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Influence of an inspiratory muscle fatigue protocol on older adults on respiratory muscle strength, muscle oxygen saturation, and functional capacity: a randomized controlled trial

Arturo Ladriñán-Maestro[1,2,3], Jorge Sánchez-Infante[3,4,5], Daniel Martín-Vera[2,6,7] and Alberto Sánchez-Sierra[2,3,5,6,8,9,10*]

Abstract

Background The fatigue of the inspiratory musculature, particularly the diaphragm, has been demonstrated to exert systemic effects on the body, impacting cardiovascular and performance outcomes. This study aimed to evaluate the influence of an inspiratory muscle fatigue protocol on respiratory muscle strength, functionality, and muscle oxygen saturation in older adults.

Methods A single-blinded randomized controlled clinical trial was conducted on twenty-four older adults aged over 60 years, who met inclusion criteria were physically independent in terms of gait and functionality. Participants were randomly assigned to one of three groups: control group, inspiratory muscle fatigue group, or activation group. Diaphragmatic ultrasonography (diaphragmatic thickness, thickening fraction, diaphragm movement curve), maximal inspiratory mouth pressure, muscle oxygen saturation, and functionality (timed up and go test, for five times sit to stand test) were used to measure the study variables at two time points: pre-intervention (T1) and post-intervention (T2).

Results In the maximum inspiratory pressure variable in the activation group an increase was found between baseline and post-treatment of 3.00 ± 0.93 cmH2O ($P < 0.01$), while in the inspiratory muscle fatigue a decrease of -6.75 ± 2.66 cmH2O ($P < 0.01$) was found. In addition, the inspiratory muscle fatigue group showed lower scores for respiratory and functional variables after performing the diaphragmatic fatigue intervention than the activation and control group ($P < 0.05$), on the other hand, the activation group showed more positive values for functional and respiratory capacity variables after performing the inspiratory muscle activation training ($P < 0.05$).

Conclusions Fatigue of the inspiratory musculature appears to negatively impact inspiratory muscle strength, peripheral muscle strength, muscular oxygenation, and functionality in older adults. Activation of the inspiratory musculature could contribute to improved respiratory muscle strength and function in these individuals.

Trial registration ClinicalTrials.gov ID: NCT06266013.

Keywords Respiratory muscle strength, Elderly, Functionality, Strength, Respiratory muscle training

*Correspondence:
Alberto Sánchez-Sierra
alberto.sanchez@universidadeuropea.es
Full list of author information is available at the end of the article

Background

As of today, population aging is an increasingly visible reality. For instance, the number of individuals over 65 years old in the European Union is higher in comparative terms than in other regions [1]. This aging, combined with various physiological changes, often leads to the onset of sarcopenia, characterized by muscle mass loss, muscle coordination alterations, decreased strength and contraction speed, and increased muscle fatigue [2]. This process also occurs at the level of respiratory muscles, resulting in a decrease in the strength of the respiratory muscles, which in turn will have a negative impact on pulmonary function, physical fitness, and quality of life [3].

The inspiratory muscles play a vital role in human life, facilitating gas exchange with the external environment and sustaining essential bodily functions. Among the main inspiratory muscles, the diaphragm stands out, which is capable of producing between 60–80% of the alveolar ventilation through its activation. Secondly, we have the external intercostals. Additionally, there are a series of accessory inspiratory muscles such as the scalenes or the sternocleidomastoid, which allow for the maintenance of this respiratory function in situations that increase the demand for gas exchange and cannot be met solely with the main inspiratory musculature [4]. Contraction of these muscles overcomes pleural pressure, facilitating gas exchange between atmospheric air and the alveolar space, taking in oxygen and releasing carbon dioxide. Furthermore, this process also regulates the acid–base balance, maintaining pH within normal values [5]. In addition to their respiratory function, inspiratory muscles serve other roles. For instance, the diaphragm, through the production and control of intra-abdominal pressure, as well as its attachment to the lumbar vertebrae, plays a pivotal role in lumbar stabilization and trunk motor control. On the other hand, its relationship with the vagus nerve via its connection to the esophagus allows this muscle to act on the parasympathetic nervous system through breathing, modulating various cardiovascular variables such as heart rate, blood pressure, or heart rate variability. Lastly, concerning its relationship with the lymphatic system, diaphragmatic contraction enables drainage of lymph nodes and vessels, especially those related to the lower limbs, due to the vacuum and suction effect produced during such contraction [6].

