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EXERCISE INTERVENTIONS IN PATIENTS WITH DIABETIC NEUROPATHY –A NARRATIVE REVIEW

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ABSTRACT

Introduction: Diabetic Peripheral Neuropathy affects a large number of populations and leads to complications like numbness, pain, tingling and burning sensations in toes and feet. Many exercise interventions are available in literature for treating these symptoms. Decision of a particular exercise intervention however is a tedious task due to unavailability of recent systematic review. Hence, this study was undertaken to describe exercise interventions administered on patients with diabetic neuropathy.

Methodology: Literature search was carried out using PUBMED, EMBASE, Cochrane and Science Direct databases to retrieve research articles about exercise interventions in diabetic neuropathy. The studies were evaluated with respect to various exercise interventions in diabetic neuropathy.

Results: After full text analysis of 32 articles, 10 studies were eligible for in depth analysis. Different treatment approaches were investigated and outcome measures like NCV,Berg Balance Scale,6 MWT,TWT, Time Up and Go Test,Star Excursion Balance Test etc. were used in these studies.

Conclusion: Aerobic training in combination with other exercises was found to be used more widely in reducing symptoms of diabetic neuropathy.

KEYWORDS : diabetic neuropathy, gait, exercise, balance.

BACKGROUND

Diabetic Mellitus is a group of metabolic diseases characterized by hyperglycemia that results from defects in insulin secretion, insulin action on target tissue or both.[1] The chronic hyperglycaemia of diabetes may lead to long-term damage, dysfunction, and failure of various organs, especially the nerves, eyes, kidneys, heart and blood vessels[2]. According to World Health Organization (WHO), the prevalence of diabetes in 2010 was 5.6% in urban areas and 2.7% in rural areas of India. It is estimated that the total number of people with diabetes in 2010 was around 50.8 million, and is expected to rise to 87.0 million by 2030[4].

Neuropathies are one of the most common long term complications of diabetes affecting up to 50% of patients Neuropathy is characterized by diffuse damage to the nerves which leads to sensory and motor deficits which often result in mobility-related dysfunction, alterations in gait characteristics and balance impairments.[4]

At the age of 55 years, around 5–8 % of all people suffer from symptomatic peripheral neuropathy, whereas in the age group above 65 years, almost one-third are estimated to have sensory symptoms attributed to peripheral neuropathy. Common symptoms include pain, altered sensation (numbness, burning, tingling, etc.), reduced or absent reflexes, muscle weakness reduced balance control, insecure gait, and higher risk of falling.[3] All of these symptoms can affect activities of daily living and subsequently reduce a patient's quality of life.

Exercise may positively influence the pathological factors associated with neuropathy by promoting microvascular dilation, reducing oxidative stress, and increasing neurotropic factors.[4]

Physical Therapy, balance training, and moderate exercise have shown increased compensation for balance deficits, increased blood flow to distal extremities and improved muscular performance with decreased muscular weakness .Moderate exercise has been shown to help reverse these effects and prevent peripheral neuropathy by increasing nitric oxide production and improving cardiovascular function.[2] Additionally, balance and gait training, closed kinetic chain exercise, and aerobic exercise have all demonstrated a decrease in the effects of peripheral neuropathy and reduce the risk of falls in patients with DM.

There are various exercises which are carried out in case of diabetic neuropathy. But many of these exercises are symptom oriented and there is no evidence as to how exercise benefits neuropathy symptoms. Patients are also uninformed as to how much they should exercise or if they should exercise during acute neuropathy.

This systemic review was performed with the aim to find the most appropriate exercise program for the treatment of diabetic neuropathy and to find the best treatment protocol for reducing the symptoms of diabetic neuropathy.

METHODOLOGY

Research question – What is the most commonly used exercise intervention to reduce symptoms of neuropathy?

Aim – To find the most commonly used exercise intervention for reducing the symptoms of diabetic neuropathy.

OBJECTIVES –

1) To analyze the literature for various exercise interventions in diabetic neuropathy.
2) To explore commonly used outcome measures to determine efficacy of treatment intervention.
3) To analyze the studies for details about the intervention and its effectiveness.

Study selection -

Literature search was carried out using PUBMED, EMBASE, Cochrane and Science Direct databases to find exercise protocols for diabetic neuropathy. Terms like 'strength training', 'endurance training' , 'gait' , 'balance', 'posture', 'diabetic neuropathy and endurance training' , 'physical fitness' , 'diabetic neuropathy and resistance training' , 'aerobic training and diabetic neuropathy' were used to carry out literature search in the database.

Inclusion criteria –

Studies in the last 5 years (2014-2019) that assessed the effect of exercise intervention on the symptoms of diabetic neuropathy in type 2 diabetes were included in the study. These mainly included RCTs, CCTs and quasi experimental studies.

Exclusion criteria –

Studies with causes of neuropathy other than diabetes (CIDT, Neuropathy of other derivation etc) Studies were also excluded if the participants had a diagnosis of type-1 diabetes mellitus, gestational diabetes in addition to T2DM. Cross sectional studies, Studies with animal subjects and studies advocating use of therapeutic footwear.

Full-text articles of the studies meeting the inclusion criteria were then critically reviewed and graded according to the Oxford levels of evidence. Only 2a and 2b RCTs and experimental studies were included.

