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Effects of Lower Extremity Exercise on the Patients with Knee Osteoarthritis on the Basis of a Meta Analysis

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Abstract: [Purpose] This study aims to explore the impacts of lower extremity exercise on the factor, the symptoms of knee osteoarthritis and the purpose of its treatments such as pain, stiffness, physical function, balance, and the quality of life.
[Participants and Methods] Electronic bibliographic data of Medline and PubMed were examined to identify studies on Randomized Controlled Trials (RCT). 22,099 publications were identified and 21 studies met inclusion and exclusion criteria. The quality assessment, Cochrane's risk of bias was used in all examined studies.
[Results]21 studies were adequate for inclusion criteria. The meta-analysis based on the random effect model was employed to testify the effectiveness of lower extremity exercise on pain, stiffness, physical function, the quality of life, and balance of patients who suffer from knee osteoarthritis. Findings showed that lower extremity exercise contributed to reducing pain (effect size .20; 95% confidence interval .06 - .34) and improving physical function(effect size .14; 95% confidence interval .01-.27). In addition, lower extremity exercise helped to significantly improve stiffness, balance, and the quality of life. However, it was statistically insufficient due to severe deviations of studies (effect size .20; 95% confidence interval -.0.13 - .53).(effect size .11; 95% confidence interval -0.02 - .25). (effect size .16; 95% confidence interval -0.01 - .32).
[Conclusion] Lower extremity exercise had affirmative effects on lowering pain which patients with knee osteoarthritis and improving stiffness, physical function, balance, and the quality of life all of which patients with knee osteoarthritis have in spite of the fact that stiffness, balance, and the quality of life were not statistically positive because of big deviations among studies

Index Terms: Osteoarthritis, Exercise, Meta analysis

I. INTRODUCTION

Osteoarthritis is defined as “a musculoskeletal condition and a chronic disease that causes inflammatory symptoms in a joint.” Inflammatory symptoms such as swelling, pain, localized heat, and a limited range of motion (ROM) are present in the joint, and are due to degeneration of soft tissues [1]. Since the condition typically affects weight-bearing joints, it frequently occurs in a knee joint [1]. Knee osteoarthritis is the most common form of osteoarthritis, causing pain and infection in the joint capsule, which in turn leads to limited ROM, muscle weakness, and stiffness [2],[3].

Osteoarthritis is associated with age, obesity, a lack of exercise, occupational factor, trauma, and gender. With aging societies globally, the burden of knee osteoarthritis is likely to increase markedly, and approximately 10-15% of individuals over 60 years old. Worldwide, suffer from some degree of osteoarthritis.[1],[4],[5]

Clinical symptoms of chronic knee osteoarthritis negatively affects daily activities. For example, knee osteoarthritis prevents patients form engaging in activities such as walking, running, and stair climbing. Thus, knee osteoarthritis is a primary cause of reduced quality of life.[6]

Key interventions for knee osteoarthritis include physical and drug therapies, acupuncture, and wearing insoles. Furthemore, arthroplasty is recommended and performed in severe cases [6]-[8]. However, these treatment modalities do not take into account musculoskeletal aspects and flexibility nevertheless knee osteoarthritis as a chronic disease, requires long-term management with a focus on alleviation symptoms, rather than a complete cure [5]. In terms of rehabilitation treatment, non-pharmacological treatments such as stretching, muscular strength, and aerobic exercise are employed[9]. For example, continuous exercise for patients with knee osteoarthritis has been studied from various perspectives. It has been reported that therapeutic exercise, is effective in reducing the symptoms of knee osteoarthritis by improving the limited joint ROM. Therapeutic exercise helps to enhance muscle strength, endurance, and agility, and helps to delay exacerbation of the disease.[5], [10].

However, previous studies on patients with knee osteoarthritis have presented the effects of particular exercises alone, making it difficult to draw comprehensive conclusions about the overall effects of exercise on knee osteoarthritis, and whether the applied comprehensive exercise had positive effects on patients with knee osteoarthritis. Accordingly, this study conducted a meta-analysis of studies on exercise used to relieve symptoms in patients with knee osteoarthritis. In particular, the effects of exercise on pain, stiffness, balance, physical function, and the QOL of patients with knee osteoarthritis were examined.