However, excessive stimulation of these muscles can lead to adverse consequences. Inspiratory muscle fatigue resulting from excessive stimulation triggers a competition for blood flow between respiratory and peripheral muscles, known as the metaboreflex. This can lead to reduced blood flow in peripheral muscles in favor of respiratory muscles, resulting in diminished blood perfusion and performance decline in affected musculature [7, 8]. Numerous studies conducted on healthy individuals and within the realm of sports have highlighted the influence of the metaboreflex on athletic performance, resulting, for example, in greater quadriceps fatigue during cycling tests, as well as an increased perception of effort [9], or leading to shorter apneas and turns in swimmers [10]. Furthermore, previous studies conducted on older adults have demonstrated the negative effects of the metaboreflex increasing blood pressure and reducing blood flow and perceived effort in the lower limbs, with a greater negative impact than that observed in younger subjects [11, 12]. Despite the available evidence on the negative effects of inspiratory muscle fatigue on variables such as blood flow, dyspnea, muscle fatigue, and perceived effort in peripheral muscles, no studies have evaluated the effects of fatigue on functionality, inspiratory muscle strength or muscle oxygen saturation in older adults. This could provide very useful information on the importance of the respiratory system and respiratory muscles in the physical condition and activities of daily living for this population, allowing for the incorporation of assessment and treatment/training of respiratory muscles to optimize or improve treatments or training programs for this population group. Therefore, the aim of this study was to objectively evaluate the acute effects of inspiratory muscle fatigue on functional capacity, inspiratory muscle strength, and muscular oxygen saturation in older adults. The hypothesis of this study is that inspiratory muscle fatigue may have a negative effect on inspiratory muscle strength, muscle oxygen saturation and functionality in older adults.

Methods

Study design

This study utilized a parallel randomized clinical trial design, conducted at the Physiotherapy Department of Residencial Montes de Toledo (Manzaneque, Spain), following the Consolidated Standards of Reporting Trials (CONSORT) guidelines [13]. Informed consent was obtained for all participants. The participants attended the laboratory on two occasions. The first visit was used to inform the participants about the study, collect informed consent and demographic data, as well as select participants based on inclusion and exclusion criteria. During the second visit, the interventions were carried out, along with the pre- and post-intervention assessments. The Research Ethics Committee of the Complejo Hospitalario Universitario de Toledo approved this study (approval number: 1070), and it was registered at ClinicalTrials.gov (NCT06266013, date of first registration: 14/02/2024).

Participants

Twenty-four older adults participated in the study and were randomized with a randomization process was performed using the randomization.com program. The participants were divided into 3 groups: inspiratory muscle fatigue group (IMFG), control group (CG) and activation group (AG). This process was performed by a third party who was not involved in the study. Both the evaluator and the data analyst were unaware of each participant's group assignment. Inclusion criteria for participants in this study were: being over 60 years of age and physical independence in terms of walking and functionality. The assessment of the exclusion criteria was conducted through interviews with the subjects. These criteria included subjects with impaired cognitive abilities, tympanic perforation or middle-internal ear pathology, pulmonary hypertension, decompensated cardiac or respiratory failure, undergoing lower extremity surgery within the last 12 months.

The sample size was determined using G*Power Software (3.1.9.2), based on maximal inspiratory mouth pressure (MIP) values data obtained on other previous study [14] with an alpha error of 0.05, a beta error of 0.2, and a medium effect size (f = 0.25 or Eta partial squared = 0.06). 30% estimated dropout rate was considered due to the study design. Therefore, a total sample size of 24 participants, divided into three groups (n = 8), was determined.

Intervention

IMFG performed the inspiratory muscle fatigue protocol using a threshold valve device (Big Breathe®; GH Innotek Co., Ltd., Busan, Republic of Korea). They breathed against submaximal inspiratory loads set at 60% of their MIP until they were unable to establish flow in at least three inspiratory efforts [15]. The AG followed a protocol of two sets of 30 repetitions at 40% of their MIP using the same threshold device as the IMFG, based on other study [16]. Finally, CG did not receive any intervention. Participants simply sat and waited for the same duration as the intervention and activation groups required to complete their protocol approximately 10 min.

Outcomes

Two measurements were taken at different times: pre-intervention (T1) and immediately post-intervention (T2). The evaluator responsible for conducting the measurements was blinded to each participant's group assignment. Firstly, the primary variables were analyzed to objectively confirm that the condition of inspiratory muscle fatigue had been achieved. Subsequently, the secondary variables were measured to assess the impact of this fatigue on functionality and muscle oxygen saturation.

Primary outcomes

MIP was measured using the Respiratory Pressure Measurement Device MicroRPM® (MicroMedical, Kent, UK) with subjects in a seated position, from residual volume to total lung capacity. To allow airflow through the mouth, the nose was plugged. Participants rested for 1 min between maneuvers and performed up to 6 maneuvers. The highest value obtained from three efforts that varied less than 5% was recorded [17].

