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Does multifactorial inspiratory muscle training improve postural stability and quality of life of patients with diabetes in Pakistan? A randomised controlled trial

Suman Sheraz ,[1] Arshad Nawaz Malik ,[1] Francesco Vincenzo Ferraro ,[2] Furqan Ahmed Siddiqi[3]

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[1]Faculty of Rehabilitation And Allied Health Sciences, Riphah International University, Islamabad, Pakistan
[2]Biomedical and Clinical Research Theme, School of Human Sciences, University of Derby, Derby, UK
[3]Foundation University College of Physical Therapy, Foundation University Islamabad, Islamabad, Pakistan

Correspondence to
Dr Suman Sheraz; suman.sheraz@riphah.edu.pk

ABSTRACT

Objective To determine the effects of multifactorial inspiratory muscle training (IMT) combined with Otago Exercise Programme (OEP) on balance and quality of life (QoL) in patients with diabetes.

Methods Pretest–post-test randomised controlled trial.

Setting Rehabilitation Department of Pakistan Railway General Hospital.

Participants 70 patients with diabetes were randomly assigned to experimental or placebo groups, out of which 59 patients completed the intervention.

Intervention Patients in the experimental group performed OEP+IMT (at 50% of baseline maximum inspiratory pressure (MIP)) whereas the placebo group performed OEP+sham IMT (at 15% of MIP). Both groups exercised for 12 consecutive weeks.

Outcome measures Outcome measures included nine variables: the Berg Balance Scale (BBS), the Biodex Postural Stability System (including postural stability test (Overall Stability Index, Anterior–Posterior Index and Mediolateral Index), fall risk test (FRT), Limits of Stability (LOS) test (time to complete test and direction control), Clinical Test of Sensory Interaction and Balance (CTSIB)) and the Audit of Diabetes Dependent Quality of Life questionnaire.

Results Out of 59 patients who completed treatment, 37.1% were men and 62.9% were women with a mean age of 58.37±5.91 years. Results show significant interaction effects on BBS scores with the mean score improving from 41.87±2.61 to 49.16±2.50 in IMT versus sham IMT group with scores improving from 41.58±2.51 to 45.74±2.30. The IMT group significantly improved in dynamic balance tested through BBS (p=0.003), anticipatory balance through LOS test (p=0.003), reactive balance tested through FRT (p=0.04), direction control (p=0.03) and sensory integration through CTSIB test (p=0.04) when compared with the sham IMT group. While no significant changes (p>0.05) between groups were observed in QoL and static balance; significant changes (p<0.05) within group were observed in both groups in QoL and static balance.

Conclusion Additional research is necessary to understand the association between inspiratory muscle strength and balance, however, we demonstrated that a multifactorial IMT intervention should be used with patients with diabetes to improve balance, postural control and reduce fall risks.

Trial registration number ClinicalTrials.gov, NCT#04947163.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This 12-week multimodal inspiratory muscle training (IMT) intervention was conducted using a prospective, single-blinded, two-arm randomised controlled trial with a repeated measure design.
- ⇒ In-depth, comprehensive assessment of multiple components of balance (static, dynamic, anticipatory, reactive balance, direction control and sensory integration) following multifactorial IMT.
- ⇒ Although the adherence rate was monitored and <80% was considered dropout, still there are limitations associated with home-based sessions.
- ⇒ Limited generalisability since the study is conducted on patients with diabetes from Pakistan only.

INTRODUCTION

Diabetes mellitus (DM) is a major public health concern globally owing to the increasing prevalence and the complications caused by the disease leading to increased morbidity and mortality.[1] In Pakistan, the prevalence of diabetes is increasing as percentage per population showed 11.77% in 2016,[2] 16.98% in 2018[3] and 17.1% in 2019.[4] According to the International Diabetes Federation, it has affected 33 000 000 Pakistani raising the prevalence to 26.7% in 2022[5] and it is estimated that 9.2 million Pakistanis will suffer from diabetes by 2030.[3]

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Complications of disease like peripheral neuropathy affect balance leading to an abnormal gait pattern, lower limb muscle weakness, impaired sensory function, decreased reflexes and high risk of falls[6] thereby lowering functional tasks abilities, limiting activities of daily life and social interactions.[6 7] Clinician goals for the management of DM are to improve the health status of patients as well as prevention of disease complications.[8 9] As reported in the National Institute for Health and Care Excellence (NICE) guidelines, multiple management strategies are currently used for controlling glycaemic index and managing comorbidities and disease-related complications.[10–12]

For the management of postural instabilities and balance deficits, different training approaches have been used in literature including Wii Fit training, Tai chi, gait training, lower limb strengthening, circuit training and task-oriented dynamic training.[13–16] Inspiratory muscle training (IMT) has demonstrated increase in diaphragm strength,[17–28] reduced dyspnoea level,[17–20 22] increased functional capacity,[17–23 29] improved thoracic mobility[30] and thereby improved quality of life (QoL) in the frail population.[17–20 22 23 31] Additionally, IMT has been used in clinical trials with chronic obstructive pulmonary disease (COPD),[19 24] asthma,[25] stroke,[26] spinal cord injury,[27] heart failure,[17 23 32] cardiac surgery patients[28] and other frailer populations.[20 21 29 31 33]

Apart from the effects on pulmonary parameters and QoL, IMT has currently been investigated for its effects on the balance ability in healthy[34] as well as patient populations including stroke[26 35] and patients with COPD.[36] Patients with DM may present pulmonary functional abnormalities which are associated with chronic hyperglycaemia. These abnormalities may include a reduction in lung volumes and carbon monoxide diffusion as well as decreased pulmonary compliance, lung elastic recoil and inspiratory muscle strength.[37–39] The weakness of the inspiratory muscles is of particular interest because it may lead to problems with balance and postural stability which is already compromised in patients with diabetes.[40] Studies have linked inspiratory muscle weakness with balance deficits[41 42] and improvements in the strength of diaphragm through IMT have been shown to improve the balance ability.[26 34–36 43] Hence, the current study aims to determine the effects of IMT on multicomponent balance, postural stability, risk of fall and QoL. The study hypothesised that multifactorial IMT intervention improves balance (dynamic, anticipatory, reactive, direction control and sensory integration) of patients with diabetes.

METHODS

The purpose of the current study is to determine the effects of IMT on balance, postural stability, risk of fall and QoL of patients with diabetes. This randomised controlled trial is a part of a comprehensive PhD project aimed at addressing different research objectives with multiple outcome measures.

