no further article was identified. Conference abstracts meeting the inclusion criteria were also included.

The inclusion criteria were as follows: study population, patients with osteoporotic vertebral fracture; intervention, exercise intervention; control, standard care; outcome measure, pain score; and study design, RCT.

Data extraction and outcome measures

The following information was extracted for the included RCTs: first author, publication year, sample size, baseline characteristics of patients, exercise intervention, control, study design, pain score, quality of life score, timed up and go, and physical function. The author would be contacted to acquire the data when necessary.

The primary outcome was pain score. Secondary outcomes included quality of life score, timed up and go, and physical function.

Quality assessment in individual studies

The Jadad Scale was used to evaluate the methodological quality of each RCT included in this meta-analysis [24]. This scale consisted of three evaluation elements: randomization (0-2 points), blinding (0-2 points), dropouts and withdrawals (0-1 points). One point would be allocated to each element if they have been mentioned in article, and another one point would be given if the methods of randomization and/or blinding had been appropriately described in detail. If methods of randomization and/or blinding were inappropriate, or dropouts and withdrawals had not been recorded, then one point was deducted. The score of Jadad Scale varied from 0 to 5 points. An article with Jadad score ≤ 2 was considered to be of low quality. If the Jadad score ≥ 3, the study was thought to be of high quality [25].

Statistical analysis

Standard Mean differences (Std. MDs) with 95% confidence intervals (CIs) for continuous outcomes (pain score, quality of life score, timed up and go, and physical function) were used to estimate the pooled effects. All meta-analyses were performed using random-effects models with DerSimonian and Laird weights. Heterogeneity was tested using the Cochran Q statistic ($P<0.1$) and quantified with the I^2 statistic, which described the variation of effect size that was attributable to heterogeneity across studies. An I^2 value greater than 50% indicated significant heterogeneity. Sensitivity analysis was performed to detect the influence of a single study on the overall estimate via omitting one study in turn when necessary. Owing to the limited number (<10) of included studies, publication bias was not assessed. $P<0.05$ in two-tailed tests was considered statistically significant. All statistical analyses were performed with Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

Results

Literature search, study characteristics and quality assessment

The flow chart for the selection process and detailed identification was presented in **Figure 1**. 749 publications were identified through the

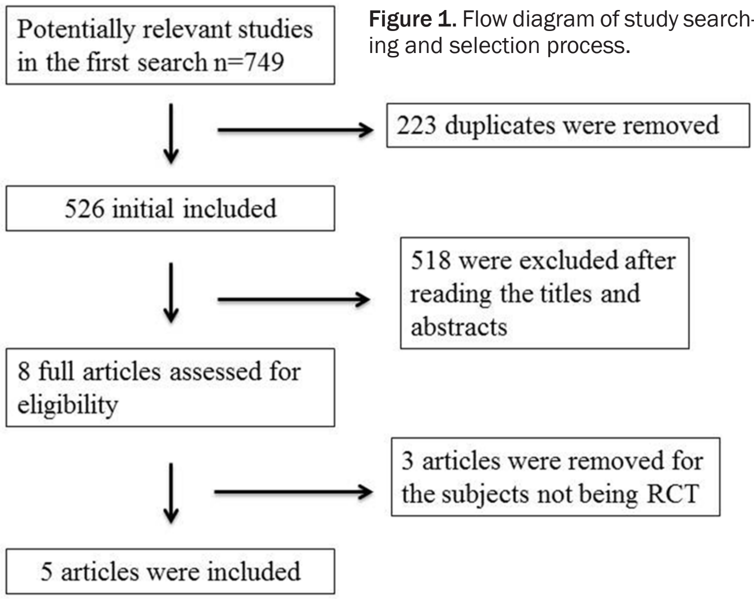

Figure 1. Flow diagram of study searching and selection process.

initial search of databases. Ultimately, six RCTs were included in the meta-analysis [5, 19-21, 26, 27].