II.PARTICIPANTS AND METHODS

This study was conducted in accordance with the Cochrane Collaboration’s Handbook for Systematic Reviews of Interventions and reporting guidelines set out by the Preferred Reporting Item for Systematic Reviews and Meta-Analysis (PRISMA). [11],[12] Literature relevant to this study

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were reviewed and studies for the final assessment were selected under consensus among the researchers participating in this study.[5],[11] We used “Knee”, “arthritis” and “exercise”. As keywords to search for studies investigating the impacts of exercise on patients with knee osteoarthritis.

For the literature review, studies using a randomized controlled trial design including male and female patients diagnosed with knee osteoarthritis, were selected. Studies of the effect of exercise that included leg exercises and that measured at least one of the symptoms of interest (pain, stiffness, balance, physical function, and the QOL), regardless of the nature of the exercise, the period of intervention, and the presence of an instructor, were included. Duplicated publications, studies in which the original text could not be confirmed, and studies that did not present appropriate findings were excluded.

Before integrating each study’s effect size, Higgins I2 statistic was used to test homogeneity between groups. When results indicated non-homogeneity, effect size was computed via the random effects model.

Effect sizes were measured by Comprehensive Meta-Analysis (Version 2.0) to compare the effects of exercise on pain, stiffness, physical function, balance and the QOL of patients with knee osteoarthritis. Effect sizes were interpreted in the following manner. First, 95% confidence intervals of the mean effect size were presented and the significance was identified based on whether 0 was included or not. Second, on the basis of the effect size interpretation criteria of Cohen [13], an effect size of $\leq$ 0.2 in standardized mean difference was defined as a small effect size; 0.5 was defined as a medium effect size; and $\geq$ 0.8 was interpreted as being a large effect size. Third, the mean of the control population under the normal distribution curve was set as 50%,; then, the mean of the experimental population was examined and the difference between the experimental and control populations was analyzed. Effect size calculation was performed using RevMan 5.0(The Nordic Cochrane Centre, Cochrane Collaboration, 2008).

III. RESULTS

A total of 22,099 studies, published between January, 2000 and December, 2016 were found. These consisted of 9,725 studies from Medline and 12,374 studies from PubMed. Using Endnote, 1,421 duplicated publications of the selected studies were identified and excluded. Additionally, 20,678 studies were excluded by reviewing titles and abstracts during the initial selection of studies. And 20,422 studies were excluded from abstract screening process . In order to select only studies pertaining to the efficacy of the exercise program, an additional 235 studies were excluded during the secondary selection process based on the aforementioned inclusion and exclusion criteria; these comprised 113 papers in which the original text was not available, 46 papers that were randomized controlled trials, 30 papers that did not cover the appropriate medical outcomes, 37 papers that were conducted with interventions other than the designated exercise program, and 9 papers for other reasons. Consequently, through these processes, a total of 21 studies were eventually included in analysis. (Figure 1, 2)

