



The Effect of Balance Training in Knee Osteoarthritis

**Marwa Mohamed Alawady Elsheikh^{1*}, Marwa Ahmed Abo El-Hawa¹,
Hanan Mohamed El-saadany¹ and Mervat Abd El Sattar Elsergany¹**

¹*Physical Medicine, Rheumatology and Rehabilitation, Faculty of Medicine, Tanta University, Tanta, Egypt.*

Authors' contributions

This work was carried out in collaboration among all authors. Author MMAE designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors MAAEI-H and HMES managed the analyses of the study. Author MAESE managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2020/v32i2430775

Editor(s):

(1) Dr. Patom Piroomchai, KhonKaen University, Thailand.

Reviewers:

(1) Felipe Marrese Bersotti, University of São Paulo, Brazil.

(2) Ns. Livana PH, M.Kep., Sp.Kep.J., Sekolah Tinggi Ilmu Kesehatan Kendal, Indonesia.

(3) Hisaya Tanioka, Tanioka Clinic, Japan.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/65146>

Original Research Article

Received 25 October 2020
Accepted 30 December 2020
Published 31 December 2020

ABSTRACT

Background: Osteoarthritis (OA) is the most common chronic disease that affects joints; especially knee joints. OA causes progressive irreversible joint damage and finally joint failure. Proprioceptive deficits are greater in people with knee OA.

Objective: The aim of this study is to assess and evaluate the effect of balance training as an additional modality in management of mild and moderate knee osteoarthritis and its effect on clinical and functional outcome.

Methods: The study included 60 patients with primary knee osteoarthritis, consecutively selected from outpatient clinic of Physical Medicine, Rheumatology and Rehabilitation Department, Faculty of Medicine, Tanta University Hospitals. They were divided into two groups: Group I: (30) Patients was trained by strength exercises rehabilitation program in addition to training program of the BSS-SD. Three sessions per week for twelve weeks. Group II: (30) Patients were trained by strength exercises rehabilitation program only by three sessions per week for twelve weeks. Patients were

*Corresponding author: E-mail: marwaalawady2020@gmail.com;

assessed by clinical evaluation (visual analogue scale (VAS), Ritchie's tenderness scale, morning stiffness, range of motion) physical performance assessments by chair stand test, functional assessment by WOMAC, assessment of postural stability and balance disturbance (postural stability test- fall risk test- limits of stability test) were performed before, 6 and 12 weeks after rehabilitation programs

Results: Our study showed improvement in both groups of clinical assessment (VAS of pain, tenderness, morning stiffness) also there was significant improvement of (active range of movement and passive range of movement and CST). There was significant improvement of pain assessed by WOMAC. There was significant improvement of (postural stability test, fall risk testing, and limits of stability). There were improvement in-group I more significant than group II.

Conclusion: Combined therapy of strength exercises rehabilitation program and training program of balance by BSS-SD have more potential effects in treatment of mild and moderate knee OA better than strength exercises rehabilitation program only.

Keywords: Knee osteoarthritis; strength exercises; balance training.

1. INTRODUCTION

Osteoarthritis (OA) is the most common chronic disease that affects joints; especially knee joints. Its prevalence increases with age, and radiographic changes of OA are seen in the knees of more than 50% of the population older than the age of 65 years [1]. Men and women are equally affected before the age of 45, but after age of 45, the prevalence is higher in women [2].

OA causes progressive irreversible joint damage and finally joint failure. Treatment of knee osteoarthritis depends on rest, external support, exercise, weight loss, physical therapy, non-steroidal anti-inflammatory drugs, intra-articular corticosteroid injections, PRP and total knee replacement, which decrease pain and improve quality of life and patient's daily activity [3].

Proprioceptive deficits are greater in people with knee OA compared with people of a similar age without disease. These deficits are also seen in contra-lateral legs of people with unilateral OA who have high risk of developing bilateral OA [4]. Proprioception deficits may result in poorly controlled, excess loading to knee during gait, initially or accelerating joint degeneration [5].