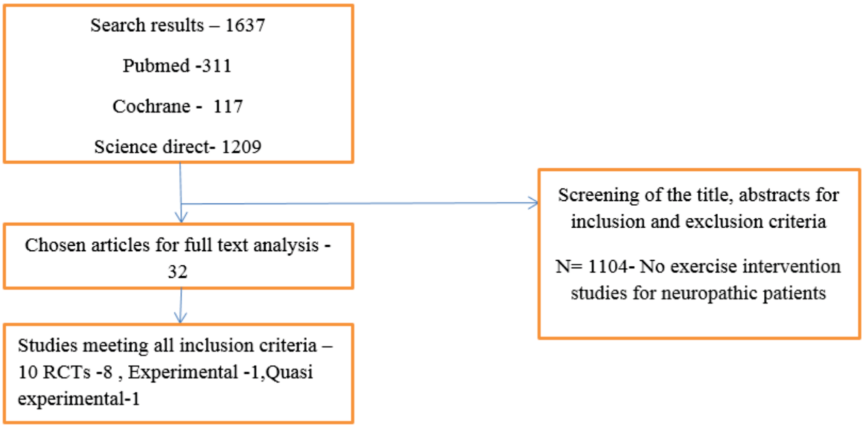

TABLE 1 Characteristics of the participants included in the studies

Sr no.	Study	Subjects	Inclusion criteria	Main exclusion criteria	Mean age (SD)
1	Snehil.Dixit et al 2014 RCT	Control arm – 47 Experimental arm – 40	clinical neuropathy score 7 on the Michigan Diabetic Neuropathy Score (MDNS)	score of 30 or > on MDNS, walking with assistive devices, part or complete foot amputation, peripheral arterial disease	70 years
2	Snehil Dixit et al 2016 RCT	36 - study group 45 - control group.	Patients with T2 DM having peripheral neuropathy, minimum score of 7 on the Michigan Diabetic Neuropathy Score.	vitamin B12 deficiency, postural hypotension, foot ulcers, walking with assistive devices, part or complete foot amputation, peripheral arterial disease,	50 – 70 years
3	S Morrison et al 2014 Experimental	(DM, n=21 DM-PN, n=16)	Presence of peripheral neuropathy based upon their total neuropathy score (TNS)	significant cardiovascular disease, unstable proliferative retinopathy, uncontrolled hypertension	mean age (58.7+1.7)
4	Eman Elsayed Fayed et al 2016 RCT	40 subjects- Study group – 20 Control group – 20 subjects	T2DM from 5- 15 years.2) peripheral diabetic neuropathy.3) BMI between 25-29.9 kg /m2	1)rheumatoid arthritis, Achilles tendinosis, post-traumatic deformities of the foot. 2) circulation problems or deep vein thrombosis. 3)Patients with diabetic open foot ulcers	45 – 55 years
5	Gholami Farhad, et al. 2018 RCT	Total patients- 31 Control group -15 Experimental group -16	Diabetes > 5 years, HbA1c between 6.6% and 12%, and diagnosed diabetic peripheral neuropathy.	Type 1 diabetes, insulin therapy	Age not considered
6	Giovanni Taveggia et al 2014 RCT	27 E- 13 C- 14	T2DM > 3 years, a diagnosis of DSP associated, able to walk autonomously.	< 5 score on the Functional Independence Measure (FIM)locomotion scale, bone instability affecting lower limb functionality	45 - 90 Years
7	Zahra Rojhani-Shirazi et al 2016 RCT	Subjects – 60 2 different intervention groups (N=20) (N=20) and a control group(N=20)	>2 scores in Michigan Neuropathy Screening Instrument (MNSI), and their Body Mass Index (BMI) was 18-30.	lower extremity complications such as fracture	45-65yrs
8	Maryam Nadi et al RCT 2017	Total – 90 45 persons in each group	Females diagnosed With T2DM, diagnosed diabetic neuropathy And diabetes duration > 5 years.	MNSI >4	20 - 55 years
9	Cory Toth et al RCT 2014	Total -54 (28-exercise and 26 – education)	perceived ability to walk on a flat surface or treadmill for at least 1 km/d at time of enrollment	(1) another cause of non-NeP source of pain that is more dominant than the peripheral NeP or that cannot be separated clinically; (2) presence of NeP for 6 months or less; (3) central nervous system cause of pain; and (4) amputation, or active neoplasia (other than forms of skin cancer	18- 80 years
10	Amin Kordi Yoosefinejad et al 2015 Quasi experimental	Total – 40 Experimental -20 Control - 20	DM, HbA1C < 8.5 %; BMI 25 - 35; Michigan Diabetic Neuropathy Score MDNS 13 - 29	epilepsy, cognitive disorders, knee or hip prosthesis, pacemaker and gall or bladder stone.	50 - 70 years.

Table 2 Levels of evidence and exercise interventions given in these studies

Sr no.	Authors	Experimental group intervention		Control group intervention	Level of evidence [16]
		Mode of Exercise	Exercise dosage		
1	Snehil.Dixit et al 2014 RCT	moderate intensity treadmill exercises	40%–60% of HRR 3–6 days/ week. 150 min/week 360 min/week of work out.	Patients were reminded telephonically every second week of the month regarding foot care and dietary habits until their final evaluation. Patients were reminded telephonically every second week of the month regarding foot care and dietary habits until their final evaluation	1c
2	Snehil Dixit et al 2016 RCT	moderate intensity treadmill exercises	3 - 6 days/ 40-60 % of HRR. 150 min/week to 360 min/week of work out	Education for foot care, and diet were given	1c
3	S Morrison et al 2014 Experimental	1)moderate intensity aerobic training (45 minutes done at 50% of HRR); or 2) vigorous intensity aerobic training (30 minutes at 75% of HRR). Aerobic exercise including treadmill walking or running, stationary cycling, and/or elliptical strider workouts.	3 times /week, supervised sessions for 12 weeks	-	2b
4	Eman Elsayed Fayed et al 2016 RCT	strengthening and stretching exercises to ankle and feet and balance and gait training	8 weeks(3 sessions/week), Each session- 60 minutes	Did not participate in exercises and took their medical treatment	2b
5	Gholami Farhad, et al. 2018 RCT	aerobic exercise program (walking,jogging or running on treadmill,	20-45 min. for 3 months (3 sessions a week,50-70% of HRR)	Habitual physical activity level and informing the researcher in case of any change	2b
6	Giovanni Taveggia et al 2014 RCT	Multimodal treatment intervention 20 minutes of treadmill, 20 minutes of isokinetic dynamometric muscle strengthening of flexor and extensor muscles of tibiotarsal joint, and 20 minutes of balance retraining on dynamic balance platform.	5 days per week, for 4 weeks – total 20 sessions	Activities to improve the endurance, manual exercises of lower limb muscle strengthening, and stretching exercises,(ie, sitting to standing, walking up and down a slope, and stair climbing)	2b
7	Zahra Rojhani-Shirazi et al 2016 RCT	Ball training- one intervention group Frenkel exercises – another intervention group	55 min, 5 days a week for 3 weeks	Information about diabetes	2b
8	Maryam Nadi et al RCT 2017	Vitamin D Supplements, simple aerobic exercises, resistance exercise movements with dumbbells (50-70% of HRR)	12 weeks and 3 sessions/week and 60 min/session.	Only received Vitamin D supplements	2b
9	Cory Toth et al RCT 2014	Exercises for stabilizing core torso muscles as well as aerobic exercises consisting of treadmill walking or running, elliptical stair climber, or cycling exercises. Exercise intensity at 40% to 60% of HRR, and then up to 85%	15 - 60 min with 3 to 5 days per week for 6 months	An educational lecture was provided by a kinesiologist for a 2-hour session Educational information provided to each patient regarding maintenance of exercise, diet, and sleep habits over the next 6 months.	2b
10	Amin Kordi Yoosefinejad et al 2015 Quasi experimental	Whole body vibration - The subjects stood barefooted with an equal weight distribution over both feet on the plate while maintaining 30° of knee flexion.	twice a week for 6 weeks (12 sessions).	Did not receive WBV and also did not participate in any physical activity training which might have affect the results.	2b

Table 3 Description of the results and conclusion

<table>
<tr><th>Study</th><th>Outcome measures</th><th>Mean – SD</th><th>Conclusion</th></tr>
<tr><td>Snehil. Dixit et al.