The baseline characteristics of the six eligible RCTs in the meta-analysis were summarized in **Table 1**. The six studies were published between 2004 and 2016, and sample sizes ranged from 20 to 185 with a total of 425. There were no significant difference of age, BMI (or body mass), and fasting glucose in pregnant woman multilevel vertebral fracture number at baseline. Exercise programs in each included study were different. For example, one included trial included patients undergoing percutaneous vertebroplasty for spinal osteoporotic compression fracture, and the exercise program consisted of three essential components: five points support, three points support and one point support training (swallow exercise) [19]. Another study reported patients received exercise program including 10 min warm up, a sequence of exercises for 40 min: walking forwards, backwards, and sideways while changing direction, avoiding and stepping over obstacles, climbing steps, getting down to and up off the floor, balance training, posture promoting and trunk and chest exercises, as well as 10 min stretching [26]. One included studies reported that patients in exercise intervention group obtained performed a specially designed 40-min program of physical exercises (including introductory Session (8 min), main Session (28 min) and final session (4 min)) twice weekly under the instructor's supervision [5]. Patients in control intervention group got usual daily activities.

Among the six RCTs, three studies reported the pain score [5, 19, 21], two studies reported the quality of life scores [5, 21], three studies reported the timed up and go [5, 20, 21], and two studies reported the physical function [5, 21]. Jadad scores of the five included studies varied from 3 to 5, all six studies were considered to be high-quality ones according to quality assessment.

Primary outcome: pain score

This outcome data was analyzed with a random-effects model, the pooled estimate of the three included RCTs suggested that compared to control group, exercise intervention was associated with a significantly decreased pain scores (Std. mean difference =-0.95; 95% CI=-1.37 to -0.53; P<0.0001), with low heterogeneity among the studies (I^2=23%, heterogeneity P=0.27) (**Figure 2**).

Sensitivity analysis

Low heterogeneity was observed among the included studies for the pain scores. Thus, we did not perform sensitivity analysis by omitting one study in each turn to detect the source of heterogeneity.

Secondary outcomes

Compared with control intervention, exercise intervention showed significantly reduced quality of life scores (Std. mean difference =-1.09; 95% CI=-1.86 to -0.31; P=0.006; **Figure 3**), but had no influence on timed up and go (Std. mean difference =-0.36; 95% CI=-0.96 to 0.24; P=0.24; **Figure 4**), physical function (Std. mean difference =-0.32; 95% CI=-0.72 to 0.08; P=0.12; **Figure 5**).

Discussion

One recent meta-analysis published in 2013 showed that exercise intervention was able to significantly reduce timed up and go after pool-

Table 1. Characteristics of included studies

NO.	Author	Exercise group				Control group				Jada scores
		Number	Age (years)	BMI (kg/m^2) or Body mass (kg)	Multilevel vertebral fractures (n)	Number	Age (years)	BMI (kg/m^2) or Body mass (kg)	Number of vertebral fractures	
1	Evstigneeva 2016	40	70.7 ± 8.1	-	-	38	67.6 ± 7.0	-	-	5
2	Chen 2012	22	70.3 ± 14.1	20.1 ± 5.2 kg/m^2	3	20	67.1 ± 15.8	19.5 ± 4.8 kg/m^2	3	4
3	Bergland 2011	38	70.8 ± 5.9	25.4 ± 4.7 kg/m^2	-	32	72.0 ± 5.8	25.6 ± 3.7 kg/m^2	-	3
4	Bennell 2010	11	66.2 ± 8.0	68.1 ± 12.8 kg	2	9	66.3 ± 11.8	68.3 ± 12.4 kg	1	4
5	Yang 2007	15	-	-	-	15	-	-	-	4
6	Gold 2004	94	80.2 ± 4.8	-	-	91	82.0 ± 6.2	-	-	3

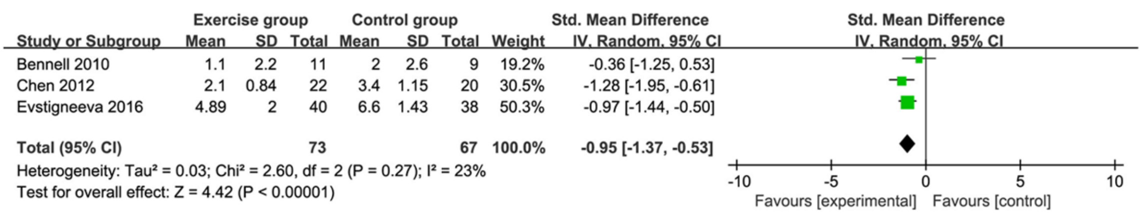

Figure 2. Forest plot for the meta-analysis of pain score. Pain score was represented as the visual analogue scale, which measured the pain on a scale of 0 to 10, with 0 indicating no pain at all and 10 indicating the maximum imaginable pain.