Diaphragmatic thickness and thickening fraction

Diaphragmatic thickness was evaluated using a linear probe (L13-3 s) and a high-resolution device (GE Healthcare, Chicago, United States) with a frequency of 3.2–12.3 MHz placed perpendicular to the chest wall, with subjects in a supine position, in the anterior and mid-axillary lines, between the 8th and 9th intercostal spaces. B-mode ultrasound was utilized to visualize the structure in the juxtaposition region. Diaphragm thickness was measured three times at the end of expiration ($Thick_{esp}$) and peak inspiration ($Thick_{insp}$), with the mean values recorded. The thickness observed at the end of expiration was designated as diaphragmatic thickness. The thickening fraction (TF%) was calculated using the formula: TF = [(Thickness at end of maximum inspiration—Thickness at end of expiration) / Thickness at end of expiration] × 100% [18].

Diaphragm movement curve

Evaluation of the diaphragmatic movement curve employed a convex probe (C5-1 s) with a frequency of 1.2–6 MHz placed on the mid-clavicular line of the right costal margin longitudinally, using the liver as an acoustic window and orienting the probe cephalically, with subjects in a supine position. M-mode was used to record the diaphragmatic movement curve during maximal deep breathing and sniff breathing. Diaphragmatic excursion (Mob_{insp} and Mob_{sniff}), inspiratory time ($Time_{insp}$ and $Time_{sniff}$), and maximum contraction velocity (Vel_{insp} and Vel_{sniff}) were analyzed in both types of breathing. Three successive respiratory cycles were measured, and the average value of each parameter was recorded [18].

Secondary outcomes

For Timed Up and Go test (TUG), patients sat on a chair with armrests and were instructed to stand up (start of trial and timing), walk 3 m, and then sit back down in the initial chair (end of timing) [19].

For Five Times Sit to Stand test (FTSST), patients sat on an armless chair with a height of 43-45 cm, with their arms crossed over their chest, and were asked to stand up and sit down 5 times in place as quickly as possible [20].

Muscle oxygen saturation levels (SmO_2) were assessed using the Moxy Monitor device (Fortiori Design LLC, Hutchinson, MN, USA). This wireless and portable device utilizes infrared spectroscopy to evaluate SmO_2. Data analysis was conducted using computer software (Moxy Software v1.5.5; Idiag, Fehraltorf, Switzerland). The measurement protocol., consists of a 180-s measurement at rest, followed by continuous measurement during all three protocols. Measurements were taken on the medial gastrocnemius of the dominant leg with the patient in a standing position. The selected values corresponded to the mean recorded during the last 30 s of each phase [21].

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics v.22.0. The significance level was set at $P < 0.05$. The normality of each variable was assessed using the Shapiro-Wilks test test, indicating a normal distribution for all variables. Descriptive statistics were applied to examine demographic with measurements presented as mean ± SD. A 2-way repeated measures ANOVA was used for outcome variables, investigating the interaction between the IMFG, AG and CG) and the time of assessment (Baseline, Posttreatment). Post hoc Bonferroni multiple-comparisons test were applied when differences were identified. The effect size (ES) was interpreted using Cohen's scale [22]: low (< 0.20), medium (0.50) and high (> 0.80).

Results

Demographic data

Twenty-four older adults were recruited for the study on February 2024 and participate on March 2024. They were distributed among IMFG (5-men, 3-women), AG (4-men, 4-women) and CG (6-men, 2-women). There were no dropouts due to complications, adverse effects or during follow up. The CONSORT flow chart was included (Fig. 1). No significant differences were found between IMFG, AG and CG in demographic characteristics (Table 1).

Changes in respiratory variables after fatigue and activation

Results for primary outcomes are presented in Table 2.

In the analysis of the MIP variable, the IMFG had lower values than the AG after performing the