2014[5]</td><td>1)peroneal motor and sural sensory nerve conduction studies.
2) MDNS</td><td>Depicting the change in mean and standard deviation for parameters of nerve conduction for peroneal and sural nerve at 8th week in two groups respectively.
<table>
<tr><th></th><th></th><th colspan="2">Control Peroneal nerve</th><th colspan="2">Experimental Peroneal nerve</th><th>p Value</th></tr>
<tr><td>8th week</td><td>Latency</td><td>37</td><td>3.16 (1.83)
(3.77–2.57)</td><td>29</td><td>4.34 (1.25)
(4.80–3.89)</td><td>0.11</td></tr>
<tr><td></td><td>Duration</td><td></td><td>10.89 (1.23)
(11.30–10.49)</td><td></td><td>10.76 (1.23)
(11.21–10.31)</td><td>0.08</td></tr>
</table>
</td><td>Aerobic exercise can halt or disrupt the progression of DPN without any major adverse events in patients suffering from diabetic peripheral neuropathy</td></tr>
</table>

<table>
<tr><td></td><td></td><td>
<table>
<tr><td></td><td>Amplitude</td><td></td><td>4.75 (2.13)
(5.45–4.05)</td><td></td><td>6.31 (2)
(7.02–5.59)</td><td>0.65</td></tr>
<tr><td></td><td>Conduction velocity</td><td></td><td>38.21 (1.31)
(38.64–37.78)</td><td></td><td>45.56 (1.24)
(46.01–45.11)</td><td>0.03</td></tr>
</table>
<table>
<tr><td></td><td></td><td colspan="2">Control
Sural nerve</td><td colspan="2">Experimental
Sural nerve</td><td>p value</td></tr>
<tr><td></td><td></td><td>n</td><td>Mean SD</td><td>n</td><td>Mean SD</td><td></td></tr>
<tr><td>8th week</td><td>Latency</td><td>37</td><td>3.39 (1.45)
(3.87–2.90)</td><td>29</td><td>3.45 (1.38)
(3.95–2.95)</td><td>0.33</td></tr>
<tr><td></td><td>Duration</td><td></td><td>1.46 (1.90)
(2.10–0.82)</td><td></td><td>1.86 (1.75)
(2.5–1.22)</td><td>0.27</td></tr>
<tr><td></td><td>Amplitude</td><td></td><td>3.94 (2.23)
(4.69–3.19)</td><td></td><td>2.14 (2.38)
(3.01–1.27)</td><td>0.85</td></tr>
<tr><td></td><td>Conduction velocity</td><td></td><td>28.53 (1.49)
(29.02–28.04)</td><td></td><td>31.39 (1.58)
(31.97 -30.81)</td><td>< 0.001</td></tr>
</table>
</td><td></td></tr>
<tr><td>Snehil Dixit et al
2014[6]</td><td>1)The Metitur Good Balance System - four conditions in quiet static standing: eyes open (EO), eyes closed (EC), and EO on foam (EOF), and EC on foam (ECF).
2)Posturography - sway</td><td>Mean values and standard deviation for postural control measures at baseline in the EO and EC conditions on a foam surface.
<table>
<tr><td>Variable</td><td colspan="2">Baseline</td><td colspan="2">Eighth Week</td><td>P value</td></tr>
<tr><td></td><td>Study group</td><td>Control group</td><td>Study group</td><td>Control group</td><td></td></tr>
<tr><td>EOF along x-axis</td><td>2.31 ± 1.19
(1.91-2.71)</td><td>2.37 ±1.21
(2.11-2.63)</td><td>2.17 ± 1.22
(1.91-2.43)</td><td>2.37 ± 1.24
(2.11-2.63)</td><td>0.17</td></tr>
<tr><td>EOF along y-axis</td><td>2.63 ± 1.19
(2.38-2.88)</td><td>2.84 ±1.19
(2.59-3.09)</td><td>2.69 ±1.18
(2.44-2.94)</td><td>2.76 ± 1.15
(2.52-3)</td><td>0.17</td></tr>
<tr><td>EOF VM</td><td>4.36 ±1.30
(4.09-4.63)</td><td>4.89 ±1.37
(4.6-5.18)</td><td>4.41 ± 1.39
(4.12-4.7)</td><td>4.76 ± 1.35
(4.7-5.05)</td><td>0.32</td></tr>
<tr><td>EOF AP displacement</td><td>2.38 ± 1.36
(2.09-2.67)</td><td>2.13 T 1.38
(1.84-2.42)</td><td>2.34 T 1.33
(2.06-2.62)</td><td>2.1 T 1.23(1.84-2.36)</td><td>0.94</td></tr>
<tr><td>EOF ML displacement</td><td>3.68 ±1.35
(3.39-3.97)</td><td>3.37 ± 1.51
(3.05-3.69)</td><td>3.96 ±1.56
(3.63-4.29)</td><td>3.48 ±1.58
(3.15-3.81)</td><td>0.49</td></tr>
<tr><td>ECF along x-axis</td><td>2.62 ± 1.27
(2.35-2.89)</td><td>2.41 ±1.23
(2.15-2.67)</td><td>8.54 ± 1.79
(8.16-8.92)</td><td>9.22 ± 1.66
(8.87-9.57)</td><td>0.04</td></tr>
<tr><td>ECF along y-axis</td><td>3.23 ±1.16
(2.98-3.48)</td><td>3.22 ±1.27
(2.95-3.49)</td><td>3.35 ±1.23
(3.09-3.61)</td><td>3.33 ± 1.16
(3.08-3.58)</td><td>0.09</td></tr>
<tr><td>ECF VM</td><td>5.35 ±1.32
(5.07-5.63)</td><td>5.34 ± 1.35
(5.05-5.63)</td><td>5.56 ± 1.37
(5.27-5.85)</td><td>6 ±1.38
(5.71-6.29)</td><td>0.16</td></tr>
<tr><td>ECF AP displacement</td><td>1.89 ±1.32
(1.61-2.17)</td><td>1.91 ±1.58
(1.58-2.24)</td><td>1.74 ± 1.35
(1.45-2.03)</td><td>1.65 ± 1.33
(1.37-1.93)</td><td>0.08</td></tr>
<tr><td>ECF ML displacement</td><td>3.30 ± 1.58
(2.97-3.63)</td><td>3.24 ±1.55
(2.91-3.57)</td><td>3.34 ± 1.54
(3.02-3.66)</td><td>2.76 ± 1.61
(2.42-3.1)</td><td>0.03</td></tr>
</table>
</td><td>Aerobic exercise training exerted a moderate effect on the Eyes Closed condition along the x-axis on foam surface in quiet standing may be helpful in reducing the risk of fall in individuals with diabetic neuropathy.</td></tr>
<tr><td>Morrison S et al [7]</td><td>1) Reaction Time-SRT task
2) Posture Assessment-Bertec balance plate, 1) eyes open/firm surface, 2) eyes closed/firm surface, 3) eyes open/foam surface, and 4) eyes closed/foam surface
3) Gait Assessment:20 ft GAITRite pressure sensitive walking surface</td><td>Significant Changes in Reaction Time, Gait and Postural (eyes closed/foam surface only) Metrics for each group before and after 12 weeks of aerobic training
<table>
<tr><td>Variable</td><td></td><td colspan="2">DM</td><td colspan="2">DM-PN</td></tr>
<tr><td></td><td></td><td>Pre-Training</td><td>Post-Training</td><td>Pre-Training</td><td>Post-Training</td></tr>
<tr><td>Reaction Time</td><td>Upper limb: Hand (ms)</td><td>219.68+2.82</td><td>210.54+1.75</td><td>232.87+2.92</td><td>217.30+2.85</td></tr>
<tr><td></td><td>Lower Limb: Foot (ms)</td><td>294.89+3.27</td><td>283.62+4.89</td><td>299.37+3.13</td><td>285.79+3.19</td></tr>
<tr><td>Gait</td><td>Gait Velocity (cm/s)</td><td>113.07+1.69</td><td>117.56+1.52</td><td>108.91+1.73</td><td>116.42+2.15</td></tr>
<tr><td></td><td>Stride Length (cm)</td><td>61.17+0.51</td><td>63.36+0.55</td><td>59.24+0.65</td><td>62.73+0.81</td></tr>
<tr><td></td><td>Step Length (cm)</td><td>123.17+0.93</td><td>126.32+1.01</td><td>122.81+1.28</td><td>125.80+1.59</td></tr>
<tr><td></td><td>Time Spent in Stance (%)</td><td>63.1+0.7</td><td>60.7+1.1</td><td>63.6+0.9</td><td>61.8+1.0</td></tr>
<tr><td></td><td>Stride Length Variability(%)</td><td>3.02+0.30</td><td>3.89+0.74</td><td>2.72+0.22</td><td>3.22+0.34</td></tr>
<tr><td>Balance</td><td>COP velocity (cm/s)</td><td>120+2.1</td><td>126+2.7</td><td>111+2.1</td><td>116+2.4</td></tr>
<tr><td></td><td>Path length (cm)</td><td>155215+7051</td><td>155766+7694</td><td>125453+4069</td><td>140045+5355</td></tr>
</table>
</td><td>T2DM individuals, with peripheral neuropathy reported more higher falls risk, slower reactions, slower gait, and altered postural control.
All persons showed improvement in balance, reaction time and gait metrics following 12 weeks of isocaloric aerobic exercise.</td></tr>
</table>