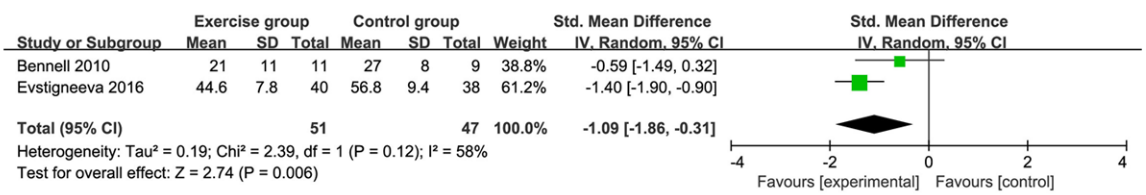

Figure 3. Forest plot for the meta-analysis of quality of life scores which consisted of 41 questions arranged in five domains: pain, physical function, social function, general health perception, and mental function. Domain scores plus a total score were scaled from 0-100 where a lower score represented better quality of life.

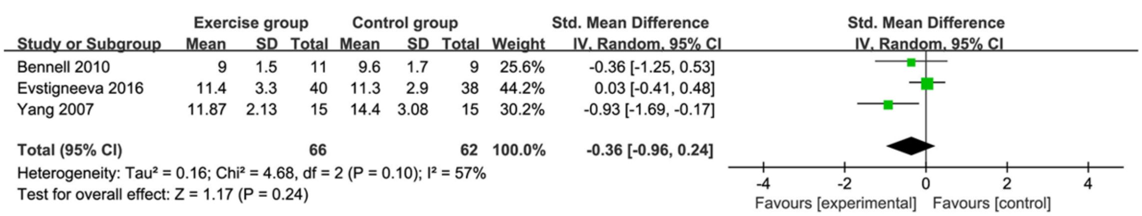

Figure 4. Forest plot for the meta-analysis of timed up and go (s). When performing this test, a patient was asked to stand up from a chair, walked three meters, then went back and sit down. The test was evaluated twice measuring the time in seconds. The best test result was recorded.

ing the results of two included RCTs [20, 26], but had no influence on posture or bone mineral density compared to daily activity control group. However, one of the two included RCTs for analyzing timed up and go reported the change of timed up and go from baseline [26], but the other trial showed the timed up and go at the end of follow up time [20].

In our meta-analysis, two recent RCTs were included [5, 19]. The results showed that exercise intervention showed no effect on functional mobility as showed by timed up and go after pooling the results of three included RCTs all of which reported the timed up and go at the end of follow-up time [5, 20, 21]. In addition, our meta-analysis clearly suggested that compared

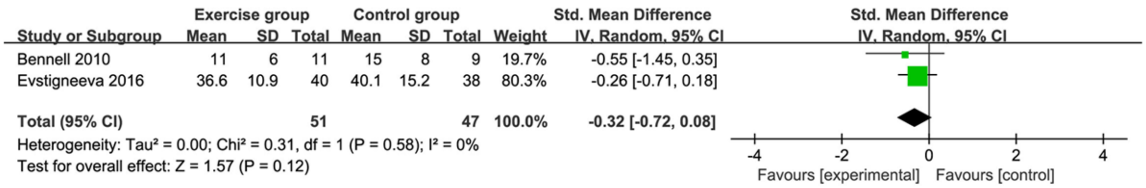

Figure 5. Forest plot for the meta-analysis of physical function.

to control intervention, exercise intervention was associated with a significantly reduced pain scores and quality of life scores, but had no influence on physical function. Quality of life was evaluated with the questionnaire which was especially designed and validated for patients with osteoporotic vertebral fractures and back pain. Assessment of the questionnaire included pain, activities of daily living, mobility, social function, general health perception, and mental function etc. The lowest quality of life score in every domain corresponds to a total of 100 points, and the highest quality of life was represented by a total score equal to 0 [5]. Thus, our results found that quality of life was substantially improved after exercise intervention. These results were consistent with previous studies reporting that exercise had a positive impact on quality of life in older people with or without osteoporosis [28, 29].