In early stages of disease, proprioception deficits may not emerge as identifiable risk factors because of effective overlapping protective strategies. Effective control of balance thus relies not only on accurate sensory input but also on a timely response of strong muscles. Individuals with knee OA display reductions in quadriceps strength and activation as well as impairments in knee joint proprioception [6].

Knee instability is considered as a significant problem in patients with knee OA because it

might lead to development of neuromuscular joint stabilization strategy that could hasten progression of disease, therefore knowledge of strategies that improve knee stability and function is important for development of treatment approaches that could improve outcomes in individuals with knee OA [7].

Biodex Stability System (BSS-SD) is a training device due to act on the somatosensory and considering neuromuscular aspects of balance, patients can control in center of gravity (COG) over the base of support (BOS) by using BSS – SD. During training, the patients try to maintain their COG over their BOS during dynamic training.

Pain associated with OA knee may play a role in balance impairments. The presence of pain may reflexively inhibit the muscles around knee, which could compromise effective and timely motor responses in postural control [8].

This study is required to find out the effect of balance exercises in conjunction with strengthen exercises and to find out whether combining balance exercises along with strengthen exercises is more effective than strengthen exercises alone [9].

The aim of this work was to assess and evaluate the effect of balance training as an additional modality in management of mild and moderate knee osteoarthritis and its effect on clinical and functional outcome.

2. PATIENTS AND METHODS

This study was performed on 60 patients with primary knee osteoarthritis diagnosed according to clinical and radiological criteria of the

American College of Rheumatology (ACR). [10], they were selected consecutively from the outpatient's clinics of Physical medicine, Rheumatology and Rehabilitation Department Faculty of Medicine Tanta University Hospitals.

2.1 Inclusion Criteria

Patients with mild or moderate primary knee osteoarthritis according to the clinical and radiological criteria of ACR. (25). All the patients had mild to moderate degree of knee osteoarthritis according to Kellgren and Lawrence classification.

2.2 Exclusion Criteria

Patients with the following criteria were excluded from the study; severe knee OA, lower limb deformity or history of any lower limb injury 12 months prior to the study, systemic disease as rheumatoid arthritis, systemic lupus erythematosus, cancer, gout, advanced hepatic, renal and other metabolic diseases, previous knee surgery, neurological disorders affecting balance as peripheral neuropathy, myopathy, hemiplegia, paraplegia, parkinsonism and multiple sclerosis, vestibular diseases or impaired visions and patients that had any medical contraindication for exercising as severe cardiac or respiratory diseases.

The patients were randomly divided into two groups:

- **Group I:** (30) Patients was trained by strength exercises rehabilitation program in addition to training program of the BSS-SD. Three sessions per week for twelve weeks.
- **Group II:** (30) Patients was trained by strength exercises rehabilitation program only by three sessions per week for twelve weeks.

All Patients will be assessed by:

2.2.1 Clinical and functional assessment

At the first visit, all patients were subjected to full history taking, general examination and local knee examination. The severity of pain was assessed by VAS, [11] Ritchie's tenderness scale, [12] morning stiffness, [13] range of motion, [14] chair stand test (CST). [15] functional assessment by WOMAC. [16]

2.2.2 Assessment of postural stability and balance disturbance

All patients underwent by using Biodex Stability System (BSS- SD) (Biodex Medical System, Shirley, NY, USA) [17].

2.3 Parameter of Assessment

By using any of five test protocols including The Postural Stability Test, Dynamic or Static Limit Of Stability (LOS) Test, Athlete Single Leg Stability Testing, Fall Risk Test , Clinical Test Of Sensory Integration and Balance – CTSIB OR m-CTSIB (MODIFIED CTSIB).(30)

The patients perform this task need coordination between neuro muscular mechanisms of proprioception with strength and power of muscle of both lower limbs and trunk [18].

The following tests were done for both patients Group (I and II) before, after six and twelve weeks from rehabilitation program.

