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# Effects of inspiratory muscle training on thoracoabdominal volume regulation in older adults: a randomised controlled trial

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## Abstract

### **Objectives:**

We investigated the effect of inspiratory muscle training (IMT) on inspiratory muscle strength, functional capacity and respiratory muscle kinematics during exercise in healthy older adults.

### **Methods:**

24 adults were randomised into an IMT or SHAM-IMT group. Both groups performed 30 breaths, twice daily, for 8 weeks, at intensities of ~50% maximal inspiratory pressure (PImax; IMT) or <15% PImax (SHAM-IMT). Measurements of PImax, breathing discomfort during a bout of IMT, six-minute walk distance, physical activity levels, and balance were assessed pre- and post-intervention. Respiratory muscle kinematics were assessed via optoelectronic plethysmography (OEP) during constant work rate cycling.

### **Results:**

PImax was significantly improved (by  $20.0\pm11.9 \text{ cmH}_2\text{O}$ ; p=0.001) in the IMT group only. Breathing discomfort ratings during IMT significantly decreased (from  $3.5\pm0.9$  to  $1.7\pm0.8$ ). Daily sedentary time was decreased (by  $28.0\pm39.8$  min; p=0.042), and reactive balance significantly improved (by  $1.2\pm0.8$ ; p<0.001) in the IMT group only. OEP measures showed a significantly greater contribution of the pulmonary and abdominal rib cage compartments to total tidal volume expansion post-IMT.

### **Conclusions:**

IMT significantly improves inspiratory muscle strength and breathing discomfort in this population. IMT induces greater rib cage expansion and diaphragm descent during exercise, thereby suggesting a less restrictive effect on thoracic expansion and increased diaphragmatic power generation.

## **1.0. Introduction**

Respiratory muscle function is impaired during the healthy ageing process due to increases in residual volume (RV) and functional residual capacity (FRC), which consequently increases the work of breathing and associated breathlessness during activities of daily living in older adults (Janssens et al., 1999). Furthermore, age-related physiological changes within the respiratory system can limit exercise tolerance in older adults due to increased ventilatory demand as well as reduced ventilatory capacity compared to their younger counterparts (Johnson et al., 1991; Molgat-Seon et al., 2018; Smith et al., 2018).

One strategy to ameliorate this demand/capacity imbalance of the respiratory system is to increase the strength and power of the respiratory pump via inspiratory muscle training (IMT) (McConnell, 2013). This method of training has been found to significantly improve respiratory muscle strength (reflected by increased maximal inspiratory pressure;  $PI_{max}$ ) in older adults, shown by a meta-analysis previously conducted by our group (Manifield et al., 2021). Furthermore, the meta-analysis on the effects of IMT on functional capacity showed a non-significant, albeit minimum clinically important difference in sixminute walk distance (6MWD; Manifield et al., 2021).

Whether improvements in respiratory muscle strength following IMT translate into: i) reductions in breathing discomfort at a given fraction of inspiratory muscle effort and/or ii) changes in breathing pattern and thoracoabdominal volume regulation during exercise in this population remains currently unknown.

Recently, optoelectronic plethysmography (OEP) has been utilised to measure changes in total and compartmental thoracoabdominal volume regulation following IMT in chronic kidney disease and advanced lung disease patients (Hoffman et al., 2021; Medeiros et al., 2019). Changes in the volumes of the rib cage compartment represent the action of the intercostal muscles and the diaphragm, whereas abdominal volume changes are effected by the function of the muscles of the abdominal wall (Aliverti, 2002). Accordingly, in patients with chronic kidney disease, Medeiros et al. (2019) observed a

significant increase of 0.1 L in the pulmonary rib cage (RCp) compartmental volume during resting inspiratory capacity manoeuvres following IMT compared to the control group. This was interpreted as an increase in external intercostal muscle strength following IMT. No difference, however, was observed during quiet breathing (QB) between groups. Hoffman et al. (2021) also reported no significant changes in breathing pattern or thoracoabdominal volume regulation during resting conditions, despite improvements in respiratory muscle strength and endurance in advanced lung disease patients. The authors stated that the main limitation of their study was the lack of OEP measurements during exercise and suggested that IMT may only elicit changes in breathing pattern when the respiratory system is placed under higher breathing demands during exercise.