	ML COP Range (cm)	1989+78	2314+108	1823+77	2038+125
	ML COP SD (cm)	383+16	459+22	369+17	456+27
	ML COP Mean (cm)	998+42	1146+55	925+43	1172+80
	Postural Coordination (Number of errors)	7.43+1.43	5.36+1.50	9.95+3.09	6.34+1.89

Eman Elsayed Fayed et al [8]	Plantar pressure distribution in 6 regions: hind foot, first metatarsal, second metatarsal, third metatarsals, forth metatarsals, fifth metatarsals	Compares the mean values of peak pressure recorded at the base line and follow up measures of the right foot in study (G1) and control (G2) groups (*significant differences)	Physiotherapeutic interventions is effective in prevention of soft tissue strain and ulceration of the planter surface of the foot among diabetic patients

Foot region	Study group				Control group			
	Mean ±SD	*t*	*p*	% imp	Mean ±SD	*t*	*p*	% imp
Hindfoot Pre	210.25 ±25.42	12.652	.001	18.10	213.25 ±40.58	-1.336	0.197	1.29
Hindfoot Post	172.20 ±17.19				216.00 ±38.90			
MH1 Pre	202.85 ±29.23	12.667	.001	18.34	202.35 ±35.32	-1.503	0.149	1.33
MH1 Post	165.65 ±33.40				205.05 ±37.57			
MH2 Pre	239.60 ±33.69	9.409	.001*	22.75	241.55 ±79.58	10.242	0.264	-1.80
MH2 Post	185.10 ±38.00				237.20 ±79.74			
MH3 Pre	218.90 ±39.99	10.486	.001	17.31	223.05 ±71.75	0.702	0.491	-1.99
MH3 Post	181.00 ±33.75				218.60 ±74.07			
MH4 Pre	167.05 ±31.58	8.638	.001	26.52	169.55 ±50.01	-0.578	0.570	1.03
MH4 Post	122.75 ±33.63				171.30 ±48.42			
MH5 Pre	119.20 ±35.60	5.426	.001	23.20	120.85 ±31.58	-1.133	0.271	4.51
MH5 Post	210.25 ±25.42				126.30 ±34.07			

SD, Standard Deviation P ≤ 0.05= significant* % imp.: Percentage of improvement MH: metatarsal head.

Compares the mean values of contact area recorded at the base line and follow up measures of the right foot in study (G1) and G2 groups.