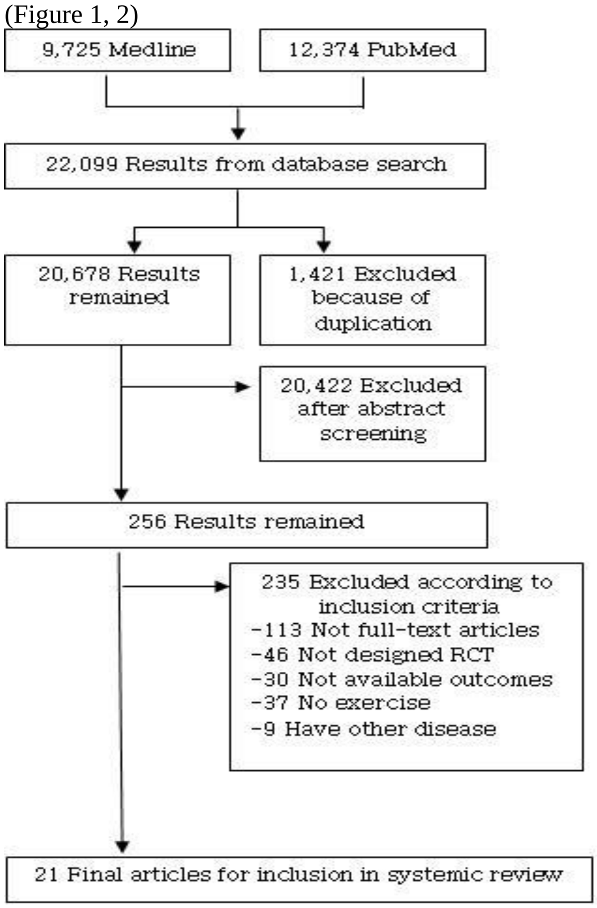

Figure 1. Study design

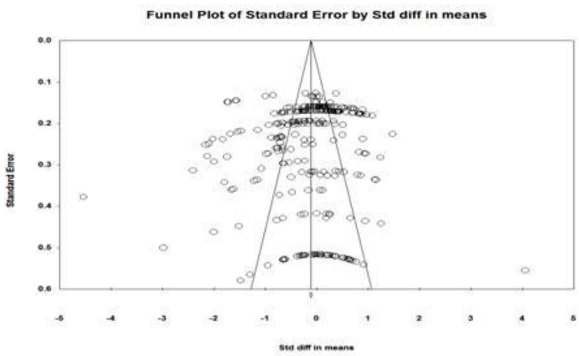

Figure 2. Funnel plot

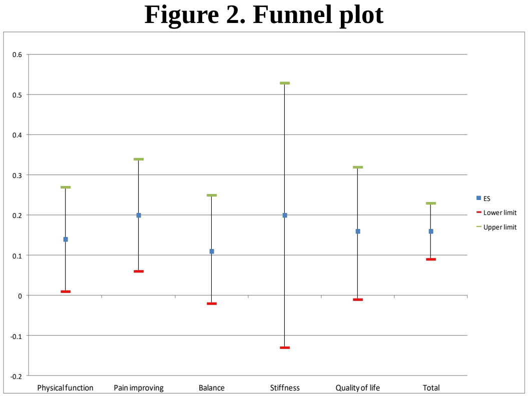

Figure 3. Forest plot

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The 21 selected articles included a total of 1,406 in an experimental group and 1,324 in a control group. The effects of exercise on pain, stiffness, physical function, balance and the QOL were measured (Table 1).

We also assessed the 21 studies qualitatively by using the Risk of Bias (RoB) tool designed by the Cochrane-Institute. Since heterogeneity emerged in the homogeneity analysis, the effect size was evaluated via a random effects model. The total effect size determined in the random effects model, including 328 effect sizes from the 21 articles, was found to be 0.16. The U3 index, which represents the percentile of the effect size, was the 56.4th percentile. This means that, with the mean score of the control population under the standard normal distribution set to the 50.0th percentile, the experimental population experienced an effect of 5.1% as compared to the control population (95% confidence interval: 0.09–0.23). Given this statistically significant result, the study hypothesis was accepted ($p < 0.05$); our meta-analysis implied that exercise improved the condition of patients with knee osteoarthritis, across various nations, including Korea (Table 2, Table3, Figure 3).

The effects of lower extremity exercise on pain were examined in 19 studies [5], [15]-[25], [27], [29]-[34]. The pain improvement effect size was small, at 0.20, but was statistically significant, (95% confidence interval: 0.06 to 0 .34).

The effects of lower extremity exercise on stiffness were inspected in 11 studies [15],[17],[19], [21], [22], [24],[25], [27], [32]-[34]. The stiffness improvement effect size was also small, at 0.20, and was not statistically significant (95% confidence interval -0.13 to 0.53).