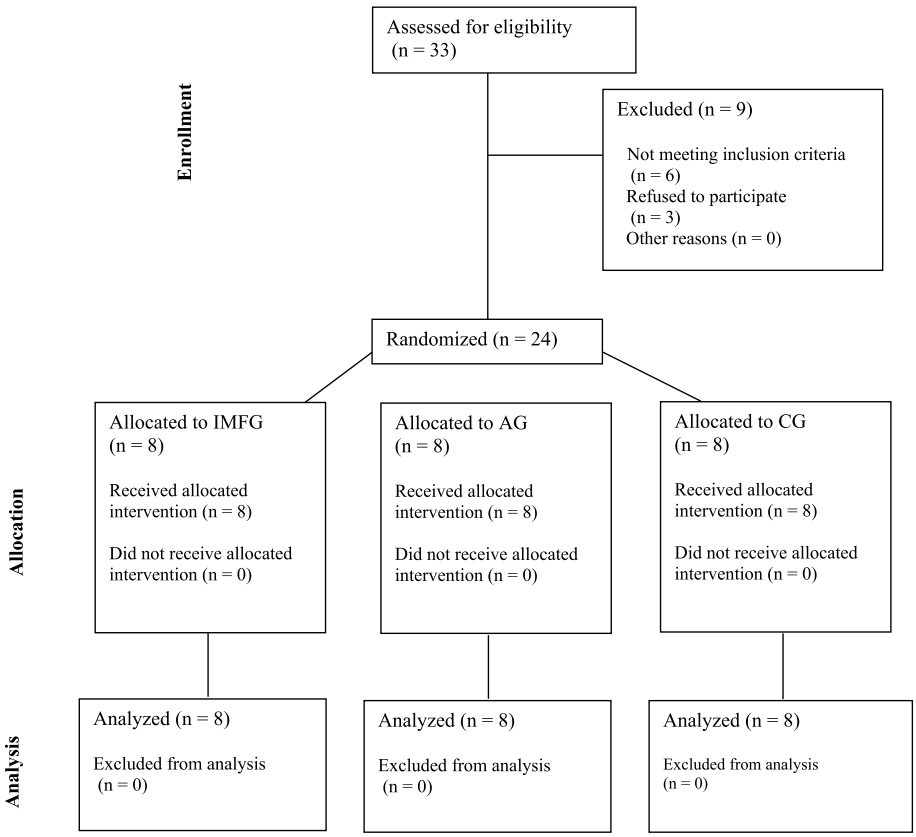

Fig. 1 CONSORT Flow diagram of the study

Table 1 Demographic and clinical characteristics of patients

	IMFG ($n=8$)	AG ($n=8$)	CG ($n=8$)	P
Sex (male/female)	5/3	4/4	6/2	
Age (yrs)	79.63 ± 6.80	78.88 ± 8.66	77.75 ± 8.46	n.s
Body Mass (kg)	68.00 ± 10.54	67.59 ± 14.24	66.17 ± 9.37	n.s
Height (cm)	171.13 ± 0.40	170.25 ± 0.71	168.50 ± 6.35	n.s
BMI (kg/m^2)	23.25 ± 3.72	23.21 ± 4.05	23.60 ± 2.47	n.s

IMFG Inspiratory muscle fatigue group, *AG* Activation group, *CG* Control group, *BMI* Body Mass Index

treatment ($P<0.05$). Within the IMFG analysis, there was a decreased between baseline and post-treatment of -6.75 ± 2.66 cmH2O ($P<0.01$; ES = 0.72; 95% CI of the difference = -8.06 to -5.44). In contrast, the AG showed an increased between baseline and post-treatment of 3.00 ± 0.93 cmH2O ($P<0.01$; ES = 0.45; 95% CI of the difference = 1.69 to 4.31).

In the analysis of the $TF_{\%}$, the IMFG had lower values than the AG and the CG after performing the treatment ($P<0.01$). Within the IMFG analysis there was a decreased between baseline and posttreatment of -22.13 ± 10.49% ($P<0.01$; ES = 1.21; 95% CI of the difference = -27.29 to -16.96). Conversely, the AG showed an increased between baseline and post-treatment of 9.72 ± 5.78% ($P<0.01$; ES = 0.61; 95% CI of the difference = 4.55 to 14.89).

In the analysis of Mob_{insp}, the IMFG had lower values than the AG and the CG after performing the treatment ($P<0.01$). Within the IMFG analysis, there was a decreased between baseline and post-treatment of -0.79 ± 0.24 cm ($P<0.01$; ES = 3.02; 95% CI of the difference = -0.96 to -0.61). Conversely, the AG showed an increased between baseline and post-treatment of 0.28 ± 0.18 cm ($P<0.01$; ES = 0.96; 95% CI of the difference = 0.10 to 0.46).

Changes in functional and muscle oxygen saturation variables after fatigue and activation

Results for secondary outcomes are presented in Table 3.

In the analysis of TUG, the inspiratory muscle fatigue group had higher values than the activation group after performing the treatment ($P<0.05$). Within the inspiratory muscle fatigue group analysis, there was an increased between baseline and post-treatment of 3.42 ± 1.11 s ($P<0.01$; ES = 0.82; 95% CI of the difference = 2.85 to 3.99), on the other hand, the activation group showed a decreased between baseline and post-treatment of -1.95 ± 0.63 s ($P<0.01$; ES = 0.59; 95% CI of the difference = -2.52 to -1.38).