Position of the patients on platform bare feet and right heel on D16 and right foot angle on 10 then left heel on D6 and left foot angle 10 with keep the eyes opening with look forward on monitor to enhancing visual feedback. The patients were asked for keeping the center of pressure in the center of target displayed on the monitor. These tests included The Postural Stability Test, The Fall Risk test, The limits of Stability (LOS) test

2.3.1 Training by the biodex stability system (BSS-SD) in Group I

The balance training protocol consisted of: Postural Stability Training, Limit of Stability Training, Weight Shift Training, Maze Control Training, The Random Control Training, Percent Weight-Bearing Training. The duration of each training was 20 minutes.

2.3.2 Training by exercise Program in Group I&II

They minimize stress on the joint as they increase its flexibility and strength of muscles [19].

It includes Leg raise (lying), Hamstring stretch (lying), Half-squat, One-leg dip, Leg stretch.

We started by a load of 2.5 kg up to 5 kg according to tolerability of patients with maximal repetition up to 10 times by exercise session, and these exercises were repeated 3 times weekly for 12 weeks.

2.4 Follow Up

Patients were evaluated clinically, functionally and postural stability and balance disturbance 6 and 12 weeks after the rehabilitation programs.

2.5 Statistical Analysis

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA Numerical variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing Student's t- test. Categorical variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered significant.

3. RESULTS

3.1 Demographic Data of Patients

This study was performed on 60 patients with primary knee osteoarthritis. Most of our patients were females. Their age ranged from 50 to 67 years. Most of our patients were hard worker.

Bilateral knee OA more dominant than unilateral. (Table 1).

3.2 Clinical Assessment

As regard clinical manifestations, there was improvement of (VAS of pain, Tenderness, Morning stiffness) in Groups I and II after 6 and 12 weeks from rehabilitation programs compared with before rehabilitation. There was significant improvement in-Group I more than Group II (Table 2).

3.3 Physical performance and functional assessments

All patients had improvement of (active range of movement and passive range of movement and CST) in both groups but the improvement in-Group I more significant than Group II after rehabilitation Programs. There was improvement of pain assessed by WOMAC in both groups but there was significance improvement in-Group I more than Group II after 6 and 12 weeks from rehabilitation programs (Table 3).

Table 1. Comparison between the two studied groups regarding demographic data

		Groups				
		Group I		Group II		P-value
Age (Years)	Mean ±SD	56.933± 4.578		56.1 ±3.566		0.578
		N	%	N	%	P-value
Sex	Male	8	26.67	9	30.00	0.774
	Female	22	73.33	21	70.00	
	Mean ±SD	24.967±1.65		25.367±1.45		
BMI	Mean ±SD	24.967 ±1.65		24.367 ±1.45		0.626
		N	%	N	%	P-value
Occupation	Manual Worker	5	16.67	6	20.00	0.988
	House wife	10	33.33	8	26.67	
	Teacher	3	10.00	3	10.00	
	Driver	2	6.67	1	3.33	
	Nurse	4	13.33	4	13.33	
	Farmer	3	10.00	4	13.33	
	Employer	3	10.00	4	13.33	
Duration (years)	Mean ±SD	4.533±1.871		4.733±1.837		0.678

Table 2. Comparison between the two groups before, after 6 and 12 weeks from rehabilitation programs regarding clinical manifestations of patients

	Group I								
	Rehabilitation program						Comparisons		
	Before		After 6 W		After 12 W		P value		
	Range	Mean ±SD	Range	Mean ±SD	Range	Mean ±SD	B-6W	B-12W	6-12W
VAS	5-9	7.200±1.518	2-6	4.533±1.279	0-6	2.933±1.721	<0.001*	<0.001*	<0.001*
Tenderness	2-3	2.467±0.507	0-3	1.667±0.758	0-2	1.267±0.521	<0.001*	<0.001*	0.003*
Morning Stiffness	10-35	17.233±7.229	4-25	11.300±5.826	0-20	5.600±4.014	<0.001*	<0.001*	<0.001*

Table 3. Comparison between the two groups before, after 6 and 12 weeks from rehabilitation programs regarding physical performance and functional assessments of patients