General design

A single-blind randomised clinical trial with a two-group pretest–post-test design was used. The study is registered at ClinicalTrials.gov and adheres to the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.[44] The principal investigator (SS) allocated patients by simple randomisation through the sealed envelope method to IMT+Otago Exercise Programme (OEP) (n=35) and sham IMT+OEP (n=35). The outcome assessor was kept blind in the study. A priori sample size of 62 patients was calculated using the G-power program (V.3.1.9.2) at a statistical power of 0.85, error probability of 0.05 and effect size of 0.20. However, four additional patients were recruited in each group to compensate for the dropouts. Final assessment was done after 12 weeks of intervention with 29 patients in the IMT group and 30 patients in the sham IMT group. Figure 1 presents the CONSORT diagram showing the number and flow of patients throughout the clinical trial.

The first week was the orientation week where supervised training sessions and written material containing instructions for the patients was provided. Also, the baseline data was recorded this week where maximum inspiratory pressure (MIP) was assessed through POWERbreathe device whereas lung volumes and capacities were assessed through a handheld spirometer. Afterwards, home-based exercise training for a period of 12 weeks was carried out three times a week on alternate days. However, patients attended one supervised session weekly. Also, a checklist was provided to ensure adherence to protocol and <80% compliance led to the dropout of patients owing to poor compliance. Assessment of fall risk, static and dynamic balance and QoL was done at baseline and after 12 weeks of intervention.

Participant characteristics

70 patients (58.3±5.9 years old) with the diagnosis of type 2 DM were recruited through a non-probability convenience sampling technique. Patients of both genders with the age ranging from 50 to 70 years were included in the study. The Berg Balance Scale (BBS) of all the patients ranged from 30 to 50. Exclusion criteria comprised of those with uncontrolled diabetes, hypertension or disease exacerbation in the last 3 months, Mini-Mental State Examination score <24 and on oxygen therapy or peripheral oxygen saturation <90% during the 6-minute walk test.

Patients who reported practising regular physical activity or any balance training in the last 6 months were also excluded. Patients with musculoskeletal comorbidities (eg, osteoarthritis, low back pain) that may impair exercise performance and previous or current experience with IMT, patients diagnosed with cardiorespiratory diseases or those with a prescription of drugs that affect

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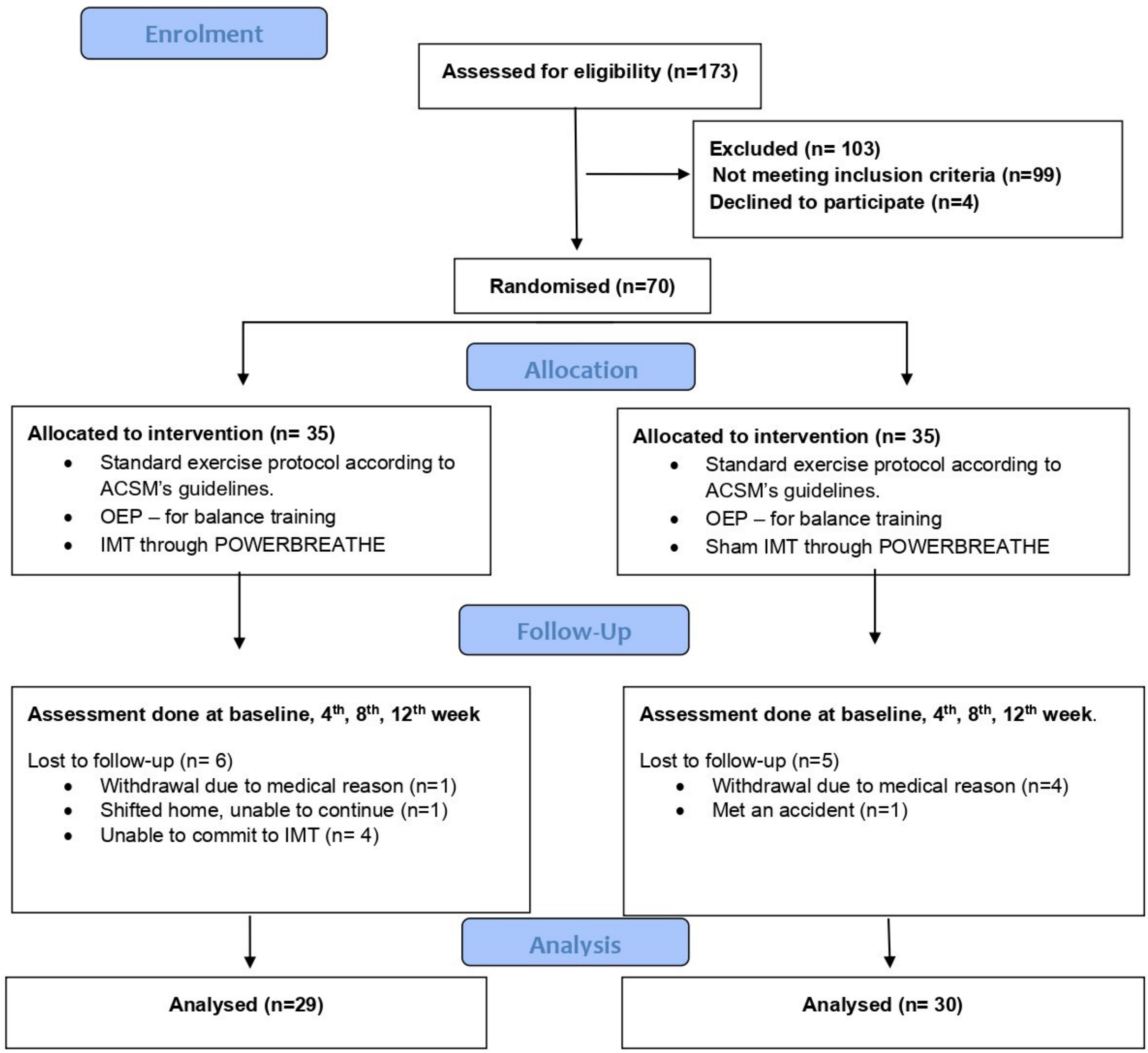

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flow diagram showing patient's pathway through the 12-week study. ACSM, American College of Sports Medicine; IMT, inspiratory muscle training; OEP, Otago Exercise Programme.

balance, for example, beta-blockers, anti-anxiety and anti-depressant drugs were also excluded.