In the analysis of FTSST, the inspiratory muscle fatigue group had higher values than the activation group after performing the treatment ($P<0.01$). Within the inspiratory muscle fatigue group analysis, there was an increased between baseline and post-treatment of 3.23 ± 1.25 s ($P<0.01$; ES = 1.44; 95% CI of the difference = 2.40 to 4.07). Conversely, the activation group showed a decreased between baseline and post-treatment of -1.73 ± 1.12 s ($P<0.01$; ES = 0.51; 95% CI of the difference = -2.57 to -0.90).

In the analysis of the SmO_2, the inspiratory muscle fatigue group had lower values than the activation group and the control group after performing the treatment ($P<0.01$). Within the inspiratory muscle fatigue group analysis, there was a decrease between baseline and post-treatment of -8.55 ± 1.50% ($P<0.01$; ES = 7.99; 95% CI of the difference = -9.21 to -7.89). Conversely, the activation group showed an increased between baseline and post-treatment of 0.55 ± 0.32% ($P<0.01$; ES = 0.21; 95% CI of the difference = 0.11 to 1.21).

Discussion

The results of our study suggest a decrease in inspiratory muscle strength, as well as a decline in functional capacity and muscle oxygen saturation when isolated inspiratory muscle fatigue occurs in older subjects. Furthermore, both inspiratory strength and functionality appear to improve with inspiratory muscle activation.

The aging process has negative effects on respiratory musculature, especially concerning the inspiratory musculature, particularly the diaphragm. Factors such as hyperinflation due to increased residual volume, increased dorsal kyphosis, or the greater rigidity of the thoracic cage induce a loss of strength in the diaphragm of around 30% in older subjects compared to younger individuals, also becoming a marker of sarcopenia [23]. Additionally, greater diaphragmatic thickening has been demonstrated in older adults, likely due to the increased need for lumbar stabilization in this population, as well as greater flattening and decreased muscle contraction velocity [3].

The results obtained in this study demonstrated reduced MIP values in the IMFG, consistent with previous studies conducted with similar protocols [24]. Inspiratory muscle fatigue involves the inability of the inspiratory muscles to overcome a given pleural pressure and is considered a limiting factor in both sports performance and exercise tolerance. Such respiratory muscle fatigue induces the appearance of the so-called respiratory metaboreflex or metaboreflex, whereby, through an afferent stimulus from type III and IV fibers, it reaches the supraspinal level, producing reflex vasoconstriction of active peripheral musculature, increasing perceived effort and decreasing performance [7] which is further intensified, with a significant increase in the vasopressor response as subject age increases [12]. Various studies

Table 2 Primary outcomes measurements (respiratory variables)