The effects of lower extremity exercise on physical function were evaluated in 21 studies [5], [15]-[34]. The effect size of these exercises on physical function improvement was small, at 0.14, but was statistically significant (95% confidence interval: 0.01 to 0.27.

The effects of a lower extremity exercise program on balance was explored in 16 studies [15], [19],[21]-[34]. The balance improvement effect size was small, at 0.11, and was not statistically significant (95% confidence interval: -0.02 to 0.25). Within the 95% confidence interval, cases with balance improvement showed a margin of improvement that was medium-sized.

The effects of lower extremity exercise on the QOL in 11 studies [5], [16]-[20], [22], [27], [28], [31], [33] were examined. The QOL improvement effect size was small, at 0.16, and was not statistically significant (95% confidence interval: -0.01 to 0.32.

IV.DISCUSSION

The effects of lower extremity exercise on pain, stiffness, physical function, balance, and QOL of patients with knee osteoarthritis were analyzed. Engaging in lower extremity exercise relieved pain and statistically significantly reduced pain. Brismee et al. [35] implemented a 6-week Tai-chi exercise program in patients with knee osteoarthritis. Patients conducted a 6-week Tai-chi exercise and then continued with Tai-chi motions at home on their own for another 6 weeks. We found that pain was considerably reduced and that joint function was improved in the experimental group. This implies that patients with knee osteoarthritis who performed such exercise could easily perform activities of daily living. Furthermore, Jorge et al. reported that patients with knee osteoarthritis who performed gradually progressive resistance exercise effect twice a week for 12 weeks were found to have experienced a positive effect when examined 6 weeks later. Taken together, it infers that an intervention period of 4 to 6 weeks is appropriate, and more frequent exercise per week may be even more effective. Moreover, considering that knee osteoarthritis is prevalent among the elderly, an exercise program for soothing knee osteoarthritis should be designed to sustain participation and to increase the frequency of participation in such exercises.

Using lower extremity exercise decreased stiffness, but the effect was not statistically significant in our meta-analysis. According to Topp et al.'s study [34], an isometric exercise program consisting of 3 sessions per week for 16 weeks yielded a significant difference in the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) stiffness score, with a decrease from 5.13 to 5.03. Song et al. [36] described that they selected patients who chronically suffered from osteoarthritis in local communities for their preliminary study. They found that stiffness scores were relatively low, and that exercise had no effect on stiffness because of these low baseline stiffness scores. While some studies identified that there was no stiffness improvement, others reported an improvement in stiffness, even if such improvement was not statistically significant. These contrasting results may be because of the type of the lower extremity exercise and the period of intervention had an impact on results. Taken together, these studies showed that adding warm-up exercise and increasing the number of exercise sessions per week were effective in decreasing stiffness. Further studies on the effect of warm-up will be required.

Applying lower extremity exercise in particular had a statistically significant effect. Fitzgerald et al. [25] classified patients with knee osteoarthritis into 2 groups. One group was instructed to perform general exercise treatments for knee osteoarthritis, such as lower extremity stretching, lower extremity strength, range of motion, and treadmill exercises. The other was instructed to perform exercises for agility, to do vibratory motions, and home exercises. All patients were monitored every two months up to 12 months. Their study revealed that exercise positively influenced knee osteoarthritis in 2 groups, and the difference in the impact of the different types of exercise was not marked. Additionally,

when patients continued exercising for 2 months,the physical function WOMAC scores in both groups were clinically significantly, although not statistically significantly, improved. Similarly, Kovaret al. [37] asked patients with knee osteoarthritis to perform walking exercise for 8 weeks, after which a self-management program was implemented. Scores representing the difficulty in performing daily activities and representing pain were decreased more at the 4-week follow-up than at the 8-week follow-up after walking. Nevertheless, the positive outcome obtained at 4 weeks after intervention was

maintained at 8 weeks. Thus, the

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improvement in physical function was not significantly influenced by the type of exercise performed, but was considerably affected by the period of keeping up the exercise program.