Moderate intensity inspiratory muscle loading (at 40% maximal inspiratory pressure;  $PI_{max}$ ) via pressure-threshold loading within a study conducted by de Souza et al. (2016) has resulted in significantly increased RCp and abdominal rib cage (RCa) contribution compared to resting levels in older adults, reflecting greater work output of both the muscles of the rib cage (i.e. external intercostals) and the diaphragm during inspiration. However, it remains unclear whether repeated bouts of inspiratory muscle loading (in the form of IMT) will translate into enduring changes in total and compartmental thoracoabdominal volume regulation during exercise, reflecting changes in respiratory muscle activation patterns.

Thus, the aim of this study was to investigate whether a programme of IMT compared to SHAM-IMT, induces changes in both breathing discomfort at a given fraction of resting inspiratory muscle effort and thoracoabdominal volume regulation during exercise in healthy older adults. Based on the available literature we reasoned that increased strength of the rib cage and diaphragm muscles following IMT would be translated into lower breathing sensations and greater pulmonary and abdominal rib cage volume perturbations reflecting greater intercostal and diaphragm muscle activity.

## 2.0 Methods

### 2.1. Study design

This was a randomised controlled study investigating the effects of IMT on thoracoabdominal volume regulation during exercise compared to SHAM-IMT. Following the baseline assessment, participants were randomly allocated to either an experimental (IMT) or control (SHAM-IMT) group using an online randomisation programme (www.sealedenvelope.com). Stratification was based on the median and interquartile range of predicted  $PI_{max}$  (88%; 74-109%) observed from our pilot study from 12 healthy older adults (age:  $67.4 \pm 2.8$  years; <88%  $PI_{max}$  or  $\geq$ 88%  $PI_{max}$ ). The present study was approved by Northumbria University Newcastle Ethics Committee (No: 23701).

### 2.2. Participants

Twenty-four older adults were initially recruited for this study. Inclusion criteria were followed and included older adults between 60-75 years who were free from injury and able to give full written consent. The exclusion criteria were current smokers, chronic pulmonary, cardiac, or neuromuscular disease, and users of medications that affect muscle strength. All participants provided full informed consent before being randomised into experimental (IMT) or control (SHAM-IMT) groups.

Estimation of sample size was based on results published by Watsford and Murphy (2008). The mean difference in  $PI_{max}$  following training between the experimental and control group (17 cmH2O), and a standard deviation (SD) of 15 cmH2O was used with an alpha significance level of 0.05 (2-sided) and 80% power. A minimum total sample size was calculated to be 12 participants in each group to detect significant differences in  $PI_{max}$  between experimental and control groups.

### 2.3. Pre-and post-intervention outcome measures

Participants visited the lab on three separate occasions. Visit one included baseline assessments of stature, mass, spirometry, blood pressure, pulmonary and respiratory muscle function, and breathing discomfort at a given level of inspiratory muscle strength. Exercise capacity (six-minute walk test [6MWT] and constant-work rate [CWR] cycling), balance (mini-balance evaluation systems test [mini-BEST]), and quality of life (36-Item Short Form Survey [SF-36]) were also assessed (specific details of these procedures are described within the following sections). Participants were then randomised into groups outlined above and trained for 8-weeks following a specific protocol (outlined within the *"interventions"* section below). Visit two occurred at the mid-point of the 8-week intervention (i.e., at the end of week 4) and involved reassessments of maximal respiratory pressures to ensure those in the experimental group were still training at the predetermined intensity. Visit three occurred immediately after the 8-week IMT or SHAM-IMT programme and involved post-intervention assessments of outcomes assessed in visit 1. Physical activity levels were assessed in the week before visit 1 and the week immediately following visit 3.