The patients were enrolled from the Rehabilitation Department of Pakistan Railway General Hospital (between July 2021 and December 2022). Informed consent was obtained from each participant prior to data collection. The study conforms to Helsinki's declaration.

Intervention

Along with IMT and sham IMT, patients in both groups underwent the standardised protocol for diabetes by the American College of Sports Medicine (ACSM). ACSM recommends 150 min of moderate-intensity or 60 min of vigorous-intensity aerobic exercise per week along with two non-consecutive days of resistance training per week at intensities between 50% and 80% of one-repetition maximum. The exercises target all major muscle groups using a scheme of 1–4 sets of 8–15 repetitions per exercise.[45] As the balance of the patients was compromised, the patients also performed a home-based OEP specifically targeting muscle strengthening and balance retraining exercises for elderly.[46]

Monitoring for this home-based exercise programme was done via record keeping of sessions in a logbook where the sessions were recorded and an adherence rate less than 80% was considered as dropout. Moreover, the patients were supposed to visit the hospital once a week to get their performance reviewed as well as load adjustment of IMT in the IMT group.

Inspiratory muscle training

Home-based IMT was performed two times a day for 12 consecutive weeks starting with 50% of MIP and increasing the load progressively using a protocol already validated and already published elsewhere.[34]

Sham—inspiratory muscle training

Home-based sham IMT was performed once a day for 12 consecutive weeks starting with 15% of MIP without

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Table 1 Details of the training protocol of patients

IMT+OEP	Sham IMT+OEP
Standard exercise protocol according to ACSM's guidelines.	Standard exercise protocol according to ACSM's guidelines.
Balance training—OEP ► Warm-up (10–15 min). ► Strengthening exercises (~20 min). ► Balance activities (~20 min). ► Cool-down (5–10 min).	Balance training—OEP ► Warm-up (10–15 min). ► Strengthening exercises (~20 min). ► Balance activities (~20 min). ► Cool-down (5–10 min).
IMT through POWERbreathe ► 30 quick breaths two times a day at an adjustable resistance (equivalent to~50% of (baseline) MIP). ► Increased up to 35 breaths as per patient's tolerance.	Sham IMT ► 60 slow breaths once daily at a load setting of 0 (corresponding to~15% (baseline) MIP). ► Training load adjustment was prevented using sticky tape applied to the device's load adjuster.
► Orientation week—supervised training+written material regarding treatment was provided to the patients. ► Training frequency: 3 days per week for 12 weeks. ► IMT/sham IMT daily two times a day. ► Assessment done at baseline and after 12 weeks of intervention.	

Frequency	Two times a day	Alternate days (Mon, Wed, Fri)	Alternate days (Tues, Thurs, Sat)
Time	10-15 min	60 min	50 min
Type	IMT/sham IMT	OEP	ACSM

ACSM, American College of Sports Medicine; IMT, inspiratory muscle training; MIP, maximum inspiratory pressure; OEP, Otago Exercise Programme.

increasing the load using a protocol already validated and already published elsewhere.[34]

Otago Exercise Programme

A home-based exercise programme for the elderly population including strength and balance exercises was followed by the patients of both groups on alternate days. The delivery of the exercise along with the type of training has been previously validated and it is reported elsewhere.[43]

Standardised protocol for patients with diabetes

The patients performed unsupervised walk for 20 min on alternate days with basic stretching exercises as warm-up and cool-down before and after the walk. They also performed basic strengthening exercises for larger muscle groups after the walk.[47] The details of the intervention protocol given to both groups are presented in table 1.

Outcome measures

Outcome measures were categorised into three main groups comprising of nine variables in total. These included the BBS; Biodex Postural Stability System, including seven variables relevant to the tests for static, reactive, anticipatory balance and sensory integration; and the Audit of Diabetes Dependent Quality of Life (ADDQoL) questionnaire.

Berg Balance Scale

Static and dynamic balance of the participants was assessed through the BBS where the patient had to perform 14 predetermined physical tasks assessing different aspects of balance. These included static, anticipatory, dynamic and sensory balance. Each task was scored from 0 to 4 where 4 indicates the person can complete the task independently with a final maximal score of 56.[48]

Postural stability system

The Biodex Postural Stability System (Biodex Medical Systems, Shirley, New York, USA) has proven to be a highly reliable (Intraclass Correlation Coefficient=0.94) measure of postural stability.[49] The system uses a circular movable platform that provides 20^{o} surface tilt in all 360^{0} directions and is interfaced with a microprocessor-based actuator.[50] Four protocols including the postural stability test (PST), Limits of Stability (LOS), Clinical Test of Sensory Interaction and Balance (CTSIB) and fall risk test (FRT) score were used for the purpose of this study following already validated protocols.[51]

Static balance of the participants was assessed through the PST that measured different indices including the Overall Stability Index (OSI), Anterior–Posterior Index (API) and Mediolateral Index (MLI). Reactive balance was assessed via the OSI computed through the FRT. LOS test was performed to assess the anticipatory balance through the time taken to complete the test (in seconds) and the overall direction control of patients. Sensory integration was assessed by computing the composite score of CTSIB.

Audit of Diabetes Dependent Quality of Life

The ADDQoL is a reliable (Cronbach's α 0.86) questionnaire[52] used to assess both overall QoL as well as the impact of diabetes on specific aspects of life in 19 different life domains. These domains include leisure activities, working life, local or long-distance journeys, holidays, physical health, family life, friendships and social life, close personal relationships, physical appearance, self-confidence, motivation to achieve things, people's reactions, feelings about the future, financial situation, living conditions, dependence on others, freedom to eat and freedom to drink. A weighted score for each domain was calculated as a multiplier of impact rating and importance rating (ranging from −9 to +3). Lower scores reflected poorer QoL. Finally, a mean weighted impact score (ADDQoL score) was calculated for the entire scale across all applicable domains.[52]

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Patient and public involvement