			Groups		T-Test
			Group I	Group II	P-value
Active range of movement	Before	Mean ±SD	76.667±11.012	75.167±11.179	0.603
	After 6W	Mean ±SD	88.000±11.033	79.500±11.843	0.006*
	After 12W	Mean ±SD	95.667±12.645	83.833±13.499	0.001*
Passive range of movement	Before	Mean ±SD	86.667±11.244	84.000±10.372	0.344
	After 6W	Mean ±SD	100.000±12.457	89.667±11.740	0.002*
	After 12W	Mean ±SD	112.667±14.487	95.167±13.031	<0.001*
C.S.T	Before	Mean ±SD	8.300±2.037	8.733±1.507	0.353
	After 6W	Mean ±SD	11.200±2.188	10.400±1.522	0.106
	After 12W	Mean ±SD	15.000±2.349	11.633±1.732	<0.001*
WOMAC (Total)	Before	Mean ±SD	57.667±9.095	58.600±10.159	0.709
	After 6W	Mean ±SD	40.367±10.297	51.200±9.876	<0.001*
	After 12W	Mean ±SD	30.933±9.709	47.767±10.057	<0.001*

Table 4. Comparison between the two groups before, after 6 and 12 weeks from rehabilitation programs regarding postural stability and balance disturbance assessment

			Groups		T-Test
			Group I	Group II	P-value
Postural Stability Test Results OASI	Before	Mean ±SD	3.372±0.157	3.428±0.225	0.262
	After 6W	Mean ±SD	3.005±0.239	3.256±0.272	<0.001*
	After 12W	Mean ±SD	2.599±0.356	3.150±0.321	<0.001*
Fall Risk Testing OASI	Before	Mean ±SD	3.703±0.397	3.513±0.501	0.109
	After 6W	Mean ±SD	2.317±0.450	3.220±0.510	<0.001*
	After 12W	Mean ±SD	1.910±0.554	2.970±0.585	<0.001*
The Limits of Stability (LOS) Test Overall	Before	Mean ±SD	37.933±2.083	37.833±4.324	0.910
	After 6W	Mean ±SD	46.733±2.288	40.867±4.232	<0.001*
	After 12W	Mean ±SD	53.067±2.876	43.833±4.324	<0.001*

3.4 Postural Stability and Balance Disturbance Assessment

There was improvement of (postural stability test, fall risk testing, and the limits of stability) in both groups but the improvement in Group- I more significant than Group II after 6 and 12 weeks from rehabilitation Programs (Table 4).

4. DISCUSSION

Osteoarthritis is the major factor of disability in elderly people around the world [2]. OA often affects weight-bearing joints, including hip, knee, and ankle; the most common large joints that are involved in this disease are knee joints. Knee osteoarthritis not only creates changes in the tissues within the joint cavity, but also influences peri-articular tissues, such as ligaments, capsule, tendons and tissues around the joint, such as muscles leading to proprioceptive deficits in extremes of joint position and body position [20]. These effects on proprioceptive sense may induce knee instability in the form of lack of ability to maintain a position or to control the movements of knee joint under various external loads [21].

Individuals with knee OA display reductions in quadriceps strength and activation as well as impairments in knee joint proprioception. [22] These deficits may result in poorly controlled, excess loading to knee during gait, initially or accelerating joint degeneration [23].

Regarding age of patients in both groups, it was found that all patients were in the middle age with no significant difference between both groups. This result was in agreement with Peixoto JG [24] and Sasaki E, et al. [25] who stated that age is the most powerful risk factor to determine the onset and progression of degenerative joint disease especially knee osteoarthritis. This is could be explained by many factors such as muscle weakness, altered gait, changes in body weight, it was also found that articular cartilage and proteoglycan content decrease with age which affect the rate of cartilage repair [26,25].

Regarding sex, the current study showed that OA predominated in females (nearly two thirds of patients) with insignificant difference between both groups. These results were agreed and supported by Sasaki E et al. [25] and Peixoto JG

[24] Who stated that men and women were affected before the age of 45 equally, but after age of 45, the prevalence was higher in women due to the effect of estrogen hormone, which has a role in maintaining the homeostasis of articular tissues and loss of ovarian function [27].