Performing lower extremity exercise did not have a statistically significant effect on balance improvement according to our meta-analysis. Ebnezar et al. [23] divided participants into 2 groups. One group was given 20-minute physical treatments, and was treated with Transcutaneous Electrical Nerve Stimulation(TENS), ultrasound for 40 minutes over a 2-week period, and were then asked to do 40-minute integrated yoga at home for 10 weeks. The other group was given TENS and ultrasound treatment for 20 minutes and then did exercise for 40 minutes. In addition, they were asked to do a therapeutic workout for 40 minutes at home for a 12-week period. They reported that the effect of exercise on knee osteoarthritis in both groups was positive and that the effect of integrated yoga was markedly greater than that of exercise as a home-based treatment. Additionally, statistically significant improvement in balance was found in a study by Lee et al. [38], which was consistent with the findings reported by Choi et al. [39], in which 8 weeks of Tai-chi exercise was performed by elderly individuals with osteoarthritis. However, Choi et al. [40], and Lee and Suh[41] found no improvement in balance, which was inconsistent with the result of Lee et al.'s study[38]. Such conflicting results may because Choi et al. [40] used a 12-week exercise intervention for the fall-risk elderly (mean age: 77.8 years), whereas Lee and Suh[41] employed a 6-week exercise intervention. Furthermore, the difference in the exercise period between the 2 studies probably affected the results. The different results obtained from studies on enhancing balance yield insights into the period of intervention and whether joints should be used individually or together during exercise. Taken together, if the period of intervention is more than 12 weeks minimum, and exercises involve using multiple joints in an integrated manner, the effects are superior. It may also be because studies on balance improvement used too many different measurement tools. More tools were used to measure balance than were used to assess stiffness, physical function, and QOL. Thus, each study reported improvement effects based on different standards and consequently, such effects were not statistically significant.

Applying lower extremity exercise did not have a statistically significant effect on QOL improvement. Messier et al. [42] reported that implementing weight loss measures and performing walking exercise resulted in QOL improvement in overweight elderly females with osteoarthritis of the knee. Also, Baker et al.[43] announced that applying leg muscle strengthening exercise significantly improved the QOL of patients with knee osteoarthritis. Among other studies on QOL, Hopman and Westhoff[44] reported that education and exercise not only alleviated pain, but also improved the QOL, muscle strength, and self-efficacy of patients with knee osteoarthritis. Their participants reported a high level of satisfaction in the post-experimental survey. However, there were many studies that ceased, which led to results lacking in statistically significant. In short, because QOL reflects a psychological aspect, motivation is crucial in applying lower extremity exercise as treatment. Furthermore, in terms of psychological and relational respects, an exercise partner should be considered.

The present study demonstrated that lower extremity exercise was effective in alleviating pain and improving physical function in patients with knee osteoarthritis. Considering that previous studies of the effects of lower extremity exercise in patients with knee osteoarthritis examined the effects of a single specific exercise, this study was meaningful in that it comprehensively analyzed the overall effects of exercise. Additionally, our findings provide the basis for future studies on lower extremity exercise patients with osteoarthritis of the knee.

In addition, the findings of this study indicated that the exercise program had no statistically significant impact on patients with knee osteoarthritis in terms of stiffness, balance, and QOL, but it was clinically meaningful. However, based on the findings of this study, future studies should use a lower extremity exercise that takes into account and reproduces those used in these previous studies.

In conclusion, performing lower extremity exercise had statistically and clinically valuable effects in patients with knee osteoarthritis in terms of reducing pain and improving physical function. Furthermore, using lower extremity exercise was shown to be more effective in patients with knee osteoarthritis when the period of the workout program was at least 12 weeks, warm-up exercise was added, and exercising was performed frequently per week. Based on the findings of this study, future studies on workout intervention for patients with knee osteoarthritis are necessary. Additionally, the major significance of this study is that findings can be used as the basis for future studies related to exercise intervention in patients with osteoarthritis of the knee. This study suggests exercise along with drug therapy is effective for relieving symptoms in these patients, and promoting exercise education and steady participation in an exercise program is necessary