None

Statistical analysis

Analysis was performed using IBM SPSS software (V.26) with the significance tested at 95% CI, $p<0.05$. Mean and SD were computed for continuous and frequency with percentages for categorical variables. The study hypothesis was tested through a 2×2 mixed model analysis of variance (ANOVA) (pre–post vs intervention type) with the balance tests as the dependent variable. Bonferroni corrections were applied to control for multiple comparisons in the analysis. The significance level was adjusted to $\alpha=0.05$. For testing the assumptions of mixed ANOVA, the homogeneity of covariance matrices was tested through Box's test of equality of covariance and assumed to be met if $p>0.05$. Normality was assessed through Shapiro-Wilk test ($p>0.05$), homogeneity of variances through Levene's test (>0.05) and sphericity was checked through Mauchly's test of sphericity. The variables in which interaction effect was observed, further analysis was carried out using the independent sample t-test for between-group comparison and paired sample t-test for within-group analysis. Effect size was interpreted via partial eta square (η_p^2) where $\eta_p^2>0.01$ was considered as small, >0.06 as medium and >0.14 was considered as large effect size. Detailed statistical plan is shared as online supplemental file. An additional analysis was conducted to follow the advice of reviewer 4, using analysis of covariance (ANCOVA), to address potential baseline differences between the groups. A statistician was consulted to ensure the robustness of our approach. The analysis was performed to assess the effects of the intervention on nine outcome variables and adjust for any minor baseline differences present. A Bonferroni correction was applied to account for multiple comparisons. The standard significance level of 0.05 was divided by the number of comparisons,[9] resulting in an adjusted significance level of 0.0055 (p=0.05/9=0.0055). This adjusted threshold was used to determine the statistical significance of the results for each outcome variable. The results of this analysis are provided as an online supplemental file.

RESULTS

59 patients out of 70 completed the study with a patient adherence rate of 82.8% in the IMT group and 85.7% in the sham IMT group. There was no adverse event (ie, fall or hypoglycaemia) during the intervention. The reasons for withdrawal are reported in figure 1 and were not related to the intervention. The mean duration of diagnosis of diabetes was 11.15±4.30 years. The majority (79%) of the patients had moderate level neuropathy, 4.8% had mild and 16.1% had severe level neuropathy evaluated by the modified Toronto Clinical Neuropathy Scoring System. 9 patients from IMT and 11 patients from the sham IMT group had a previous history of fall. Both groups were similar in terms of age, body mass index and pulmonary function at baseline (p>0.05) as reported in table 2.

Table 2 Baseline characteristics of patients in IMT+OEP and sham IMT+OEP group

	IMT+OEP Mean±SD	Sham IMT+OEP Mean±SD	p value
Age (years)	57.32±5.23	59.42±6.58	0.17
Gender (M/F)	11/20	12/19	–
BMI (kg/m^2)	28.19±3.83	27.02±4.34	0.26
MIP (cmH$_2$O)	24.8±8.09	24.5±8.93	0.88
FEV1 (L)	1.34±0.50	1.25±0.59	0.54
FVC (L)	1.52±0.62	1.62±0.74	0.56
PEFR (L/min)	1.84±0.72	1.71±0.65	0.20

All p values are non-significant (>0.05) and computed through independent sample t-test.
BMI, body mass index; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; IMT, inspiratory muscle training; MIP, maximum inspiratory pressure; OEP, Otago Exercise Programme; PEFR, peak expiratory flow rate.

The MIP of the patients in the study ranged from 11.11 to 41.90 cmH$_2$O. After 12 weeks of multifactorial intervention, the percentage change in MIP from pre-treatment to post-treatment of the IMT group was 78.22% whereas a pre–post change of only 24.2% was observed in the MIP values of the sham IMT group.

After 12 weeks, a significant group × time interaction effect ($p<0.05$) of the treatments in IMT and sham IMT groups was observed in all variables except for ADDQoL and PST-OSI. Within the group, results showed that all the types of balance and postural control improved after training in both the groups. For between-group results, there was a significant improvement ($p<0.05$) in the FRT, LOS and CTSIB test. However, no significant differences ($p>0.05$) were found in static balance and in QoL ($p>0.05$) between groups. Table 3 summarises between and within differences and interaction effects for all the balance measures. The reported p values include the p value for the within-groups effect, reflecting overall change over time in each group; the p value for the between-groups effect, comparing the treatment effects between both groups; and the p value for the interaction effect, indicating how the treatment effect varied over time between the groups. The within-groups effect combines both the intervention and placebo effects which can complicate the interpretation of the treatment effect while the between-groups effect may be less precise if baseline values are similar due to randomisation, potentially underestimating the treatment impact. Therefore, it is important to focus on the interaction effect being the most meaningful indicator of the treatment's effectiveness.

Berg Balance Scale

Both groups were similar initially ($p>0.05$) tested through independent sample t-test, however, there were

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Table 3 Showing mean±SD of balance measures of patients in IMT+OEP and sham IMT+OEP group and the p values for interaction effect, between and within group comparisons computed from 2×2 mixed model ANOVA

Outcome		IMT+OEP (n=29) Baseline	IMT+OEP (n=29) Follow-up	Sham IMT+OEP (n=30) Baseline	Sham IMT+OEP (n=30) Follow-up	p value
BBS		41.87±2.61	49.16±2.50	41.58±2.51	45.74±2.30	1. Int≤0.001 2. b/w=0.003 3. w/i≤0.001
PST	OSI	2.20±0.87	1.01±0.46	2.16±0.96	1.44±0.99	1. Int=0.07 2. b/w=0.35 3. w/i≤0.001
	API	1.88±0.98	0.81±0.54	1.85±0.97	1.41±0.87	1. Int=<0.001 2. b/w=0.21 3. w/i≤0.001
	MLI	1.20±0.60	0.61±0.41	1.32±0.68	0.98±0.64	1. Int=0.04 2. b/w=0.09 3. w/i≤0.001
FRT	OSI	2.35±0.77	1.27±0.58	2.35±0.89	1.98±0.57	1. Int≤0.001 2. b/w=0.04 3. w/i≤0.001
LOS	Time to complete test (s)	118.96±21.61	68.58±11.78	111.58±2252	99.83±24.94	1. Int≤0.001 2. b/w=0.03 3. w/i≤0.001
	Overall direction control	24.22±8.74	42.10±8.16	25.80±8.65	32.50±9.65	1. Int≤0.001 2. b/w=0.03 3. w/i≤0.001
CTSIB	Composite score	2.06±0.45	1.53±0.43	2.08±0.47	2.00±0.51	1. Int≤0.001 2. b/w=0.04 3. w/i≤0.001
ADDQoL	AWI score	−0.35±1.34	0.19±1.28	−0.38±1.64	0.15±1.43	1. Int=0.97 2. b/w=0.93 3. w/i≤0.001

ADDQoL, Audit of Diabetes Dependent Quality of Life; ANOVA, analysis of variance; API, Anterior-Posterior Index; AWI, Average Weighted Impact Score; BBS, Berg Balance Scale; b/w, p value for between group comparison; CTSIB, Clinical Test of Sensory Interaction and Balance; FRT, fall risk test; IMT, inspiratory muscle training; Int, p value of interaction effect; LOS, Limits of Stability; MLI, Mediolateral Index; OEP, Otago Exercise Programme; OSI, Overall Stability Index; PST, postural stability test; w/i, p value for within group changes.

significant interaction effects for BBS score of experimental compared with the placebo group after 12 weeks of intervention as reported in table 3, with moderate effect size (F=50.9,[1 53] p <0.001, η_p^2=0.45).