	Baseline	Post-treatment		f	P	n^2	pot
MIP (cmH2O)							
IMFG	62.75 ± 9.36	56.00 ± 7.46**$^{\#\#}$	Group	1.19	0.33	0.10	0.23
AG	62.00 ± 6.63	65.00 ± 6.85**	Time	11.09	< 0.01	0.35	0.89
CG	64.50 ± 6.52	64.63 ± 5.63	Group x Time	63.53	< 0.01	0.86	1
$Thick_{insp}$ (cm)							
IMFG	0.43 ± 0.09	0.39 ± 0.08**	Group	0.44	0.65	0.04	0.11
AG	0.44 ± 0.10	0.46 ± 0.10**	Time	13.46	< 0.01	0.39	0.94
CG	0.43 ± 0.08	0.43 ± 0.08	Group x Time	69.64	< 0.01	0.87	1
$Thick_{esp}$ (cm)							
IMFG	0.23 ± 0.04	0.24 ± 0.04**	Group	0.36	0.70	0.03	0.10
AG	0.23 ± 0.04	0.23 ± 0.04	Time	3.77	0.06	0.15	0.46
CG	0.22 ± 0.03	0.22 ± 0.03	Group x Time	7.00	< 0.01	0.40	0.89
$TF_{\%}$							
IMFG	85.83 ± 18.32	63.71 ± 12.48**$^{\#\#}$	Group	5.35	0.01	0.78	0.28
AG	90.40 ± 15.89	100.12 ± 19.60**	Time	10.53	< 0.01	0.33	0.87
CG	95.19 ± 8.28	93.63 ± 9.11^{++}	Group x Time	42.19	< 0.01	0.80	1
Mob_{insp} (cm)							
IMFG	5.51 ± 0.26	4.72 ± 0.23**$^{\#\#}$	Group	8.17	< 0.01	0.44	0.93
AG	5.47 ± 0.29	5.75 ± 0.35**	Time	13.38	< 0.01	0.39	0.94
CG	5.49 ± 0.26	5.46 ± 0.29^{++}	Group x Time	41.10	< 0.01	0.80	1
$Time_{insp}$ (ms)							
IMFG	2002.50 ± 155.54	2080.00 ± 145.60$^{\#\#}$	Group	5.71	0.01	0.35	0.81
AG	1911.25 ± 136.74	1770.00 ± 134.70**	Time	0.21	0.65	0.01	0.07
CG	1990.00 ± 176.72	2012.50 ± 118.05$^{\$\$}$	Group x Time	4.77	0.02	0.31	0.73
Vel_{insp} (cm/s)							
IMFG	2.76 ± 0.13	2.30 ± 0.15**$^{\#\#}$	Group	21.78	< 0.01	0.68	1
AG	2.86 ± 0.22	3.26 ± 0.27**$^{++}$	Time	1.07	0.31	0.05	0.17
CG	2.77 ± 0.16	2.69 ± 0.21$^{\$\$}$	Group x Time	32.02	< 0.01	0.75	1
Mob_{sniff} (cm)							
IMFG	1.68 ± 0.19	1.55 ± 0.15*$^{\#\#}$	Group	2.33	0.12	0.18	0.42
AG	1.67 ± 0.13	1.83 ± 0.08**	Time	0.35	0.56	0.02	0.09
CG	1.67 ± 0.20	1.59 ± 0.16$^{\$\$}$	Group x Time	8.24	< 0.01	0.44	0.93
$Time_{sniff}$ (ms)							
IMFG	167.50 ± 19.09	213.75 ± 15.06**$^{\#\#}$	Group	9.51	< 0.01	0.48	0.96
AG	168.75 ± 18.08	158.75 ± 17.27	Time	6.22	0.02	0.23	0.66
CG	165.00 ± 21.38	160.00 ± 15.12^{++}	Group x Time	18.53	< 0.01	0.64	1
Vel_{sniff} (cm/s)							
IMFG	10.12 ± 0.64	7.20 ± 0.68**$^{\#\#}$	Group	20.63	< 0.01	0.66	1
AG	9.92 ± 0.53	11.59 ± 1.13**$^{++}$	Time	14.71	< 0.01	0.41	0.96
CG	10.22 ± 0.68	9.96 ± 0.64$^{\$\$}$	Group x Time	102.15	< 0.01	0.91	1

Values are mean ± SD

IMFG Inspiratory muscle fatigue group, *AG* Activation group, *CG* Control group, *MIP* Maximal inspiratory pressure, $Thick_{insp}$ Diaphragmatic thickness in inspiration, $Thick_{esp}$ Expiratory diaphragmatic thickness, *TF* Thickness ratio inspiration/expiration, Mob_{insp} Maximal inspiration diaphragmatic mobility, $Time_{insp}$ Maximum inspiratory contraction time, Vel_{insp} Maximum inspiration contraction velocity, Mob_{sniff} Diaphragmatic mobility sniff, $Time_{sniff}$ Sniff contraction time, Vel_{sniff} Sniff contraction velocity

* $P < 0.05$, $^{**}P < 0.01$, post-treatment, with baseline

$^{\#}$ $P < 0.05$, $^{\#\#}P < 0.01$, comparisons between the IMFG and AG groups at corresponding time points

$^{+}$ $P < 0.05$, $^{++}P < 0.01$, comparisons between the IMFG and CG groups at corresponding time points

$^{\$}$ $P < 0.05$, AGP < 0.01, comparisons between the AG and CG groups at corresponding time points

Table 3 Secondary outcome measurements (functional and muscle oxygen saturation variables)

	Baseline	Post-treatment		f	P	n^2	pot
TUG (s)							
IMFG	17.98 ± 4.19	21.39 ± 4.83**##	Group	2.01	0.16	0.16	0.37
AG	16.62 ± 3.29	14.66 ± 3.07**	Time	5.69	0.03	0.21	0.62
CG	17.82 ± 4.29	17.49 ± 4.38	Group x Time	101.35	< 0.01	0.91	1
FTSST (s)							
IMFG	16.09 ± 2.25	19.32 ± 2.57**##	Group	3.50	0.05	0.25	0.59
AG	14.74 ± 3.41	13.00 ± 4.30**	Time	4.13	0.06	0.16	0.49
CG	16.19 ± 2.69	16.11 ± 2.03	Group x Time	39.43	< 0.01	0.79	1
SmO_2 (%)							
IMFG	37.43 ± 1.07	28.88 ± 1.64**##	Group	3.99	0.03	0.28	0.95
AG	35.91 ± 2.63	36.46 ± 2.69	Time	213.84	< 0.01	0.91	1
CG	35.91 ± 2.98	35.91 ± 2.89++	Group x Time	260.98	< 0.01	0.96	1