One included RCT reported the exercise intervention resulted in 5% new vertebral fractures in patients with osteoporotic vertebral fractures, but 5.3% new vertebral fractures occurred in control group. New non-vertebral fractures were found more frequently in the control group (13.2%) compared to the exercise group (5%) [5]. The timed up and go test was used to assess functional mobility. A patient was asked to stand up from a chair, walk three meters, then went back and sit down. The test was evaluated twice measuring the time in seconds. The best test result was included in the analysis when performing this test. One recent meta-analysis found that exercise intervention could significantly reduce the test time after pooling the results of two included RCTs [30], but our meta-results showed that there was no significant difference of test time between exercise group and control group after analyzing three included RCTs. In addition, the time of Sit-to-Stand test was also used to evaluate functional mobility, and exercise intervention was not associated with a significantly reduced time of Sit-to-Stand test, which also confirmed that exercise intervention had no influence on functional mobility [5].

Several limitations should be taken into account. Firstly, our analysis was based on only six RCTs and five of them have a relatively small sample size (n<100). Overestimation of the treatment effect was more likely in smaller trials compared with larger samples. More clinical trials with large sample were needed to explore this issue. The methods, duration time and intensity of exercise in the included studies were different and it may have an influence on the pooling results. Next, the follow-up time of include studies ranged from 6 to 24 months, which affected the pooling results. There was only one included RCT reporting the incidence of new bone fracture, and it was hard to evaluate the influence of exercise intervention on new fracture occurrence. Finally, some unpublished and missing data might lead bias to the pooled effect.

Conclusion

Exercise intervention showed an important ability to reduce pain and improve the quality of life in patients with osteoporotic vertebral fractures. Exercise intervention was recommended to be administrated in osteoporotic vertebral fracture patients, but more studies should investigate the optimal methods and duration time exercise.

Disclosure of conflict of interest

None.

Address correspondence to: Zhengu Huang, Department of Orthopaedics, The People's Hospital of Dazu District Chongqing, Longgang West Road NO. 138, Dazu District, Chongqing 400016, P. R. China. Tel: 15086963806; E-mail: dazuhuangzhengu@163.com

References

[1] Noordin S and Glowacki J. Parathyroid hormone and its receptor gene polymorphisms: implications in osteoporosis and in fracture healing. Rheumatol Int 2016; 36: 1-6.

[2] Black DM and Rosen CJ. Postmenopausal osteoporosis. N Engl J Med 2016; 374: 2096-2097.

[3] Black DM and Rosen CJ. Clinical practice. Postmenopausal osteoporosis. N Engl J Med 2016; 374: 254-262.

[4] Miazgowski T. The prospective evaluation of the osteoporotic vertebral fractures incidence in a random population sample. Endokrynol Pol 2005; 56: 154-159.

[5] Evstigneeva L, Lesnyak O, Bultink IE, Lems WF, Kozhemyakina E, Negodaeva E, Guselnikova G and Belkin A. Effect of twelve-month physical exercise program on patients with osteoporotic vertebral fractures: a randomized, controlled trial. Osteoporos Int 2016; 27: 2515-2524.

[6] Cosman F, Hattersley G, Hu MY, Williams GC, Fitzpatrick LA and Black DM. Effects of abaloparatide-SC on fractures and bone mineral density in subgroups of postmenopausal women with osteoporosis and varying baseline risk factors. J Bone Miner Res 2017; 32: 17-23.

[7] Johnell O and Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int 2006; 17: 1726-1733.

[8] Lems WF. Clinical relevance of vertebral fractures. Ann Rheum Dis 2007; 66: 2-4.

[9] Briot K, Fechtenbaum J and Roux C. Clinical relevance of vertebral fractures in men. J Bone Miner Res 2016; 31: 1497-1499.

[10] Lloret A, Coiffier G, Couchouron T, Perdriger A and Guggenbuhl P. Risk factors of mortality during the first year after low energy osteoporosis fracture: a retrospective case-control study. Clin Cases Miner Bone Metab 2016; 13: 123-126.

[11] Barnes TR; Schizophrenia Consensus Group of British Association for Psychopharmacology. Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British association for psychopharmacology. J Psychopharmacol 2011; 25: 567-620.