### 2.3.1. Pulmonary function measurements

Pulmonary function was assessed via spirometry tests using a metabolic gas exchange analyser (Cortex; Metalyzer 3B, Leipzig, Germany). The cortex device was calibrated in line with the manufacturer's instructions before spirometry manoeuvres were performed. The variables measured included: forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), FEV<sub>1</sub>/FVC ratio, and peak expiratory flow (PEF). These tests were performed to confirm all participants' eligibility to the study by confirming no presence of pulmonary disease (FEV<sub>1</sub>/FVC: >70%; FEV<sub>1</sub>: >80% predicted) (Rabe et al., 2007) and were conducted in line with current guidelines (Graham et al., 2019). After a minimum of three manoeuvres were performed, the manoeuvre which showed the highest values were used (Graham et al., 2019). Maximal voluntary ventilation (MVV) was predicted by multiplying FEV<sub>1</sub> by 40 (Miller et al., 2005).

### 2.3.2. Respiratory muscle function measurements

Maximal inspiratory and expiratory pressures ( $PI_{max}$  and  $PE_{max}$ , respectively) were assessed using a handheld pressure transducer (MicroRPM; Micro Medical Ltd, Rochester, Kent, UK). Participants were seated and performed forceful inspiratory efforts (Mueller manoeuvre) from both residual volume (RV) and functional residual capacity (FRC) for  $PI_{max}$ , and forceful expiratory efforts (Valsalva manoeuvre) from total lung capacity (TLC) for  $PE_{max}$ , for at least 1.5 seconds against an occluded airway (Laveneziana et al., 2019). Initially, participants performed 3 inspiratory-muscle warm up manoeuvres at self-determined 50%  $PI_{max}$  and 3 at 75%  $PI_{max}$  to be familiarised with the manoeuvre. Maximal measurements were repeated at least five times until three consecutive manoeuvres had less than 10% variability with the highest of these values used (Laveneziana et al., 2019). Predicted  $PI_{max}$  values (in cmH<sub>2</sub>O) were calculated using equations outlined by Black and Hyatt (1969) and were used to determine the percentage predicted (% pred) values for each participants  $PI_{max}$ . Furthermore, breathing discomfort at a given fraction of  $PI_{max}$  was assessed during all 3 visits (baseline, mid 8-week and at 8 weeks) via the 10-point modified Borg scale following a bout of IMT (30 breaths at 50% baseline  $PI_{max}$ ).

## 2.3.3. Six-minute walk test (6MWT)

The 6MWT is a self-paced measure of exercise capacity and involved participants walking as far as possible along a 30-metre flat course in accordance with ATS/ERS guidelines (Holland et al., 2014). Participants were instructed to walk as far as possible in 30m shuttles at their own pace for six minutes. The 6MWT distance (6MWD) was recorded by tallying the number of 30m laps covered by the participants and the number of meters achieved in the final partial lap (Holland et al., 2014). Predicted values were calculated using equations published by Troosters et al. (1999).

### 2.3.4. Constant work rate exercise test

Constant work rate (CWR) exercise tests were performed on a cycle ergometer. Participants predicted work rate max levels were calculated using equations from Lewthwaite et al. (2020). These equations were validated by the authors who found that the predicted values were statistically equivalent to values measured at peak cardiopulmonary exercise testing (Lewthwaite et al., 2020).

Following a warm-up of 3 minutes unloaded pedalling, participants performed the CWR test at 75% predicted work rate peak with a pedalling frequency of 60 rpm to their perceived limit of tolerance (Tlim). Inspiratory capacity (IC) manoeuvres were performed at rest, and every two minutes during the CWR test as previously described (O'Donnell & Webb, 1993) to establish thoracoabdominal volumes at total lung capacity (TLC). Operational thoracoabdominal volumes and central haemodynamic responses were measured continuously via OEP and bio-impedance cardiography (PhysioFlow, Enduro, PF-07, Manatec Biomedical, France) respectively. Perceived dyspnoea and leg discomfort were assessed via the modified 10-point Borg scale at rest, and every two minutes of exercise. The exact same absolute load and protocol was used following the intervention. Participants reported the reason for exercise termination (dyspnoea, leg discomfort, a combination, or other) following the test.