Regarding occupation of the studied patients, the current study showed that knee OA was common among manual workers followed by house wives and other patients with heavy duties with insignificant difference between both groups of the studied patients ($P= 0.988$). These results were supported with Verbeek, et al. [28] who found that subchondral micro-fractures may induce OA. Micro-fractures may occur when the joint is in extreme positions or when physical workload exceeds a critical level.

As regard the side of affection, the current study showed that bilateral knee OA predominated among the studied patients in both groups (80% in-Group I and 73% in-Group II) with no significant difference between both groups. These results were supported by Komatsu, et al. [29] and Culvenor AG [30] who stated that knee OA is common bilaterally mostly due to its degenerative background. Deficits in proprioception lead to impairment of the dynamic mechanisms for knee stability and loss of balance. [29]

Regarding clinical evaluation of the studied patients by VAS, morning stiffness and tenderness the current study showed significant improvement in-Group I and Group II at 6 and 12 weeks of rehabilitation programs (P value $<0.001^*$) while the comparison between both groups showed significant improvement in Group I more than Group II in VAS and Tenderness after 6 and 12 weeks while Morning stiffness show better improvement after 6weeks but significant improvement after 12 weeks from rehabilitation programs.

These results were supported by Kunduracilar, et al. [31], Ashtiani, et al. [32] and Goh SL [33] who found that patients with knee OA showed better improvement by using balance training plus strengthening exercises than patients who use either procedure alone. They found the positive additive effects of kinesthesia and balance training to increase the functional capacities of knee OA patients and improvement of neuromuscular adaptations and pain that is in agreement with the current findings [7].

The initial goals of OA therapy are reducing pain intensity, maintaining functional status, and minimizing deformity and instability of the knee. Theoretically, the balance training and kinesthesia affect knee proprioception more than the exercises that are based on standard strengthening only.

There is a relationship between knee OA and proprioceptive loss, and improvement in proprioception could be another reason for pain reduction in this group.

The current study showed significant improvement of AROM, PROM and C.S.T in Group I and Group II after 6 and 12 weeks from rehabilitation programs but the improvement in Group I more significant improvement than Group II in AROM and PROM after 6 and 12 weeks while CST show better improvement after 6weeks but significant improvement after 12 weeks from rehabilitation programs.

These results were supported by Kim et al. [34], and Levinger et al. [35] who stated that painful joints have deleterious effects on muscle strength and consequently affect the joint range of movement, so, therapeutic muscle-strengthening exercises will lead to decrease in articular pain and functional improvement of the legs [34].

As regard adding balance exercises to muscle-strengthening exercises, they found significant improvement of knee stability of the OA patients.

Regarding functional assessment of the studied patients by WOMAC, the current study showed significant improvement in-Group I and II at 6 and 12 weeks of rehabilitation programs (P value= 0.001^*) significant improvement in Group I than Group II.

These results were supported by Levinger, et al. [35], Kim, et al. [34] Who found that combining balance exercises to strengthening exercises improve the functional ability of OA knee patients more than the strengthening exercises alone. It has been suggested that functional ability is also affected by poor proprioception [36].

Knee joint proprioception encompasses the sense of joint position and the sense of motion. These senses are partially derived from neural inputs arising from mechanoreceptors in joints, muscles, tendons and associated tissue [37].

In addition, it has been shown that patients with poor proprioception show more limitation in functional ability but this relationship is rather weak, and in patients with poor proprioception, muscle weakness has a stronger impact on limitations in functional ability than in patients with accurate proprioception [35].

They also show that knee joint proprioception is essential for accurate modulation and activation of muscles, thus providing adequate neuromuscular control of knee joint position and joint movement, and ultimately the performance of physical tasks. When proprioceptive acuity decreases, functional ability can only be maintained if there is sufficient muscle strength to compensate for the decrease in accuracy of modulation and activation of muscles. This implies that functional ability will be more strongly affected in the presence of both proprioceptive inaccuracy and muscle weakness [36].

Regarding postural stability and balance disturbance assessment by BSS-SD (postural stability test, fall risk testing OASI, and The Limits of Stability (LOS) Test Overall), the current study showed that significant improvement in Group I and Group II at 6 and 12 weeks (P value <0.001*) of rehabilitation programs. It was found that Group I had significant improvement in comparison to Group II at the same rehabilitation programs.