[12] Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, Christmas DM, Davies S, Fineberg N, Lidbetter N, Malizia A, McCrone P, Nabarro D, O'Neill C, Scott J, van der Wee N and Wittchen HU. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British association for Psychopharmacology. J Psychopharmacol 2014; 28: 403-439.

[13] Belhassen M, Confavreux CB, Cortet B, Lamezec L, Ginoux M and Van Ganse E. Anti-osteoporotic treatments in France: initiation, persistence and switches over 6 years of follow-up. Osteoporos Int 2017; 28: 853-862.

[14] Ratnasingam J, Ibrahim L, Paramasivam S, Lim LL, Boon AT and Vethakkan S. Asymmetrical bone loss in a patient with poliomyelitis: an indication for anti-osteoporotic therapy. Clin Cases Miner Bone Metab 2016; 13: 61-63.

[15] Swift DL, Johannsen NM, Lavie CJ, Earnest CP and Church TS. The role of exercise and physical activity in weight loss and maintenance. Prog Cardiovasc Dis 2014; 56: 441-447.

[16] Sinaki M. Exercise for patients with osteoporosis: management of vertebral compression fractures and trunk strengthening for fall prevention. PM R 2012; 4: 882-888.

[17] Bonaiuti D, Arioli G, Diana G, Franchignoni F, Giustini A, Monticone M, Negrini S and Maini M. SIMFER rehabilitation treatment guidelines in postmenopausal and senile osteoporosis. Eura Medicophys 2005; 41: 315-337.

[18] Giangregorio LM, Papaioannou A, Macintyre NJ, Ashe MC, Heinonen A, Shipp K, Wark J, McGill S, Keller H, Jain R, Laprade J and Cheung AM. Too fit to fracture: exercise recommendations for individuals with osteoporosis or osteoporotic vertebral fracture. Osteoporos Int 2014; 25: 821-835.

[19] Chen BL, Zhong Y, Huang YL, Zeng LW, Li YQ, Yang XX, Jiang Q and Wang CH. Systematic back muscle exercise after percutaneous vertebroplasty for spinal osteoporotic compression fracture patients: a randomized controlled trial. Clin Rehabil 2012; 26: 483-492.

[20] Yang L HC, Xie W, Lan Q. Effect of pain-free exercises on female osteoporosis patients with spinal compressive fracture. Journal of Clinical Rehabilitative Tissue Engineering Research 2007; 11: 9108-111.

[21] Bennell KL, Matthews B, Greig A, Briggs A, Kelly A, Sherburn M, Larsen J and Wark J. Effects of an exercise and manual therapy program on physical impairments, function and quality-of-life in people with osteoporotic vertebral fracture: a randomised, single-blind controlled pilot trial. BMC Musculoskelet Disord 2010; 11: 36.

[22] Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009; 339: b2535.

[23] Higgins JPT GS. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration 2011. Available from www.cochrane-handbook.org.

[24] Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ and McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17: 1-12.

[25] Kjaergard LL, Villumsen J and Gluud C. Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. Ann Intern Med 2001; 135: 982-989.

[26] Bergland A, Thorsen H and Karesen R. Effect of exercise on mobility, balance, and health-related quality of life in osteoporotic women with a history of vertebral fracture: a randomized, controlled trial. Osteoporos Int 2011; 22: 1863-1871.

[27] Gold DT, Shipp KM, Pieper CF, Duncan PW, Martinez S and Lyles KW. Group treatment improves trunk strength and psychological status in older women with vertebral fractures: results of a randomized, clinical trial. J Am Geriatr Soc 2004; 52: 1471-1478.

[28] Langlois F, Vu TT, Chasse K, Dupuis G, Kergoat MJ and Bherer L. Benefits of physical exercise training on cognition and quality of life in frail older adults. J Gerontol B Psychol Sci Soc Sci 2013; 68: 400-404.

[29] Liu-Ambrose TY, Khan KM, Eng JJ, Lord SR, Lentle B and McKay HA. Both resistance and agility training reduce back pain and improve health-related quality of life in older women with low bone mass. Osteoporos Int 2005; 16: 1321-1329.

[30] Giangregorio LM, Macintyre NJ, Thabane L, Skidmore CJ and Papaioannou A. Exercise for improving outcomes after osteoporotic vertebral fracture. Cochrane Database Syst Rev 2013; CD008618.