Values are mean ± SD

IMFG Inspiratory muscle fatigue group, *AG* Activation group, *CG* Control group, *TUG* Timed up and go test, *FTSST* Five times sit to stand test, SmO_2 Muscle oxygen saturation

* $P < 0.05$, ** $P < 0.01$, post-treatment, with baseline

# $P < 0.05$, ## $P < 0.01$, comparisons between the IMFG and AG groups at corresponding time points

+ $P < 0.05$, ++ $P < 0.01$, comparisons between the IMFG and CG groups at corresponding time points

$ $P < 0.05$, AGP < 0.01, comparisons between the AG and CG groups at corresponding time points

throughout current scientific literature have examined the effects of inducing fatigue on respiratory musculature. For example, in another study, it was demonstrated that inducing diaphragmatic fatigue in healthy subjects resulted in decreased exercise tolerance, as well as increased sensation of dyspnea and leg discomfort [25].

Regarding the ultrasound measurements obtained, they appear to be reduced in the IMFG, yielding results similar to those found in previous studies [26]. Ultrasound constitutes a non-invasive imaging technique that allows for objective evaluation of muscle structure and function, in our case, of respiratory musculature, specifically the diaphragm, and is also a reliable and reproducible assessment method [18]. There is evidence regarding the different correlations between diaphragmatic thickness measurements made with the B-mode and diaphragmatic mobility measurements made using the M-mode. Regarding diaphragmatic thickness measurement, its correlation with inspiratory muscle strength and pulmonary function has been demonstrated, while diaphragmatic mobility correlates equally with inspiratory muscle strength, transdiaphragmatic pressure, and esophageal pressure, specifically through deep breathing and sniff maneuvers [27, 28]. On the other hand, another determinant of diaphragmatic functionality, in addition to the force it can develop, is diaphragmatic contraction velocity, which is also not influenced by other variables such as thoracic stiffness or pulmonary distensibility, allowing for an accurate reflection of diaphragmatic contraction efficiency [29]. Previous studies analyzing diaphragmatic dysfunction using ultrasound demonstrated a decrease in respiratory time, thickening fraction, strength, and diaphragmatic contraction velocity in subjects with sepsis-induced diaphragmatic dysfunction [30]. Among the potential effects that may explain these negative outcomes, we find that fatigue can affect the ability of the muscles to generate pressure and force, resulting in a decrease in diaphragm thickness and mobility during contraction [31, 32]. On the other hand, the improvements observed in the AG could be explained by the neuromuscular and biochemical enhancements resulting from the activation of the inspiratory muscles [33].

Muscle oxygen saturation measurements using infrared spectroscopy devices have proven to be an effective measurement method both during activity and at rest, whether for research or training purposes [34]. The lower values of muscle oxygen saturation found in the fatigue group may be due to peripheral vasoconstriction and blood flow redistribution resulting from excessive inspiratory muscle work and the appearance of the metaboreflex, leading to reduced blood supply to the area and thus reduced oxygen delivery [35, 36], also occurring in the lower limbs at rest [37]. It should be noted that in older adults, there is already dysfunction of the cardiovascular system, leading to reduced vasodilatory capacity during exercise, as well as slower oxygen uptake at the onset of exercise [38, 39]. Our results align with another previous study, where subjects subjected to increased respiratory work showed increased blood flow in accessory

respiratory musculature, as well as a decrease in locomotor musculature [40].

TUG is a commonly used test in clinical practice to assess functionality and fall risk in older adults [41]. Additionally, it is widely validated and integrated into the management of respiratory pathology due to its ease of use and its ability to stratify frailty in COPD patients [42]. On the other hand, FTSST is a widely validated test in older adults aimed at assessing lower limb strength, as well as postural control and balance [43]. Currently, there are no studies investigating the relationship between inspiratory muscle fatigue and functionality, balance, and strength in older adults. Although these tests may initially seem too short in duration, it is important to consider that the negative effects of the metaboreflex can be triggered by short-duration stimuli that involve significant effort for the patient [44], such as performing five squats or walking three meters as quickly as possible for an older adult. Our results demonstrate a significant increase in the execution time of TUG and FTSST in the IMFG. We can hypothesize that, as a decrease in blood flow and oxygen supply to peripheral musculature induced by the metaboreflex occurs [35, 36], ischemia may lead to a loss of muscle contractile capacity and strength [38]. This ischemia may present the same issue in respiratory musculature, considering that the diaphragm plays a fundamental role in lumbar stability through control and generation of intra-abdominal pressure [45].