These results were agreed and supported by, Nguyen, et al. [38] and Choi HS, et al. [39] and who stated that combining balance exercises to strengthening exercises improves the functional ability of OA knee patients more than the strengthening exercises alone. It has been suggested that functional ability is also affected by poor proprioception [36].

5. CONCLUSION

Combined therapy of strength exercises rehabilitation program and training program of balance by BSS-SD more potential effects in treatment of mild and moderate knee OA better than strength exercises rehabilitation program only. Combined therapy produced significant improvement of pain assessed by VAS, tenderness, morning stiffness, active and passive range of motion (ROM), physical performance and Postural stability and balance disturbance.

CONSENT AND ETHICAL APPROVAL

All tests were explained to all patients before having their written informed consents to participate in this study. This study approved by Local Research Ethics Committee of Faculty of Medicine Tanta University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Prieto-Alhambra D, Judge A, Javaid MK, et al. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: Influences of age, gender and osteoarthritis affecting other joints. *Ann Rheum Dis.* 2014;73(9):1659-64. Available:<http://dx.doi.org/10.1136/annrheumdis-2013-203355>
2. Pereira D, Peleteiro B, Araujo J, et al. The effect of osteoarthritis definition on prevalence and incidence estimates: A systematic review. *Osteoarthritis Cartilage.* 2011;19(11):1270-85. Available:<https://doi.org/10.1016/j.joca.2011.08.009>
3. Leung GJ, Rainsford KD, Kean WF. Osteoarthritis of the hand I: Aetiology and pathogenesis, risk factors, investigation and diagnosis. *J Pharm Pharmacol.* 2014; 66(3):339-46. Available:<https://doi.org/10.1111/jphp.12196>
4. Baert IA, Mahmoudian A, Nieuwenhuys A et al. Proprioceptive accuracy in women with early and established knee osteoarthritis and its relation to functional ability, postural control, and muscle strength. *J Clin Rheumatol.* 2013; 32(9):1365-74. Available:<https://doi.org/10.1007/s10067-013-2285-4>
5. Wang H, Ji Z, Jiang G, et al. Correlation among proprioception, muscle strength, and balance. *J Phys Ther Sci.* 2016; 28(12):3468-72. Available:<https://doi.org/10.1589/jpts.28.3468>
6. Vuillerme N, Pinsault N, Chenu O et al. Sensory supplementation system based on electrotactile tongue biofeedback of head position for balance control. *Neurosci Lett.* 2008;431(3):206-10.