Biodex Postural Stability System

The group × time interaction was found to be highly significant for PST-API (F=15.4,[1 54] p =<0.001, η_p^2=0.21) and PST-MLI (F=4.35,[1 54] p =0.04, η_p^2=0.07) indicating that the multifactorial intervention had a differential effect on anterior-posterior and mediolateral stability over time. However, no significant interaction (F=6.23,[1 54] p =0.07, η_p^2=0.09) was observed for OSI.

Decreases in OSI showing reactive balance through FRT (F=4.1,[1 54] p <0.001, η_p^2=0.06) and composite score for sway index showing sensory integration computed through CTSIB test (F=4.17,[1 54] p <0.001, η_p^2=0.06) were observed (table 3).

Anticipatory balance when tested through LOS test showed that the time needed to complete the test decreased significantly (F=4.67,[1 54] p <0.001, η_p^2=0.07) and the overall direction control improved significantly (F=4.58,[1 54] p <0.001, η_p^2=0.07) in IMT group when compared with sham IMT group, refer to table 3.

Figure 2 shows the percentage of changes in IMT+OEP and sham IMT+OEP group for balance, postural stability and QoL outcomes.

The estimated marginal means of all the outcome measures of balance and postural stability are added as online supplemental figure 1.

ADDQoL

Before the start of the intervention, 19.4% patients in the experimental and 9.7% of placebo group reported to have a very bad QoL. Both groups reported that the QoL would have been much better if they had not had

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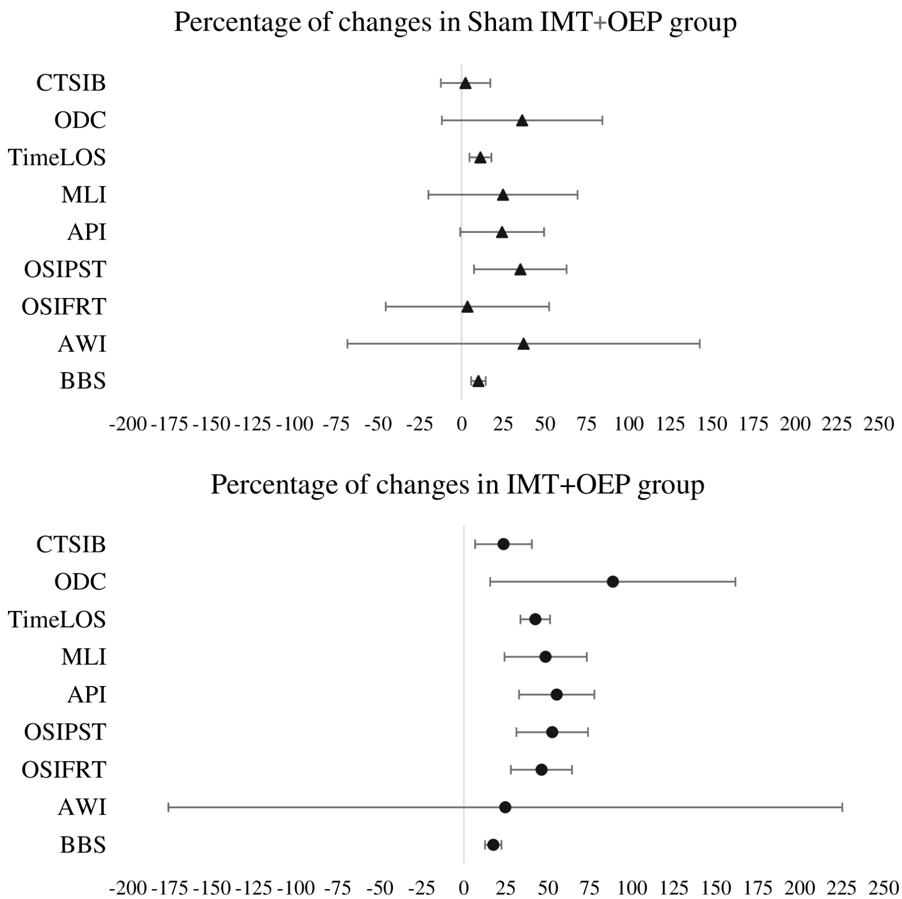

Figure 2 Forest plot showing the percentage of changes in sham IMT+OEP and IMT+OEP group for and Clinical Test of Sensory Interaction and Balance (CTSIB) score, overall direction control (ODC) in Limits of Stability (LOS) test, time to perform LOS test, Mediolateral Index (MLI), Anterior–Posterior Index (API), Overall Stability Index from Postural Stability Test (OSI-PST), Overall Stability Index from Fall Risk Test (OSI-FRT), Average Weighted Score (AWI) of Audit of Diabetes Dependent Quality of Life (ADDQoL) questionnaire and Berg Balance Scale Scores (BBS). IMT, inspiratory muscle training; OEP, Otago Exercise Programme.

diabetes (29% in the experimental and 58.1% in the placebo groups).

No significant group × time interaction (p=0.97) was observed in the average weighted score of ADDQoL. Although, significant improvement (F=13.7,[1 53] p <0.001, η_p^2=0.18) in QoL was observed within both groups but no significant difference between group (p=0.93) was seen on average weighted impact score of 19 daily life activities reflecting the QoL of patients with diabetes as shown in table 3. Weighted score of each domain before and after the intervention in both groups are shown in online supplemental figure 2.

Baseline scores of balance tests and QoL outcomes of the groups were compared using ANCOVA to adjust for any initial differences. The adjusted means and standard errors for each group are attached as an online supplemental file. As expected, there were no significant differences between the groups at baseline after adjustment.