## 2.3.5. Operational thoracoabdominal volume regulation

Operational thoracoabdominal volumes were assessed by optoelectronic plethysmography (OEP; BTS Bioengineering, Milan, Italy) during QB and CWR exercise. This system allows for the non-invasive measurements of total and compartmental tidal volume ( $V_T$ ), end-inspiratory ( $V_{EI}$ ) and end-expiratory ( $V_{EE}$ ) volumes, along with breathing frequency (bf), and minute ventilation ( $V_E$ ).  $V_{EE}$  was set to zero at QB and  $V_{EI}$  was defined as  $V_{EE} + V_T$ . Both  $V_{EE}$  and  $V_{EI}$  were expressed as changes from baseline, and as both absolute values (L) and as percentages of FVC (% FVC) to normalise for lung size.

In order to capture this, eight infrared cameras (Smart System, BTS Bioengineering, Milan, Italy), positioned around the participants, tracked infrared-reflective markers attached to the participants chest wall in a previously calibrated space (Massaroni et al., 2017). The participants were seated in an upright position, and grasped handles located laterally and positioned in line with their mid sternum to ensure

that their arms were lifted away from their chest wall. Participants were familiarised with the cycling exercise whilst maintaining this body position. During QB measurements at baseline and following 3-4 normal tidal breaths, the participants were instructed to perform a maximal inspiratory capacity (IC) manoeuvre from FRC to TLC as previously described (O'Donnell & Webb, 1993). This manoeuvre was repeated at least twice to ensure accurate measurements.

Eighty-nine 6- and 10-mm diameter hemispherical or spherical markers (Massaroni et al., 2017) were attached to the participants, and arranged on different levels in anatomical structures between the sternal notch and the clavicles to the anterior superior iliac crest (Aliverti & Pedotti, 2002; Parreira et al., 2012). Overall, 37 markers were attached to the anterior, 42 to the posterior, and 10 laterally on each participant (Aliverti & Pedotti, 2002).

The positioning of the markers on the thoracoabdominal surface is designed to allow adequate sampling of its complex shape and subdivision of the total volume into three different compartments: the pulmonary rib cage (RCp), the abdominal rib cage (RCa), and the abdomen (AB) (Aliverti & Pedotti, 2002, 2014). This allows for the detailed study of respiratory muscle kinematics as it takes into consideration the different pressures that the lung- (RCp) and diaphragm-apposed (RCa) sections of the rib cage are exposed to during inspiration (Agostoni & d'Angelo, 1985; Aliverti & Pedotti, 2002). Furthermore, it also allows for the consideration that the diaphragm acts directly on RCa, and non-diaphragmatic inspiratory muscles (such as the external intercostals, parasternal, scalene, and neck muscles) act largely on RCp only (Aliverti & Pedotti, 2002; Massaroni et al., 2017). The change in abdominal volume is defined as the volume swept by the abdominal wall (Konno & Mead, 1967), resulting from the action of the diaphragm during inspiration and muscles of the abdominal wall (such as the rectus and transverse abdominis, and the internal and external obliques) during expiration (Aliverti & Pedotti, 2014).

## 2.3.6. Physical activity levels

Physical activity levels were assessed via accelerometery (Actigraph wGT3X; ActiGraph, Pensacola, FL, USA) during the week preceding, and the week following completion of, the IMT or SHAM-IMT intervention. Specifically, the outcome measures recorded by the ActiGraph were daily steps, movement intensity (vector magnitude units per minute; VMU/min), sedentary, light, and moderate to vigorous physical activity (MVPA) levels (min/day).

The initialisation of the Actigraph was set to record for seven days (starting the day after the administration to the participant). The Actigraph was deployed in delay mode during day 0 and commenced logging at 07:00 hrs with a 7-day stop time indicated. The data collection sample rate was set to 100 Hz and an epoch length of 60 seconds. Participants were instructed to wear the ActiGraph around their waist during all hours of wakefulness. During data processing, a valid recording was defined as at least 8 hours (480 minutes) of wear time during waking hours (Demeyer et al., 2014). A minimum of 4 valid days were required to be included within the data analysis (Demeyer et al., 2021).