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I. APPENDIX

Table 1. Characteristics of Selected 21 Articles

No.	Author, year	Types of studies	Mean age(±SD)	Exercise group	Control group	Exercise Type	Length of Intervention(weeks)	1 weeks of day	Outcome measures 1)Pain 2)Stiffness 3)Physical function 4)Balance 5)Quality of life
1	Abbott et al, 2015[15]	RCT	61~75	19 19	19 18	aerobic, muscle strengthening, muscle stretching, neuromuscular control exercise, prescribed individually exercise	48weeks	7	1)WOMAC-NRS, NPRS 2)WOMAC 3)WOMAC 4)The timed up-and-go test, The 30-second sit-to-stand test, The 40-meter fast-paced walk test 5)NA
2	Crossley et al, 2015[16]	RCT	53~56	44	48	Patellofemoral joint target exercise	12weeks	4	1)VAS, KOOS 2)NA 3)KOOS 4)NA 5)KOOS
3	Jorge et al, 2015[17]	RCT	59.9~68.1	29	31	Progressive resistance exercise	12weeks	2	1)VAS, WOMAC 2)WOMAC 3)WOMAC 4)NA 5)SF-36
4	Henriksen et al, 2014[18]	RCT	61.3~74.4	31	29	Facility-based functional and individualized exercise	12weeks	3	1)KOOS 2)NA 3)KOOS 4)NA 5)KOOS
5	Peungsuwan et al, 2014[19]	RCT	67.8~69.8	24	20	thai physical therapy	8weeks	2	1)VAS 2)WOMAC 3)WOMAC 4)6MWT 5)SF-36
6	Henriksen et al, 2014[20]	RCT	61.3~65.9	31	29	functional/individualized exercise	12weeks	3	1)PPT 2)NA 3)KOOS 4)NA 5)KOOS
7	Oliveira et al, 2012[21]	RCT	58.8~61.5	50	50	exercise group	8weeks	2	1)WOMAC, Lequesne index 2)WOMAC 3)WOMAC, Lequesne index 4)TUG Test 5)NA
8	Bruce-Brand et al, 2012[22]	RCT	63.4~65.2	14	14 13	home- based resistance training exercise program	6weeks	3	1)WOMAC 2)WOMAC 3)WOMAC 4)25m walk test, repeated chair rise test, stair climb test 5)SF-36

9	Ebnezar et al, 2012[23)]	RCT	59.4~59.6	125		125	hatha yoga	12weeks	7	1)WP 2)NA 3)KDS 4)WT 5)NA
10	Simao et al, 2012[24)]	RCT	69~75	12	11	12	squat+whole body vibration	12weeks	3	1)WOMAC 2)WOMAC 3)WOMAC, 4)BBS, gait speed,6minute walk test 5)NA
11	Fitzgerald et al, 2011[25)]	RCT	63.3~64.6	92		91	agility+perturbation training with standard exercise	8weeks		1)WOMAC, self-reported pain 2)WOMAC 3)WOMAC 4)self-reported knee instability, GUAG test 5)NA
12	Paulo et al, 2011[26)]	RCT	63.8~65	75		84	standard exercise +agility [stepping, braiding]	8weeks		1)NA 2)NA 3)WOMAC ,LEFS, ADLS 4)ADLS 5)NA
13	Akyol et al, 2010[27)]	RCT	56.6~60	20		20	short wave diathermy+isokinetic muscular strengthening exercise	4weeks	3	1)VAS,WOMAC 2)WOMAC 3)WOMAC 4)6MWD 5)SF-36
14	Chaipinyo et al, 2009[28)]	RCT	62~70	24		24	home-based exercise programs (balance training or strength training)	4weeks	5	1)NA 2)NA 3)KOOS-function in daily living/ sport and recreation 4)get up and go, walk upstairs/downstairs 5)KOOS-Knee related quality of life
15	Jan et al, 2008[29)]	RCT	61.8~63.3	34	34	34	high/low-resistance exercise	8weeks	3	1)WOMAC 2)NA 3)WOMAC 4)Stairs 5)NA
16	Lim et al, 2008[30)]	RCT	60.8~67.2	53		54	home based quadriceps strengthening	12weeks	5	1)WOMAC 2)NA 3)WOMAC 4)step test 5)NA
17	Mikesky et al, 2006[8)]	RCT	68.6~69.4	113		108	strength training	12weeks	3	1)WOMAC 2)NA 3)WOMAC 4)NA 5)SF-36
18	Bennell et al, 2005[31)]	RCT	67.4~69.8	73		67	physiotherapy treatment	12weeks	3	1)VAS, KPS, SF-36 2)NA 3)WOMAC, SF-36 4)Step Test 5)AQoL
19	Deyle et al, 2005[32)]	RCT	62.2~64.0	68		66	supervised exercise, individualized manual therapy	8weeks		1)WOMAC, VAS 2)WOMAC 3)WOMAC 4)6MWT 5)NA
20	McCarthy et al, 2004[33)]	RCT	64.5~64.9	111		103	home-based exercise supplemented with class based exercise	8weeks	2	1)VAS,ALF 2)ROM 3)WOMAC, ALF 4)ALF 5)SF-36, EuroQolqustionnaires
21	Topp et al, 2002[34)]	RCT	60.9~65.6	35	32	35	isometric/dynamic resistance	16weeks	3	1)WOMAC 2)WOMAC 3)WOMAC 4)Getting down to and up off the floor, descending and ascending stairs 5)NA