Foot region	Study group				Control group			
	Mean ±SD	T	p	% imp	Mean ±SD	t	p	% imp
Hindfoot Pre	22.15 ±6.40	-2.795	.012	16.02	19.85 ±4.39	-1.398	0.178	7.30
Hindfoot Post	25.70 ±4.28				21.30 ±3.96			
MH1 Pre	7.90± 5.98	-5.409	.001*	48.73	9.50± 3.26	1.732	0.099	-18.42
MH1 Post	11.75 ±4.30				7.75± 3.38			
MH2 Pre	5.75± 3.65	-6.453	.001*	54.93	6.60± 1.69	0.637	0.531	-5.30
MH2 Post	8.90± 4.11				6.25± 1.91			
MH3 Pre	5.55± 4.19	-9.404	.001*	81.98	7.55± 3.76	-0.459	0.652	5.30
MH3 Post	10.10 ±4.17				7.95± 2.92			
MH4 Pre	5.25± 3.33	-7.464	.001*	63.80	6.85± 3.88	0.483	0.635	5.84
MH4 Post	8.60± ±2.60				6.45± 2.94			
MH5 Pre	5.10± 3.52	-16.709	.001	90.19	5.95± 1.35	-1.535	0.141	3.53
MH5 Post	9.70± 3.18				6.80± 2.91			

<table>
<tr>
<td>Farhad Gholami et al [9]</td>
<td>NCV-The sural nerve for sensory nerve conduction and peroneal and tibial nerves for motor nerve conduction study</td>
<td>Values of body composition and calorie intake at baseline and at the end of experimental period

Comparison of values for outcome measures before and after the experimental period between groups (mean ± SD).
<table>
<tr><td>Group</td><td colspan="2">Experimental ($n = 12$)</td><td colspan="2">Control ($n = 12$)</td></tr>
<tr><td></td><td>pre</td><td>post</td><td>pre</td><td>post</td></tr>
<tr><td colspan="5"><i>Variable</i></td></tr>
<tr><td>SNCV (m/s)</td><td>35.2 ± 4.3</td><td>37.3 ± 6.2</td><td>33.7 ± 2.5</td><td>33.0 ± 2.8</td></tr>
<tr><td>PNCV (m/s)</td><td>39.0 ± 3.6</td><td>40.4 ± 4.4</td><td>41.8 ± 4.4</td><td>42.0 ± 5.2</td></tr>
<tr><td>TNCV (m/s)</td><td>38.3 ± 6.6</td><td>40.2 ± 6.1</td><td>40.0 ± 3.9</td><td>40.5 ± 4.8</td></tr>
<tr><td>SNAPA (_V)</td><td>7.1 ± 2.6</td><td>7.4 ± 2.5</td><td>6.7 ± 2.1</td><td>6.8 ± 2.1</td></tr>
<tr><td>PNAPA (mV)</td><td>3.2 ± 1.7</td><td>3.3 ± 1.3</td><td>3.0 ± 0.6</td><td>3.1 ± 0.6</td></tr>
<tr><td>TNAPA (mV)</td><td>5.0 ± 1.3</td><td>5.4 ± 1.5</td><td>4.7 ± 2.0</td><td>4.8 ± 1.8</td></tr>
<tr><td>Fasting glucose (mmol/L)</td><td>11.22 ± 3.8</td><td>8.58 ± 2.7*</td><td>10.90 ± 3.6</td><td>9.99 ± 4.46</td></tr>
<tr><td>2hpp (mmol/L)</td><td>15.76 ± 2.5</td><td>14.21 ± 2.5</td><td>15.15 ± 4.8</td><td>15.27 ± 4.5</td></tr>
<tr><td>HbA1c (%)</td><td>8.3 ± 1.4</td><td>7.7 ± 1.5</td><td>8.6 ± 1.4</td><td>8.5 ± 1.8</td></tr>
<tr><td>EST (min)</td><td>8.85 ± 1.4</td><td>10.12 ± 1.0</td><td>8.68 ± 1.1</td><td>8.47 ± 1.2</td></tr>
</table>
SNCV: sural nerve conduction velocity; PNCV: peroneal nerve conduction velocity; TNCV: tibial nerve conduction velocity; SNAPA: sural nerve action potential amplitude; PNAPA: peroneal nerve action potential amplitude; TNAPA: tibial nerve action potential amplitude; 2hpp: two hours postprandial glucose level; EST: exercise stress test. * Significantly ($P < 0.05$) different from pre-test values. ** Time × group interaction is significant ($P < 0.05$).</td>
<td>Improved sensory nerve conduction velocity and glucose control denotes that patients with PN may benefit from supervised exercise programs.</td>
</tr>
<tr>
<td>Zahra Rojhani-Shirazi et al[11]</td>
<td>1)One Leg Stance (OLS)test
2)Berg Balance Scale (BBS)
3)Star Excursion Balance Test (SEBT)</td>
<td>Balance measures before and after the intervention
<table>
<tr><td></td><td colspan="2">Ball training group (N=20)</td><td colspan="2">Frenkel training group (N=20)</td><td colspan="2">Control group (N=20)</td></tr>
<tr><td></td><td>Pre</td><td>Post (Mean± SD)</td><td>Pre</td><td>Post (Mean± SD)</td><td>Pre</td><td>Post (Mean± SD)</td></tr>
<tr><td colspan="7">OLS (s)</td></tr>
<tr><td>EO (right)</td><td>5.12± 1.66</td><td>9.22± 1.63</td><td>5.54± 1.89</td><td>7.88± 1.84</td><td>6.15± 1.67</td><td>6.26± 1.17</td></tr>
<tr><td>(left)</td><td>3.84± 1.31</td><td>6.49± 1.69</td><td>4.12± 1.21</td><td>5.41± 1.21</td><td>4.38± 1.07</td><td>4.28± 1.20</td></tr>
<tr><td>EC (right)</td><td>2.84± 0.89</td><td>5.19± 1.24</td><td>3.45± 1.19</td><td>4.23± 1.17</td><td>3.45± 1.00</td><td>3.26± 1.26</td></tr>
<tr><td>(left)</td><td>2.61± 1.00</td><td>4.34± 1.19</td><td>3.19± 0.64</td><td>3.45± 0.97</td><td>2.74± 0.94</td><td>2.37± .093</td></tr>
<tr><td>BBS (score)</td><td>44.50± 5.17</td><td>47.35± 2.64</td><td>42.35± 3.66</td><td>44.05± 3.34</td><td>41.55± 4.01</td><td>41.35± 3.89</td></tr>
<tr><td colspan="7">SEBT (distance)</td></tr>
<tr><td>Ant</td><td>51.24± 10.90</td><td>59.85± 10.99</td><td>50.15± 11.69</td><td>51.82±11 .50</td><td>44.32± 7.44</td><td>42.98± 7.33</td></tr>
<tr><td>Post-med</td><td>45.48± 12.03</td><td>54.64± 11.93</td><td>42.77± 11.06</td><td>46.78± 10.68</td><td>45.27± 9.69</td><td>39.01± 7.19</td></tr>
<tr><td>Post-lat</td><td>53.71± 8.71</td><td>64.85± 10.29</td><td>54.51± 11.72</td><td>58.13± 8.39</td><td>54.11± 8.44</td><td>51.35± 6.75</td></tr>
</table>
OLS = One leg stance; EO = Eye open; EC = Eye closed; BBS = Berg balance scale; SEBT = Star excursion balance test</td>
<td>Frenkel and Swiss ball exercises are efficient in improvement of balance in diabetic patients.
Swiss ball was preferred over Frenkel training</td>
</tr>
<tr>
<td>Maryam Nadi, et al[12]</td>
<td>Pain
Sense of touch
Knee and ankle reflex</td>
<td>Frequency distribution of diabetic neuropathy
<table>
<tr><td>Variable</td><td>Period</td><td>Period</td><td colspan="2"><i>n</i> (%)</td><td colspan="2">Statistics</td></tr>
<tr><td></td><td></td><td></td><td>Has</td><td>Does not have</td><td>$\chi2$</td><td><i>P</i></td></tr>
<tr><td>Pain</td><td>Pretest</td><td>Control</td><td>23 (56.1)</td><td>18 (43.9)</td><td>0.99</td><td>0.32</td></tr>
<tr><td></td><td></td><td>Experiment</td><td>18 (45)</td><td>22 (55)</td><td></td><td></td></tr>
<tr><td></td><td>Posttest</td><td>Control</td><td>23 (56.1)</td><td>18 (43.9)</td><td>9.56</td><td>0.002</td></tr>
<tr><td></td><td></td><td>Experiment</td><td>9 (22.5)</td><td>31 (77.5)</td><td></td><td></td></tr>
<tr><td>Sense of touch</td><td>Pretest</td><td>Control</td><td>23 (56.1)</td><td>18 (43.9)</td><td>0.3</td><td>0.58</td></tr>
<tr><td></td><td>Posttest</td><td>Experiment</td><td>24 (58.5)</td><td>17 (41.5)</td><td>7.9</td><td>0.005</td></tr>
<tr><td></td><td></td><td>Control</td><td>11 (27.5)</td><td>29 (72.5)</td><td></td><td></td></tr>
</table></td>
<td>Doing exercises in parallel of Vitamin D supplementation could have an extra effect on decreasing the complication of diabetic neuropathy.</td>
</tr>
</table>