### 2.3.7. Balance tests

A range of balance measures were assessed using the mini-balance evaluation systems test (mini-BEST) (Franchignoni et al., 2010) at baseline and post-intervention. This test is comprised of 14 tasks divided into four domains: anticipatory postural adjustments, reactive postural responses, sensory orientation, and dynamic balance during gait (Franchignoni et al., 2010). The mini-BEST test was developed from the original balance evaluation systems test (BESTest) (Horak et al., 2009) via psychometric (Factor and Rasch) analysis to significantly reduce the time taken to administer from 30-45 minutes to 10-15 minutes (Franchignoni et al., 2010; Potter & Brandfass, 2015). Each task within the mini-BEST is scored on a 3-point ordinal scale (0 = severely impaired, 1 = moderately impaired, and 2 = normal) with a maximum scorer of 28 points and a cut-off score of 16 to define older adults with balance disorders (Yingyongyudha et al., 2016).

### 2.3.8. Quality of life

Quality of life (QoL) was assessed via the 36-Item Short Form Survey (SF-36) (Ware Jr & Sherbourne, 1992). This questionnaire consists of 36 questions across eight dimensions of health: physical function, role physical, bodily pain, general health perception, vitality, social function, role emotional, and mental health. Scores for each dimension were coded, summed, and transformed onto a scale ranging from 0 (worst health) to 100 (best health) (Brazier et al., 1992).

### 2.4. Interventions

The training programme within this study consisted of two daily, home-based sessions of 30 breaths, 7 days/week for 8 weeks using a pressure-threshold IMT device (POWERbreathe Classic [medium resistance], POWERbreathe International Ltd., Southam, UK). The IMT group trained at an intensity corresponding to approximately 50% of their baseline  $PI_{max}$ , ensuring maximum inspirations were achieved during each breath, and aiming for Borg scale ratings of 4-6 for perceived breathing discomfort following each session. As this was mainly a home-based intervention, participants were coached through the correct technique prior to the intervention. This included inspiring forcefully against the resistance (lasting 1-2 seconds) followed by a slow expiration to residual volume (lasting around 4 seconds) (McConnell, 2013). Participants were recommended to perform each training session in an upright seated position and if sensations of light-headedness occur, they should take a short pause of 2-3 seconds following exhalation.

Training diaries were administered to monitor adherence to the intervention, and participants were instructed to record the intensity (level 1-9 on the POWERbreathe Classic device which was converted to % baseline  $PI_{max}$  during analysis), duration (number of breaths achieved; should always be around 30), and breathing discomfort (using a modified 10-point Borg scale provided) following each session. Participants were encouraged to increase the training load by a one quarter turn of the load tensioner (2-3 cmH<sub>2</sub>O) if they reached the 30 breaths with ease (Borg rating of perceived breathing discomfort <<4). The control (SHAM-IMT) group trained in the same manner as the experimental group but at an

unaltered intensity of <15%  $PI_{max}$  (or lowest possible intensity on the device; 10 cmH<sub>2</sub>O) for the entire 8 weeks.

After 4 weeks, all participants were required to return to the laboratory for a mid-intervention visit to re-assess  $PI_{max}$  and adjust the training load if necessary to ensure that those in the IMT group were training at approximately 50% of their current  $PI_{max}$ .

### 2.5. Statistical analysis

Normal distribution was assessed using the Shapiro-Wilk test, with a p value >0.05 indicating normally distributed data. Data are presented as mean  $\pm$  SD unless stated otherwise. Baseline characteristics between groups were assessed via independent t-tests. Two-way repeated measures ANOVAs with Bonferroni adjustments were employed to determine within (pre-post/pre-mid-post [baseline, mid-, and post-intervention] and time [exercise isotime; 25, 50, 75, and 100%]) and between group (intervention [IMT vs. control]) interactions following training.

Isotime was defined as the duration of the shortest CWR test (pre- or post-intervention) for each individual and exercise isotime data are reported as a fraction of the shortest CWR test (i.e., 25, 50, 75, and 100%). Paired samples t-tests were employed to assess within group pre- vs post-intervention differences. Pearson's correlation analysis was performed to determine the association between changes from QB (delta  $\Delta$ ) in rib cage volume and changes from QB in total thoracoabdominal volume, as well as between changes from QB in abdomen volume and changes from QB in total thoracoabdominal volume, during CWR exercise. T-tests were employed to determine between and within group differences in regression slopes. For all analyses, the level of significance was set to p<0.05.