DISCUSSION

This is the first study to compare the effects of 12 weeks of multifactorial IMT on multiple components of balance including static, reactive, anticipatory balance, LOS, sensory integration and dynamic stability in patients with diabetes. The findings supported the study hypothesis that OEP+IMT improves all components of balance except for the static balance ability. These findings are consistent with the results of studies that have demonstrated the effects of IMT alone on balance.[34 43]

Following multifactorial IMT for 12 weeks, the MIP of the patients with diabetes was largely improved (78.22%) as compared with healthy older adults (66%) in a previous study[43] following 8 weeks of IMT intervention. The MIP of patients who underwent sham IMT also improved but to a much lesser extent (24.08%) like those reported for older adults by Ferraro *et al*.[34] The possible reason for this is not the remodelling of respiratory muscles rather the increased neural activation because of sham training protocol.[34]

Balance outcomes

The BBS score improved significantly in the IMT group as compared with the sham IMT group which is consistent with the findings of Tounsi with patients with COPD.[36] Similar results were observed by Beauchamp with a significant

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improvement in balance[55] which might be explained by the potential mechanisms postulated by Hodges[56 57] and reported by Ferraro *et al*.[43] The first mechanism explains the segmental linkages between the upper and lower body according to which perturbations in the upper body activate the diaphragm in a feedforward manner and increased diaphragmatic strength will support the evidence of these segmental linkages.[57] A second mechanism is the increase in intra-abdominal pressure as a consequence of an increment in diaphragmatic strength which helps in stabilise the spine improving balance ability.[58] A third potential mechanism postulated by Witt explains that there is reduced sympathetic activity, reduced firing of afferent fibres from the diaphragm after training and reduced inspiratory muscle metaboreflex.[54 59]

The current study highlights the decrease in the risk of falls and an increase in postural stability and balance with increased strength of diaphragm depicted by increased MIP. This can be attributed to the multifaceted role of diaphragm in the regulation of balance owing to its anatomical position, physiological function and biomechanical action. The multiple physiological mechanisms working together result in improvement in multicomponent balance linked to increased strength of the diaphragm.

IMT strengthens the diaphragm depicted by increased MIP, this reduces the metaboreflex and decreases fatigue in peripheral muscles by improving the blood flow to the peripheral locomotor muscles. Also, the perturbations to the upper limb also activate the diaphragm in a feedforward manner to maintain balance which would be improved with the strengthened diaphragm. The role of the diaphragm in creating optimal abdominal pressure helps maintenance of dynamic and reactive balance. All these factors when combined tend to improve multiple aspects of balance by enhancing the role of the diaphragm in postural stability and balance ability.

Postural stability outcomes

Four different test protocols including PST, FRT, LOS and CTSIB were used. A significant group × time interaction reflecting an improvement of all components of postural stability was demonstrated indicating improved postural stability and reduction of fall risk However, no significant differences between groups were observed in the static component of balance assessment.

These results are similar to those of Ferraro *et al*[34] where improvements in dynamic stability were observed. The activation of inspiratory muscles, particularly the diaphragm, is minimal during static balance tasks as compared with the dynamic movements as postulated by Hodges.[56–58] The lack of effect on the static component assessed through PST was probably because the challenges posed during PST did not require the recruitment of the musculature of trunk muscles.

In agreement, previous studies have also demonstrated improvement in dynamic stability.[34 35 43 60] However, previous studies have used different balance assessment tests with dynamic component assessment through the Mini-Balance Evaluation Systems Test.[34 43] The present study also reported improvement in reactive balance tested through LOS test and CTSIB test with a medium effect size.

The efficacy of home-based, unsupervised training has been proven in healthy community-dwelling older adults declaring it as a feasible and effective treatment for improving their balance ability. The improvement in balance after IMT was reported not only in healthy older adults (with a mean age of 74 years) but also in COPD, heart failure and patients who had chronic stroke.[34 35 55 60]

Quality of life

IMT had no significant effects on the overall QoL of patients as within the group significant changes were observed in both groups performing OEP but the inclusion of IMT in intervention did not add any benefit and both the groups were having similar QoL scores after intervention.

The ADDQoL 19 questionnaire reported the QoL in 19 different life domains but not all life domains were equally applicable to all the patients decreasing the response rate in a few specific domains. This brings the limitation to interpret the results of individual and average weighted scores with caution. Similar results were observed in a study by Ping Lun Hsieh where no significant changes were observed after 12 weeks of resistance training in patients with type DM.[53] Few other studies with different exercise regimens have reported inconsistent results on the QoL of younger adults.[61 62]

In response to reviewer #4's feedback, an additional analysis using ANCOVA was conducted to adjust for baseline differences between the groups for balance tests and ADDQoL scores. This adjustment was minor but necessary to ensure the robustness of our findings. The analysis confirmed that there were no significant baseline differences between the groups consistent with the results reported previously. This supports the validity of our original findings and confirms that any observed effects are not due to initial differences between the groups.

Limitations and recommendations

This is a single-centre, small, randomised study with limited generalisability. The current study lacks the use of a group where IMT alone is given to better understand the effects of IMT and does not study the physiological links between IMT and balance. The questionnaire used for QoL reported it in 19 different life domains but all those life domains are not equally applicable to every individual making it a limitation to generalise results considering this.[53] Future research should also consider the outcome measures like work of breathing and blood oxygenation so that the underlying mechanisms associated with balance improvement can be explored.

CONCLUSION

This is the first study to evaluate the effects of 12 weeks of multifactorial IMT (IMT and OEP) for reducing the risk

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of fall, improving balance and postural stability of patients with diabetes. The study shows that the combined intervention reduced the risk of fall, improved the reactive, anticipatory and dynamic balance outcomes enhancing the overall postural control of patients.