<table>
<tr>
<td>Cory Toth et al[13]</td>
<td>VAS of the short form McGill Pain Questionnaire</td>
<td>
<table>
<tr><td colspan="5">Timepoints</td></tr>
<tr><td>Characteristics</td><td>Baseline Exercise (n=28)</td><td>Baseline Education (n=26)</td><td>Endpoint Exercise (n=28)</td><td>Endpoint Education (n=26)</td></tr>
<tr><td colspan="5">European Quality of Life-5 Domains (EQ-5D)</td></tr>
<tr><td>EQ-5D utility score</td><td>64.3±4.3</td><td>63.2±6.2</td><td>68.6±4.9</td><td>65.2±7.0</td></tr>
<tr><td>EQ-5D index score</td><td>0.58±0.06</td><td>0.54±0.07</td><td>0.61±0.07</td><td>0.56±0.06</td></tr>
<tr><td colspan="5">Medical Outcomes Study Sleep Scale (MOSSS)</td></tr>
<tr><td>Characteristic MOSSS sleep problems index</td><td>32.9±1.9</td><td>32.5±2.3</td><td>29.8±2.1</td><td>31.0±2.4</td></tr>
<tr><td colspan="5">Hospital Anxiety and Depression Scale (HADS)</td></tr>
<tr><td>Characteristic HADS-A (anxiety)</td><td>7.8±0.9</td><td>7.4±1.2</td><td>7.4±1.1</td><td>7.1±1.3</td></tr>
<tr><td>HADS-D(depression)</td><td>5.6±0.6</td><td>5.8±1.3</td><td>5.5±0.8</td><td>5.7±1.4</td></tr>
<tr><td colspan="5">Karnofsky Performance Scale</td></tr>
<tr><td>Karnofsky mean Score</td><td>68.2±6.5</td><td>66.7±7.3</td><td>70.6±7.3</td><td>65.8±8.4</td></tr>
<tr><td>Weight (kg)</td><td>78.2±9.8</td><td>79.7±9.3</td><td>77.6±10.5</td><td>79.9±9.5</td></tr>
<tr><td>Body mass indices (Kg/m2)</td><td>27.4±3.5</td><td>27.7±3.7</td><td>27.2±3.4</td><td>27.7±3.7</td></tr>
</table>
</td>
<td>Impact of an exercise program for patients with DPN may increase exercise capacity, but failed to impact significantly upon pain severity.</td>
</tr>
<tr>
<td>Amin Kordi Yoosefinejad et al.[14]</td>
<td>Timed Up & Go Test (TUGT) Unilateral Stance Test (UST) Balance evaluation - eight diff</td>
<td>TUGT-Timed Up & Go Test; UST- Unilateral Stance Test; ONF- Open eye No foam; OF-Open eye with foam; CNF- Closed eye No foam; CF- Closed eye with Foam
<table>
<tr><td>Parameter</td><td>F-value</td><td>ICC</td><td>P-value</td></tr>
<tr><td>mean velocity (ONF)</td><td>20.42</td><td>0.95</td><td><0.001*</td></tr>
<tr><td>mean velocity (CNF)</td><td>23.45</td><td>0.95</td><td><0.001*</td></tr>
<tr><td>mean velocity (OF)</td><td>42.78</td><td>0.97</td><td><0.001*</td></tr>
<tr><td>mean velocity (CF)</td><td>50.42</td><td>0.98</td><td><0.001*</td></tr>
<tr><td>quadriceps strength</td><td>10.07</td><td>0.89</td><td><0.001*</td></tr>
<tr><td>tibialis anterior strength</td><td>15.00</td><td>1.23</td><td><0.001*</td></tr>
<tr><td>general strength</td><td>50.30</td><td>0.90</td><td><0.001*</td></tr>
<tr><td>TUGT</td><td>5.22</td><td>0.80</td><td><0.001*</td></tr>
<tr><td>UST</td><td>4.30</td><td>0.76</td><td><0.001*</td></tr>
</table>
ICC of Outcomes</td>
<td>Whole Body Vibration enhances the muscle isometric strength and improves the mobility and balance in type 2 diabetic patients with peripheral neuropathy.</td>
</tr>
<tr>
<td>Giovanni Taveggia et al [10]</td>
<td>6-Minute Walk Test. 10-Meter Walking Test</td>
<td>6MWT, 6-meter walking test; DBP, diastolic blood pressure; Exp, experimental group; F, F ratio; FEO2, fraction of expired air that is oxygen; FIM, functional independence measure; HR, heart rate; REE, resting energy expenditure; RR, respiratory rate; SBP, systolic blood pressure; SpO2, oxygen saturation; TWT, 10-meter walking test; VE, expired minute volume; VO2max, maximal oxygen consumption; SCG, standard care group; SS, sum of squares;.
<table>
<tr><td>Outcome</td><td colspan="3">Difference Between Groups</td></tr>
<tr><td></td><td>Pretreatment</td><td>Post treatment</td><td>Follow-up</td></tr>
<tr><td></td><td>Exp minus SCG</td><td>Exp minus SCG</td><td>Exp minus SCG</td></tr>
<tr><td>6MWT</td><td>16.3
(−117, 149)</td><td>22.2
(−90.2, 134.6)</td><td>−44.1
(−173, 85.0)</td></tr>
<tr><td>TWT</td><td>−0.04
(−0.3, 0.3)</td><td>−0.17
(−0.6, 0.3)</td><td>0.47
(−0.3, 0.4)</td></tr>
<tr><td>FIM</td><td>−0.6
(−7.3, 6.01)</td><td>−1.6
(−7.1, 4.0)</td><td>−3.5
(−10.0, 3.0)</td></tr>
<tr><td>Tinetti scale walk</td><td>−0.2
(−2.1, 1.8)</td><td>1.0
(1.9, 3.9)</td><td>−0.4
(−2.3, 1.5)</td></tr>
<tr><td>SBP</td><td>−1.8
(−12.9, 9.3)</td><td>−3.5
(−18.7, 11.5)</td><td>3.6
(−11.5, 18.7)</td></tr>
<tr><td>DBP</td><td>2.4
(−8.9, 13.8)</td><td>−1.1
(−14.3, 12.1)</td><td>2.9
(−10.2, 16.0)</td></tr>
<tr><td>RR</td><td>−1.3
(−4.6, 1.9)</td><td>−0.5
(−1.9, 0.9)</td><td>0.5
(−0.9, 1.9)</td></tr>
<tr><td>HR</td><td>−0.3
(−19.0, 18.4)</td><td>−12.1
(−41.7, 17.5)</td><td>−6.2
(−23.1, 10.7)</td></tr>
<tr><td>VO2max</td><td>−231
(−666, 203)</td><td>29.0
(−235, 293)</td><td>−217
(−676, 241)</td></tr>
<tr><td>SPO2</td><td>−2.8
(−5.5, -0.2)</td><td>1.2
(−0.5, 3.0)</td><td>−2.0
(−7.0, 3.1)</td></tr>
<tr><td>REE</td><td>0.4
(−466, 467)</td><td>−232
(−538, 73.3)</td><td>101
(−611, 812)</td></tr>
</table>
</td>
<td></td>
</tr>
</table>