## **3.0. Results**

### 3.1. Participant baseline characteristics

Initially, 24 participants were recruited for this study, however, one participant within the IMT group dropped out due to illness. Demographic, spirometric, and respiratory muscle strength variables at baseline are outlined in Table 1. Other than a significant difference in age (p=0.048), no differences in baseline characteristics were observed between IMT and SHAM-IMT groups. Adherence to the training sessions was  $95.5 \pm 6.5\%$  and  $92.2 \pm 8.8\%$  in the IMT and SHAM-IMT groups, respectively, and were not significantly different (p=0.213). Weekly training intensity progression and breathing discomfort ratings in both the IMT and control groups are outlined in Figure 1.

Table 1. Participant baseline characteristics.

	All participants (n=23)	IMT (n=11)	SHAM-IMT (n=12)
Men/Women (n)	11/12	5/6	6/6
Age (years)	$68.3 \pm 2.5$	$69.5\pm2.3$	$67.3 \pm 2.5$ <sup>\$</sup>
Stature (cm)	$168.9\pm9.9$	$167.9\pm8.2$	$169.8 \pm 11.8$
Mass (kg)	$75.6 \pm 17.2$	$79.8\pm20.7$	$71.7 \pm 13.9$
BMI (kg/m <sup>2</sup> )	$26.3\pm5.0$	$28.1\pm5.8$	$25.1\pm3.8$
SBP (mmHg)	$129.0\pm15.1$	$132.0\pm15.0$	$126.3\pm16.0$
DBP (mmHg)	$81.1\pm8.5$	$84.4\pm7.8$	$78.2\pm8.7$
$FEV_1(L)$	$2.9\pm0.8$	$2.7\pm0.8$	$3.0 \pm 0.9$
FEV <sub>1</sub> (% predicted)	$104.3 \pm 14.8$	$102.5\pm13.2$	$106.2\pm16.6$
FVC (L)	$3.6 \pm 1.0$	$3.5\pm0.9$	$3.8 \pm 1.1$
FVC (% predicted)	$102.3\pm13.9$	$100.3 \pm 12.9$	$104.3 \pm 15.5$
FEV <sub>1</sub> /FVC (%)	$78.6\pm4.0$	$78.7\pm4.7$	$78.4\pm3.6$
PEF (L/s)	$6.9 \pm 2.3$	$6.9\pm2.4$	$6.9\pm2.5$
PEF (% predicted)	$98.9\pm21.8$	$101.1\pm24.1$	$96.7\pm21.4$
MVV (predicted; L/min)	$117.5 \pm 32.2$	$114.8\pm26.3$	$120.0\pm38.0$
PI <sub>max</sub> at RV (cmH <sub>2</sub> O)	$80.5\pm25.7$	$77.3\pm26.5$	$83.4\pm25.7$
PImax at RV (% predicted)	$94.1 \pm 25.3$	$91.5\pm25.9$	$96.4\pm26.7$
PImax at FRC (cmH2O)	$67.1\pm22.6$	$65.5\pm22.2$	$68.7\pm23.7$
PE <sub>max</sub> at TLC (cmH <sub>2</sub> O)	$120.6\pm38.4$	$122.5\pm42.9$	$118.7\pm37.3$
6MWD (m)	$594.6\pm54.4$	$588.7\pm56.4$	$600.6\pm54.0$
6MWD (% predicted)	$97.6\pm7.8$	$99.3\pm6.9$	$96.1\pm8.5$

Data presented as mean $\pm$ SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity; PEF, peak expiratory flow; PI<sub>max</sub>, maximal inspiratory pressure; RV, residual volume; FRC, functional residual capacity; PE<sub>max</sub>, maximal

expiratory pressure; TLC, total lung capacity. \$ indicates significant difference between IMT and SHAM-IMT groups.