1)TUG=Timed Up and Go
2)KPS=Knee Pain Scale
3)AQoL=Assessment of Quality of Life index
4)6MWT=6 minute walk time
5)PPT=Pressure pain thresholds
6)KOOS=Knee osteoarthritis outcome score
7)WP=Walking pain
8)KDS=Knee disability score

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9)WT=Walking time
10)BBS=Berg balance scale
11)GUAG=Get up and go
12)LEFS=Lower extremity functional scale
13)ADLS=Activity of daily living scale of the knee outcome survey

Table 2.Homogeneity testing of sampling

N	Q^b	p	I^2
328	2820.65	0.000***	88.41

N: Effect size number, Qb: Homogeneity test statistic, p : Significance level of homogeneity test statistic I^2: Percentage of actual variance

*** : p <.001

Table 3.Risk of bias summary search risk of bias item for each included study

No	Author	Allocation concealment	Blinding of participant	Blinding of care provider	Blinding of outcome assessor	Incomplete outcome data	Selective reporting	Other bias
	Abbott, 2015	?	?	?	+	+	?	+
2	Crossley 2015	+	+	+	+	+	+	+
3	Jorge 2015	?	?	?	+	+	+	+
4	Henriksen 2014	?	?	+	+	+	+	+
5	Punnee 2014	?	?	+	+	+	+	+
6	Henriksen 2014	+	+	+	+	+	+	+
7	Oliveira 2012	?	?	+	+	+	+	+
8	Bruce-Brand 2012	+	+	+	+	+	+	+
9	Ebnezar 2012	+	+	+	+	+	+	+
10	Simao 2012	?	?	+	+	+	+	+
11	Fitzgerald 2011	+	+	+	+	+	+	+
12	Teixeira 2011	+	+	+	+	+	+	+
13	Akyol 2010	?	?	+	+	+	+	+
14	Chaipinyo 2009	+	+	+	+	+	+	+
15	Jan 2008	+	+	+	+	+	+	+
16	Lim 2008	+	+	+	+	+	+	+
17	Mikesky 2006	?	?	+	+	+	+	+
18	Bennell 2005	+	+	+	+	+	+	+
19	Deyle 2005	+	+	+	+	+	+	+
20	McCarthy 2004	?	?	+	+	+	+	+
21	Topp 2002	?	?	+	+	+	+	+

'+ '=Low risk of bias, '−'=High risk of bias, '?'=Uncertain risk of bias

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