			VE (L/m)	−0.08 (−3.38, 3.22)	0.249 (−1.83, 2.33)	−0.092 (−1.82, 1.64)	
			FEO2 (%)	−0.21 (−0.81, 1.23)	0.613 (0.058, 1.167)	−0.382 (−1.72, 0.959)	

DISCUSSION –

Studies from the last 5 years have been considered in the study hinting that more research has been carried out in the field of diabetic neuropathy.We can say that the evidence for exercise interventions in neuropathic patients has improved, although study quality is diverse.One of the major aspects to be considered is the absence of long term follow up in most of the studies.The overall study quality for the studies analyzed is 2b signifying the need for high quality studies to be performed in this field.[16]

Three studies out of ten have considered MDNS score as an inclusion criteria,two studies have considered MNSI score as while one has considered Total Neuropathy Score as an inclusion criteria in their study.[5][6][14]Other studies have considered peripheral neuropathy based on the diagnosis of physician.Almost all studies have included participants with age more than 45 years except for one study by Maryam Nadi et al where the participants ranged between 20-55 years old were included in the study.[9] Gholami et al have not taken into consideration age as inclusion criteria in their study.[12] The Exclusion criteria are varied in all the studies, the most common being lower extremity complications like foot ulcers or amputations and deep vein thrombosis.

In various articles that were analyzed , exercise interventions in the form of aerobic treadmill training, strengthening exercises for lower limbs, Swiss ball exercises, frenkel exercises, multimodal treatment in the form of dynamometry and lower limb strengthening and whole body vibration were given to reduce symptoms of diabetic neuropathy.Aerobic treadmill training has been used as an intervention in five studies out of ten signifying the importance of aerobic exercises for reducing symptoms of neuropathy.The intervention period has been different in different studies and ranges from merely 3 weeks to 6 months.

Since the symptoms of diabetic neuropathy are varied, it is impossible to study symptoms using only one outcome measure. Hence various outcome measures like Nerve Conduction Velocity , Posturography , One Leg Stance (OLS)test ,Berg Balance Scale (BBS),Reflexes, 6 Minute walk test,10 meter walk test(TWT), Time Up and Go Test, Star Excursion Balance Test(SEBT) etc have been used to study the effect of exercise intervention on diabetic neuropathy symptoms.[5][6][7][8][9][10]

The most commonly given exercise intervention among the analyzed studies was aerobic training and strengthening exercises. In studies by Dixit et al, Morrison et al,Gholami et al,Fayed et al,Maryam Nadi et al,aerobic training was used as the main exercise intervention.[5][6][9][12]Other interventions in combination with aerobic training included strengthening exercise ,balance and gait training and whole body vibration techniques.[4][6][7][10]

Mild to moderate intensity exercises do show improvements in diabetic patients experiencing neuropathy.[6][8]The outcomes of each study vary in respect to what is being measured. Some studies focused on alleviating pain or pain interference while others focused on preventing further complications such as falling, ulcers, or amputations. Because the exercises have different intentions, making a comparison to rank which exercise is most beneficial for patients with neuropathy is not possible.

Each show improvements in patient outcomes including quality of life, decreased pain intensities, and improved balance and gait. However, when comparing the different studies, there are no set guidelines, requirements, or measurement outcome tools utilized in DPN for every study. Because of the varieties in the types of outcome tools, the data cannot be fairly compared. The studies in this research have shown that mild to moderate intensity treadmill training are successful in disrupting progression of diabetic neuropathy. Aerobic training has also proved successful in improving Nerve Conduction Velocity thus reducing symptoms of neuropathy.[5][6][7][9][12]

As research in DPN develops, more trials in exercises should be completed. Specifically, combination of exercise and medication therapies, comparisons in length and duration of exercises, and studies in types of exercises could contribute noteworthy evidence for DPN patients striving to manage their symptoms. One underlying issue with each of these studies is the lack of a gold standard in measuring outcomes to determine any quantitative or qualitative improvements; therefore, integrating a system of universal measurements in DPN is imperative.