- Available:<https://doi.org/10.1016/j.neulet.2007.11.049>
7. Khalaj N, Osman NA, Mokhtar AH, et al. Balance and risk of fall in individuals with bilateral mild and moderate knee osteoarthritis. *PLoS One*. 2014;9(3): 92270.
Available:<https://doi.org/10.1371/journal.pone.0092270>
 8. Gurudut P, Welling AA, Naik R. Comparative effect of calisthenic and proprioceptive exercises on pain, proprioception, balance and function in chronic osteoarthritis of knee. *Journal of Exercise Science & Physiotherapy* 2018; 14(2).
DOI:10.18376/jesp/2018/v14/i2/111310
 9. Law TY, Nguyen C, Frank RM, Rosas S, & McCormick F. Current concepts on the use of corticosteroid injections for knee osteoarthritis. *The Physician and Sportsmedicine*. 2015;43(3):269-273.
Available:<https://doi.org/10.1080/00913847.2015.1017440>
 10. Arifin N, Osman NAA, Abas WABW. Intrarater test-retest reliability of static and dynamic stability indexes measurement using the Biodex Stability System during unilateral stance. *Journal of applied biomechanics*. 2014;30(2):300-304.
Available:<https://doi.org/10.1123/jab.2013-0130>
 11. Singh AK, KAIvAni AK, AggArwAl PK, Gupta SK. Prevalence of osteoarthritis of knee among elderly persons in urban slums using American College of Rheumatology (ACR) criteria. *J Clin Diagn Res*. 2014;8(9):JC09.
DOI:10.7860/JCDR/2014/7763.4868
 12. Klimek L, Bergmann K-C, Biedermann T, et al. Visual analogue scales (VAS): Measuring instruments for the documentation of symptoms and therapy monitoring in cases of allergic rhinitis in everyday health care. *Allergo J Int*. 2017; 26(1):16-24.
DOI:10.1007/s40629-016-0006-7
 13. Henrotin Y, Pesesse L, Sanchez C. Subchondral bone and osteoarthritis: biological and cellular aspects. *Osteoporos Int*. 2012;23(8):847-51.
DOI:10.1007/s00198-012-2162-z
 14. Ludin A, Sela JJ, Schroeder A et al. Injection of vascular endothelial growth factor into knee joints induces osteoarthritis in mice. *Osteoarthritis Cartilage*. 2013;21(3):491-7.
Available:<https://doi.org/10.1016/j.joca.2012.12.003>
 15. Gaballah A, Hussein NA, Risk M, et al. Correlation between synovial vascular endothelial growth factor, clinical, functional and radiological manifestations in knee osteoarthritis. *Rheumatol Int*. 2016;38(1):29-34.
Available:<https://doi.org/10.1016/j.ejr.2015.01.002>
 16. Basaran S, Guzel R, Seydaoglu G, Guler-Uysal F. Validity, reliability, and comparison of the WOMAC osteoarthritis index and *Lequesne algofunctional* index in Turkish patients with hip or knee osteoarthritis. *Clinical Rheumatology*. 2010;29(7):749-756.
DOI: 10.1007/s10067-010-1398-2
 17. Jose AP, Pedro RO, Ana CB et al. Test-Retest reliability of Biodex Balance SD on physically active old people. *J Sports Med Phys Fitness*. 2011;6(2):444-51.
DOI: 10.4100/jhse.2011.62.25
 18. Colen S, van den Bekerom MP, Mulier M et al. Hyaluronic acid in the treatment of knee osteoarthritis. *BioDrugs*. 2012; 26(4):257-68.
Available:<https://doi.org/10.1007/BF03261884>
 19. Evcik D. Non pharmacological knee osteoarthritis treatment. *Ann Phys Rehabil Med*. 2015;58:33.
Available:<https://doi.org/10.1016/j.rehab.2015.07.084>
 20. Gallagher B, Tjoumakaris FP, Harwood MI, et al. Chondroprotection and the prevention of osteoarthritis progression of the knee: a systematic review of treatment agents. *Am J Sports Med*. 2015;43(3):734-744.
Available:<https://doi.org/10.1177%2F0363546514533777>
 21. Mat S, Tan MP, Kamaruzzaman SB, Ng CT. Physical therapies for improving balance and reducing falls risk in osteoarthritis of the knee: A systematic review. *Age Ageing*. 2014;44(1):16-24.
Available:<https://doi.org/10.1093/ageing/afu112>
 22. Mermerci BB, Garip Y, Uysal RS et al. Clinic and ultrasound findings related to pain in patients with knee osteoarthritis. *Clin Rheumatol*. 2011; 30(8):1055-62.
DOI 10.1007/s10067-011-1701-x
 23. Knoop J, Steultjens MP, Van der Leeden M, et al. Proprioception in knee