Hence it is possible to conceive that IMT, home-based, cost-effective training can be integrated in the multicomponent management of patients with diabetes along with the OEP and can be incorporated in the daily management of the disease as recommended by the multifactorial approaches in NICE guidelines.[12]

X Suman Sheraz @sumansherax and Francesco Vincenzo Ferraro @fferraro5

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ORCID iDs
Suman Sheraz http://orcid.org/0000-0002-1441-1455
Arshad Nawaz Malik http://orcid.org/0000-0002-2661-9499
Francesco Vincenzo Ferraro http://orcid.org/0000-0002-4902-7760

REFERENCES

1 Diabetes. 2023. Available: https://www.who.int/news-room/fact-sheets/detail/diabetes
2 Type 2 Diabetes Mellitus in Pakistan: Current Prevalence and Future Forecast, 2023. Available: https://pubmed.ncbi.nlm.nih.gov/27924966/
3 Aamir AH, Ul-Haq Z, Mahar SA, *et al*. Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. *BMJ Open* 2019;9:e025300.
4 Pakistan - International Diabetes Federation, 2023. Available: https://idf.org/our-network/regions-and-members/middle-east-and-north-africa/members/pakistan/
5 Azeem S, Khan U, Liaquat A. The increasing rate of diabetes in Pakistan: a silent killer. *Ann Med Surg (Lond)* 2022;79:103901.
6 D'Silva LJ, Lin J, Staecker H, *et al*. Impact of diabetic complications on balance and falls: contribution of the vestibular system. *Phys Ther* 2016;96:400–9.
7 Mustapa A, Justine M, Mohd Mustafah N, *et al*. Postural control and gait performance in the diabetic peripheral neuropathy: a systematic review. *Biomed Res Int* 2016;2016:9305025.
8 Harris-Hayes M, Schootman M, Schootman JC, *et al*. The role of physical therapists in fighting the type 2 diabetes epidemic. *J Orthop Sports Phys Ther* 2020;50:5–16.
9 Thent ZC, Das S, Henry LJ. Role of Exercise in the Management of Diabetes Mellitus: the Global Scenario. 2013; Available from: www.plosone.org
10 Asfaw MS, Dagne WK. Physical activity can improve diabetes patients' glucose control; a systematic review and meta-analysis. *Heliyon* 2022;8:e12267.
11 Shah SZA, Karam JA, Zeb A, *et al*. Movement is improvement: the therapeutic effects of exercise and general physical activity on glycemic control in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Ther* 2021;12:707–32.
12 NICE. Recommendations | type 2 diabetes in adults: management | guidance. 2015. Available: https://www.nice.org.uk/guidance/ng
13 Zhou Z, Zhou R, Li K, *et al*. Effects of tai chi on physiology, balance and quality of life in patients with type 2 diabetes: a systematic review and meta-analysis. *J Rehabil Med* 2019;51:405–17.
14 Morrison S, Simmons R, Colberg SR, *et al*. Supervised balance training and wii fit-based exercises lower falls risk in older adults with type 2 diabetes. *J Am Med Dir Assoc* 2018;19:185.
15 Ahmad I, Noohu MM, Verma S, *et al*. Effect of sensorimotor training on balance measures and proprioception among middle and older age adults with diabetic peripheral neuropathy. *Gait Posture* 2019;74:114–20.
16 Chapman A, Meyer C, Renehan E, *et al*. Exercise interventions for the improvement of falls-related outcomes among older adults with diabetes mellitus: a systematic review and meta-analyses. *J Diabetes Complications* 2017;31:631–45.
17 Tanriverdi A, Savci S, Ozcan Kahraman B, *et al*. Effects of high intensity interval-based inspiratory muscle training in patients with heart failure: a single-blind randomized controlled trial. *Heart & Lung* 2023;62:1–8.
18 Buran Cirak Y, Yilmaz Yelvar GD, Durustkan Elbasi N. Effectiveness of 12-week inspiratory muscle training with manual therapy in patients with COPD: a randomized controlled study. *Clin Respir J* 2022;16:317–28.
19 Beaumont M, Forget P, Couturaud F, *et al*. Effects of inspiratory muscle training in COPD patients: a systematic review and meta-analysis. *Clin Respir J* 2018;12:2178–88.
20 McNarry MA, Berg RMG, Shelley J, *et al*. Inspiratory muscle training enhances recovery post-COVID-19: a randomised controlled trial. *Eur Respir J* 2022;60:2103101.
21 Luo Z, Qian H, Zhang X, *et al*. Effectiveness and safety of inspiratory muscle training in patients with pulmonary hypertension: a systematic review and meta-analysis. *Front Cardiovasc Med* 2022;9:999422.
22 Zaki S, Moiz JA, Mujaddadi A, *et al*. Does inspiratory muscle training provide additional benefits during pulmonary rehabilitation in people with interstitial lung disease? A randomized control trial. *Physiother Theory Pract* 2023;39:518–28.
23 Sadek Z, Salami A, Youness M, *et al*. A randomized controlled trial of high-intensity interval training and inspiratory muscle training for chronic heart failure patients with inspiratory muscle weakness. *Chronic Illn* 2022;18:140–54.
24 Ammous O, Feki W, Lotfi T, *et al*. Inspiratory muscle training, with or without concomitant pulmonary rehabilitation, for chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst Rev* 2023;1:CD013778.