CONCLUSION –

Since DPN symptoms are diverse, single exercise intervention is ineffective for treating diabetic neuropathy and hence combination of exercise interventions are needed to reduce neuropathic symptoms. Also, mild to moderate aerobic training in combination with other exercise interventions can prove most beneficial for the treatment of diabetic neuropathy.

REFERENCES –

1) Gu Y, Dennis SM. Are falls prevention programs effective at reducing the risk factors for falls in people with type-2 diabetes mellitus and peripheral neuropathy: a systematic review with narrative synthesis. Journal of diabetes and its complications. 2017 Feb 1;31(2):504-16.
2) Chapman A, Meyer C, Renehan E, Hill KD, Browning CJ. Exercise interventions for the improvement of falls-related outcomes among older adults with diabetes mellitus: A systematic review and meta-analyses. Journal of diabetes and its complications. 2017 Mar 1;31(3):631-45.
3) Johnson CE, Takemoto JK. A Review of Beneficial Low-Intensity Exercises in Diabetic Peripheral Neuropathy Patients. Journal of Pharmacy & Pharmaceutical Sciences. 2019 Jan 1;22(1):22-7.
4) Streckmann F, Zopf EM, Lehmann HC, May K, Rizza J, Zimmer P, Gollhofer A, Bloch W, Baumann FT. Exercise intervention studies in patients with peripheral neuropathy: a systematic review. Sports medicine. 2014 Sep 1;44(9):1289-304.
5) Dixit S, Maiya AG, Shastry BA. Effect of aerobic exercise on peripheral nerve functions of population with diabetic peripheral neuropathy in type 2 diabetes: a single blind, parallel group randomized controlled trial. Journal of Diabetes and its Complications. 2014 May 1;28(3):332-9.
6) Dixit S, Maiya A, Shastry BA, Guddattu V. Analysis of postural control during quiet standing in a population with diabetic peripheral neuropathy undergoing moderate intensity aerobic exercise training: a single blind, randomized controlled trial. American journal of physical medicine & rehabilitation. 2016 Jul 1;95(7):516-24.
7) Morrison S, Colberg SR, Parson HK, Vinik AI. Exercise improves gait, reaction time and postural stability in older adults with type 2 diabetes and neuropathy. Journal of Diabetes and its Complications. 2014 Sep 1;28(5):715-22.
8) Monteiro RL, Sartor CD, Ferreira JS, Dantas MG, Bus SA, Sacco IC. Protocol for evaluating the effects of a foot-ankle therapeutic exercise program on daily activity, foot-ankle functionality, and biomechanics in people with diabetic polyneuropathy: a randomized controlled trial. BMC musculoskeletal disorders. 2018 Dec;19(1):400.
9) Gholami F, Nikookheslat S, Salekzamani Y, Boule N, Jafari A. Effect of aerobic training on nerve conduction in men with type 2 diabetes and peripheral neuropathy: a randomized controlled trial. Neurophysiologie Clinique. 2018 Sep 1;48(4):195-202.
10) Taveggia G, Villafañe JH, Vavassori F, Lecchi C, Borboni A, Negrini S. Multimodal treatment of distal sensorimotor polyneuropathy in diabetic patients: a randomized clinical trial. Journal of Manipulative and Physiological Therapeutics. 2014 May 1;37(4):242-52.
11) Rojhani-Shirazi Z, Barzintaj F, Salimifard MR. Comparison the effects of two types of therapeutic exercises Frenkele vs. Swiss ball on the clinical balance measures in patients with type II diabetic neuropathy. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2017 Nov 1;11:S29-32.
12) Nadi M, Marandi SM, Esfarjani F, Saleki M, Mohammadi M. The comparison between effects of 12 weeks combined training and vitamin D supplement on improvement of sensory-motor neuropathy in type 2 diabetic women. Advanced biomedical research. 2017;6.
13) Toth C, Brady S, Gagnon F, Wigglesworth K. A randomized, single-blind, controlled, parallel assignment study of exercise versus education as adjuvant in the treatment of peripheral neuropathic pain. The Clinical journal of pain. 2014 Feb 1;30(2):111-8.
14) Yoosefinejad AK, Shadmehr A, Olyaei G, Talebian S, Bagheri H, Mohajeri-Tehrani MR. Short-term effects of the whole-body vibration on the balance and muscle strength of type 2 diabetic patients with peripheral neuropathy: a quasi-randomized-controlled trial study. Journal of Diabetes & Metabolic Disorders. 2015 Dec;14(1):45.
15) Boulé NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. Diabetologia. 2003 Aug 1;46(8):1071-81.
16) Philipps B, Ball C, Sackett D, et al. Oxford Centre for Evidence based Medicine-Levels of evidence. March 2009.
17) Sigal RJ. Diabetes Canada clinical practice guidelines: What's new in the physical activity chapter. Diabetes. 2018 Oct 5.
18) Allet L, Armand S, De Bie RA, Golay A, Monnin D, Aminian K, Staal JB, De Bruin ED. The gait and balance of patients with diabetes can be improved: a randomised controlled trial. Diabetologia. 2010 Mar 1;53(3):458-66.
19) Pop-Busui R, Boulton AJ, Feldman EL, Bril V, Freeman R, Malik RA, Sosenko JM, Ziegler D. Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes care. 2017 Jan 1;40(1):136-54.
20) Colberg SR, Parson HK, Nunnold T, Holton DR, Swain DP, Vinik AI. Change in cutaneous perfusion following 10 weeks of aerobic training in Type 2 diabetes. Journal of diabetes and its complications. 2005 Sep 1;19(5):276-83.
21) Ibáñez J, Gorostiaga EM, Alonso AM, Forga L, Argüelles I, Larrión JL, Izquierdo M. Lower muscle strength gains in older men with type 2 diabetes after resistance training. Journal of diabetes and its complications. 2008 Mar 1;22(2):112-8.
22) Balducci S, Iacobellis G, Parisi L, Di Biase N, Calandriello E, Leonetti F, Fallucca F. Exercise training can modify the natural history of diabetic peripheral neuropathy. Journal of diabetes and its complications. 2006 Jul 1;20(4):216-23.