Regarding the improvements obtained by the AG, several studies available in the current scientific literature evidence the various effects produced by activation of respiratory musculature. On one hand, improvements in MIP and various ultrasound variables may be due to improved neuromuscular function of the diaphragm and accessory inspiratory musculature [46]. Additionally, moderate loads like those used in our study also allowed for a decrease in dyspnea sensation and increased oxygen supply to active muscles [47] thus improving exercise tolerance [48] with improvements also found in lung function [16].

Although the results of this study should be interpreted with caution, they seem to have a number of interesting clinical implications. Firstly, there appear to be a series of negative functional implications resulting from respiratory muscle fatigue. Secondly, it seems that the activation of the inspiratory muscles may have beneficial effects on functionality in older adults. Therefore, these results suggest that inspiratory muscle training should be considered in clinical contexts, both rehabilitative and preventive, as part of treatment and training programs for older adults. Among the possible limitations of this study, we found that only pre and post measurements of the different variables were performed, not allowing for the objective assessment of how long the effects of the interventions may last. For its part, neither respiratory rate or tidal volume were standardized; the breathing pattern was free as long as the ratio of two seconds of expiration for every second of inspiration was maintained. On the other hand, although other correlated measurements were employed, the application of specific measurements such as phrenic stimulation at the cervical level or transdiaphragmatic pressure could have provided greater objectivity to inspiratory muscle fatigue. Future lines of research may focus on evaluating the long-term effects of inspiratory muscle fatigue on functionality, as well as examining its effects on other variables or parameters such as time to task failure, muscle strength, or aerobic capacity.

Conclusions

Fatigue of the inspiratory musculature seems to have a detrimental effect on inspiratory muscle strength, peripheral muscle strength, muscular oxygenation and functionality in older adults. On the other hand, activation of the inspiratory musculature appears to contribute to improvements in respiratory muscle strength and functionality in these individuals.

Abbreviations

IMFG	Inspiratory muscle fatigue group
AG	Activation group
CG	Control group
MIP	Maximal inspiratory pressure
$Thick_{insp}$	Diaphragmatic thickness in inspiration
$Thick_{esp}$	Expiratory diaphragmatic thickness
TF	Thickness ratio inspiration/expiration
Mob_{insp}	Maximal inspiration diaphragmatic mobility
$Time_{insp}$	Maximum inspiratory contraction time
Vel_{insp}	Maximum inspiration contraction velocity
Mob_{sniff}	Diaphragmatic mobility sniff
$Time_{sniff}$	Sniff contraction time
Vel_{sniff}	Sniff contraction velocity
TUG	Timed up and go test
FTSST	Five times sit to stand test
SmO_2	Muscle oxygen saturation

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

ALM and ASS carried out the design and idea of the project, ASS and ALM and DMV wrote the introduction to the manuscript, DMV and ALM wrote the methodology and JSI statistics part, and ASS, JSI and ALM wrote the Discussion and conclusions part. ASS, DMV and JSI reviewed the manuscript.

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Data availability
We have the availability of the data, and the materials are available at the request of the publisher.

Declarations

Ethics approval and consent to participate
The current study was approved by the Research Ethics Committee of Toledo University Hospital Complex.
(Spain). In addition, written informed consent was obtained from the participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]School for Doctoral Studies and Research, Universidad Europea de Madrid, Calle Tajo S/N. 28670, Villaviciosa de Odón, Madrid, Spain. [2]Research Group On Exercise Therapy and Functional Rehabilitation, Faculty of Sports Sciences, Universidad Europea de Madrid, Madrid, Spain. [3]Faculty of Physiotherapy and Nursing of Toledo, Universidad de Castilla-La Mancha, Toledo, Spain. [4]Faculty of Health Sciences, Universidad Francisco de Vitoria, Madrid, Spain. [5]Physiotherapy Research Group of Toledo (GIFTO), Faculty of Physiotherapy and Nursing, Universidad de Castilla-La Mancha, Toledo, Spain. [6]Faculty of Sports Sciences, Universidad Europea de Madrid, Madrid, Spain. [7]Clínica Axium Salud Funcional, Madrid, Spain. [8]Clínica Sierra Varona SL, Toledo, Spain. [9]Department of Physiotherapy, Faculty of Health, Camilo José Cela University, Villanueva de La Cañada, Madrid, Spain. [10]Department of Physical Therapy, Faculty of Health Sciences, Universidad Alfonso X El Sabio, Madrid, Spain.

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