- osteoarthritis: A narrative review. *Osteoarthritis Cartilage*. 2011;19(4):381-8. Available:<https://doi.org/10.1016/j.joca.2011.01.003>
24. Peixoto JG, de Souza Moreira B, Diz JB et al. Analysis of symmetry between lower limbs during gait of older women with bilateral knee osteoarthritis. *Aging Clin Exp Res*. 2019;31(1): 67-73. Available:<https://doi.org/10.1007/s40520-018-0942-9>
 25. Sasaki E, Ota S, Chiba D, et al. Early knee osteoarthritis prevalence is highest among middle-aged adult females with obesity based on new set of diagnostic criteria from a large sample cohort study in the Japanese general population. *Knee Surg Sports Traumatol Arthrosc*. 2020;28(3): 984-94. Available:<https://doi.org/10.1007/s00167-019-05614-z>
 26. Silverwood V, Blagojevic-Bucknall M, Jinks C et al. Current evidence on risk factors for knee osteoarthritis in older adults: A systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2015;23(4):507-515. Available:<https://doi.org/10.1016/j.joca.2014.11.019>
 27. Madry H, Kon E, Condello V et al. Early osteoarthritis of the knee. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(6): 1753-1762. DOI: 10.1007/s00167-016-4068-3
 28. Verbeek J, Mischke C, Neuvonen K, et al Occupational exposure to knee loading and the risk of osteoarthritis of the knee: A systematic review and a dose-response meta-analysis. *Saf Health Work*. 2017;8(2): 130-42. Available:<https://doi.org/10.1016/j.shaw.2017.02.001>
 29. Komatsu D, Ikeuchi K, Hasegawa Y, et al. Laterality of radiographic osteoarthritis of the knee. *Laterality: Asymmetries of Body, Brain Cogn*. 2017;22(3):340-53. Available:<https://doi.org/10.1080/1357650X.2016.1199560>
 30. Culvenor AG, Hart HF, Stefanik JJ, et al. Prevalence of knee osteoarthritis features on magnetic resonance imaging in asymptomatic uninjured adults: A systematic review and meta-analysis. *Br J Sports Med*. 2019;53(20):1268-78. Available:<http://dx.doi.org/10.1136/bjsports-2018-099257>
 31. Kunduracilar Z, Sahin HG, Sonmezer E, Sozay S. The effects of two different water exercise trainings on pain, functional status and balance in patients with knee osteoarthritis. *Complementary therapies in clinical practice*. 2018;31:374-378. Available:<https://doi.org/10.1016/j.ctcp.2018.01.004>
 32. Ashtiani ARA, Akbari NJ, Mohammadi M, Nouraisarjou S. The Effect of Balance Exercises on Knee Instability and Pain Intensity in Patients with Knee Osteoarthritis: A Randomized Clinical Trial. *Journal of Research in Medical and Dental Science*. 2018;6(2):74-82. Available:<https://doi.org/10.5455/jrmds.20186213>
 33. Goh SL, Persson MS, Stocks J et al. Relative efficacy of different exercises for pain, function, performance and quality of life in knee and hip osteoarthritis: Systematic review and network meta-analysis. *Sports Med*. 2019;49(5):743-61. Available:<https://doi.org/10.1007/s40279-019-01082-0>
 34. Kim K, Lee HY, Lim SJ. Effects of increased standing balance on pain in patients with knee osteoarthritis. *J Phys Ther Sci*. 2016;28(1):87-89. Available:<https://doi.org/10.1589/jpts.28.87>
 35. Levinger P, Dunn J, Bifera N et al. High-speed resistance training and balance training for people with knee osteoarthritis to reduce falls risk: Study protocol for a pilot randomized controlled trial. *Trials*. 2017;18(1):384. DOI: 10.1186/s13063-017-2129-7
 36. Takacs J, Krowchuk NM, Garland SJ, Carpenter MG, Hunt MA. Dynamic balance training improves physical function in individuals with knee osteoarthritis: a pilot randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*. 2017;98(8): 1586-1593. Available:<https://doi.org/10.1016/j.apmr.2017.01.029>
 37. Baker K, McAlindon T. Exercise for knee osteoarthritis. *Current Opinion in Rheumatology*. 2000;12(5):456-463. Available:<https://doi.org/10.1002/14651858.CD004376.pub3>
 38. Nguyen C, Lefevre-Colau MM, Poiraudou. Rehabilitation exercise and strength training and osteoarthritis: A critical narrative review. *Annals of Physical and Rehabilitation Medicine*. 2016;59(3): 190-195.

- Available:<https://doi.org/10.1016/j.rehab.2016.02.010>
39. Choi HS, Shin WS. Effects of game-based balance training with constraint-induced movement therapy on lower extremity function and balance confidence levels in women with total knee replacement. *Physical Therapy Rehabilitation Science*. 2019;8(1):8-14. Available:<https://doi.org/10.14474/ptrs.2019.8.1.8>

© 2020 Elsheikh et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/65146>