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25 Wang Q, Yang F, Gao L, *et al*. Effects of inspiratory muscle training and high-intensity interval training on lung function and respiratory muscle function in asthma. *Respir Care* 2022;1465–75:.
26 Aydoğan Arslan S, Uğurlu K, Sakizli Erdal E, *et al*. Effects of inspiratory muscle training on respiratory muscle strength, trunk control, balance and functional capacity in stroke patients: a single-blinded randomized controlled study. *Top Stroke Rehabil* 2022;29:40–8.
27 Woods A, Gustafson O, Williams M, *et al*. The effects of inspiratory muscle training on inspiratory muscle strength, lung function and quality of life in adults with spinal cord injuries: a systematic review and meta-analysis. *Disabil Rehabil* 2023;45:2703–14.
28 Cook A, Smith L, Anderson C, *et al*. The effect of preoperative threshold inspiratory muscle training in adults undergoing cardiac surgery on postoperative hospital stay: a systematic review. *Physiother Theory Pract* 2023;39:690–703.
29 Hockele LF, Sachet Affonso JV, Rossi D, *et al*. Pulmonary and functional rehabilitation improves functional capacity, pulmonary function and respiratory muscle strength in post COVID-19 patients: pilot clinical trial. *Int J Environ Res Public Health* 2022;19:14899.
30 Azab AR, Abdelbasset WK, Alrawaili SM, *et al*. Effect of chest resistance and expansion exercises on respiratory muscle strength, lung function, and thoracic excursion in children with a post-operative congenital diaphragmatic hernia. *Int J Environ Res Public Health* 2022;19:6101.
31 Del Corral T, Fabero-Garrido R, Plaza-Manzano G, *et al*. Home-based respiratory muscle training on quality of life and exercise tolerance in long-term post-COVID-19: randomized controlled trial. *Ann Phys Rehabil Med* 2023;66:101709.
32 Andrade CCF, Silva RT, Brunherotti M de A. Effects of inspiratory muscle training in patients with class III and IV heart failure. *Curr Probl Cardiol* 2022;47:101307.
33 Bostanci Ö, Mayda H, Yılmaz C, *et al*. Inspiratory muscle training improves pulmonary functions and respiratory muscle strength in healthy male smokers. *Respir Physiol Neurobiol* 2019;264:28–32.
34 Ferraro FV, Gavin JP, Wainwright T, *et al*. The effects of 8 weeks of inspiratory muscle training on the balance of healthy older adults: a randomized, double-blind, placebo-controlled study. *Physiol Rep* 2019;7:e14076.
35 Oh D, Kim G, Lee W, *et al*. Effects of inspiratory muscle training on balance ability and abdominal muscle thickness in chronic stroke patients. *J Phys Ther Sci* 2016;28:107–11.
36 Tounsi B, Acheche A, Lelard T, *et al*. Effects of specific inspiratory muscle training combined with whole-body endurance training program on balance in COPD patients: randomized controlled trial. *PLoS ONE* 2021;16:e0257595.
37 Sonoda N, Morimoto A, Tatsumi Y, *et al*. A prospective study of the impact of diabetes mellitus on restrictive and obstructive lung function impairment: the Saku study. *Metab Clin Exp* 2018;82:58–64.
38 Khateeb J, Fuchs E, Khamaisi M. Diabetes and lung disease: a neglected relationship. *Rev Diabet Stud* 2019;15:1–15.
39 Mauricio D, Alonso N, Gratacòs M. Chronic diabetes complications: the need to move beyond classical concepts. *Trends Endocrinol Metab* 2020;31:287–95.
40 Vaz MM, Costa GC, Reis JG, *et al*. Postural control and functional strength in patients with type 2 diabetes mellitus with and without peripheral neuropathy. *Arch Phys Med Rehabil* 2013;94:2465–70.
41 Hyodo Y, Jiroumaru T, Mori K, *et al*. Relationship between respiratory muscle strength and static balance in older people requiring support and care. *OJTR* 2023;11:90–7.
42 Azevedo IG, da Câmara SMA, Maciel ACC, *et al*. Relationship between inspiratory muscle strength and balance in women: a cross-sectional study. *PLoS One* 2023;18:e0280465.
43 Ferraro FV, Gavin JP, Wainwright TW, *et al*. Comparison of balance changes after inspiratory muscle or Otago exercise training. *PLoS One* 2020;15:e0227379.
44 Schulz KF, Altman DG, Moher D, *et al*. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Med* 2010;8:1–9.
45 Postprandial Exercise and Glucose Regulation for Type II Diabetics: Considerations for ACSM Guidelines, Available: https://www.acsm.org/blog-detail/acsm-certified-blog/2018/06/29/postprandial-exercise-and-glucose-regulation-for-type-ii-diabetics-considerations-for-acsm-guidelines
46 Day L. The Otago strength and balance exercise programme lowers the risk of death and falls in the older people at 12 months. *Evid Based Nurs* 2011;14:76–8.
47 Onaade O, Maples JM, Rand B, *et al*. Physical activity for blood glucose control in gestational diabetes mellitus: rationale and recommendations for translational behavioral interventions. *Clin Diabetes Endocrinol* 2021;7:7.
48 Patel K, Naik N, M.P.Th, Assistant professor, P.P. Savani College of Physiotherapy, Kosamba, Surat, Gujarat, India, *et al*. To compare the functional balance between normal elderly, elderly with diabetes, elderly with diabetic polyneuropathy. *IJPR* 2019;6:2970–5.
49 Cachupe WJC, Shifflett B, Kahanov L, *et al*. Reliability of biodex balance system measures. *Meas Phys Educ Exerc Sci* 2001;5:97–108.
50 Aly FA, Fawzy E, Ibrahim M, *et al*. Assessment of stability deficits in patients with diabetic peripheral neuropathy. *Bull Fac Ph Th Cairo Univ* 2007;12.
51 Eftekhar-Sadat B, Azizi R, Aliasgharzadeh A, *et al*. Effect of balance training with biodex stability system on balance in diabetic neuropathy. *Ther Adv Endocrinol Metab* 2015;6:233–40.
52 Bradley C, Todd C, Gorton T, *et al*. The development of an individualized questionnaire measure of perceived impact of diabetes on quality of life: the ADDQoL. *Qual Life Res* 1999;8:79–91.
53 Hsieh PL, Tseng CH, Tseng YJ, *et al*. Resistance training improves muscle function and cardiometabolic risks but not quality of life in older people with type 2 diabetes mellitus: a randomized controlled trial. *J Geriatr Phys Ther* 2018;41:65–76.
54 Witt JD, Guenette JA, Rupert JL, *et al*. Inspiratory muscle training attenuates the human respiratory muscle metaboreflex. *J Physiol* 2007;584:1019–28.
55 Beauchamp MK, Janaudis-Ferreira T, Parreira V, *et al*. A randomized controlled trial of balance training during pulmonary rehabilitation for individuals with COPD. *Chest* 2013;144:1803–10.
56 Hodges PW, Butler JE, McKenzie DK, *et al*. Contraction of the human diaphragm during rapid postural adjustments. *J Physiol* 1997;505 (Pt 2):539–48.
57 Hodges PW, Gandevia SC. Activation of the human diaphragm during a repetitive postural task. *J Physiol* 2000;522 Pt 1:165–75.
58 Hodges PW, Gandevia SC. Changes in intra-abdominal pressure during postural and respiratory activation of the human diaphragm. *J Appl Physiol (1985)* 2000;89:967–76.
59 Mello PR, Guerra GM, Borile S, *et al*. Inspiratory muscle training reduces sympathetic nervous activity and improves inspiratory muscle weakness and quality of life in patients with chronic heart failure: a clinical trial. *J Cardiopulm Rehabil Prev* 2012;32:255–61.
60 Bosnak-Guclu M, Arikan H, Savci S, *et al*. Effects of inspiratory muscle training in patients with heart failure. *Respir Med* 2011;105:1671–81.
61 Plotnikoff RC, Eves N, Jung M, *et al*. Multicomponent, home-based resistance training for obese adults with type 2 diabetes: a randomized controlled trial. *Int J Obes* 2010;34:1733–41.
62 Reid RD, Tulloch HE, Sigal RJ, *et al*. Effects of aerobic exercise, resistance exercise or both, on patient-reported health status and well-being in type 2 diabetes mellitus: a randomised trial. *Diabetologia* 2010;53:632–40.

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