### 3.2. Respiratory muscle pressures

Significant intervention x pre-mid-post interactions were observed for: 1)  $PI_{max}$  at residual volume (RV; expressed as both absolute [p=0.001] and % predicted [p<0.001] values), 2)  $PI_{max}$  at functional residual capacity (FRC; p=0.041) and 3) breathing discomfort (p<0.001; Table 2; Figure 2). For  $PI_{max}$  variables, these interactions were attributable to significant increases in the IMT group only from baseline to mid-intervention (PI<sub>max</sub> at RV: p=0.001, % pred; p<0.001; PI<sub>max</sub> at FRC: p=0.005), baseline to post-intervention (p<0.001 for all variables), and from mid- and post-intervention (PI<sub>max</sub> at RV: p=0.036, % pred; p=0.043; PI<sub>max</sub> at FRC: p=0.008).

Borg ratings for breathing discomfort during a bout of IMT at 50% baseline  $PI_{max}$  significantly decreased in the IMT group only, from both baseline to mid-intervention and from baseline to post-intervention (both p<0.001; Figure 2). No significant change in breathing discomfort in the IMT group was observed between mid- and post-intervention (p=0.080). No significant intervention x pre-mid-post interaction was observed for  $PE_{max}$  (p=0.832). No changes between intervention time-points were observed for any variable within the SHAM-IMT group. No significant correlation was found within the IMT group between baseline  $PI_{max}$  and post-intervention change in  $PI_{max}$  expressed as absolute values (n=11, *r*=0.461, p=0.153; Figure 3a) or as percentage predicted (n=11, *r*=0.472, p=0.136; Figure 3b).

		IMT		SHAM-IMT		
	Baseline	Mid- intervention	Post- intervention	Baseline	Mid- intervention	Post- intervention
PI <sub>max</sub> at RV (cmH <sub>2</sub> O)	77.3 ± 26.5	92.1 ± 25.0*	97.3 ± 23.6* <sup>#†</sup>	83.4 ± 25.7	84.0 ± 21.6	85.8 ± 19.5
PI <sub>max</sub> at RV (% predicted)	91.5 ± 25.9	109.3 ± 21.9*	116.2 ± 23.0* <sup>#†</sup>	96.4 ± 26.7	97.4 ± 23.0	99.5 ± 21.0
PI <sub>max</sub> at FRC (cmH <sub>2</sub> O)	65.5 ± 22.2	$76.3 \pm 20.6*$	$\begin{array}{c} 80.9 \pm \\ 19.8^{* \# \dagger} \end{array}$	68.7 ± 23.7	72.8 ± 19.4	$74.8 \pm 15.9$
PE <sub>max</sub> at TLC (cmH <sub>2</sub> O)	122.5 ± 42.9	$123.6 \pm 54.7$	$130.7\pm45.8$	118.7 ± 37.3	$118.4 \pm 44.6$	$123.0\pm41.6$

Table 2. Baseline, mid- and post-intervention values for respiratory muscle strength.

Data presented as mean±SD. PI<sub>max</sub>, maximal inspiratory pressure; RV, residual volume; FRC, functional residual capacity; PE<sub>max</sub>, maximal expiratory pressure; TLC, total lung capacity; Breathing discomfort rating based on the 1-10 Borg scale. \* denote significant difference from pre-intervention; \*significant difference from mid-intervention, <sup>†</sup>significant intervention x pre-post interaction.

### 3.3. Exercise capacity

No intervention x pre-post interaction was found for 6MWD (p=0.114) or CWR time (p=0.725). Paired t-tests showed that 6MWD significantly increased by  $18.8 \pm 28.4$  m in the IMT group (from  $588.7 \pm 56.4$  m to  $607.5 \pm 48.0$  m; p=0.042) but did not change within the SHAM-IMT group (from  $600.6 \pm 54.0$  to  $600.1 \pm 54.8$ ; p=0.956; Table 3).

No significant intervention x pre-post x time interaction was observed for dyspnoea (p=0.440) and leg discomfort ratings (p=0.227; supplementary material A; Table 4), or cardiac output (p=0.732), stroke volume (p=0.540), or heart rate (p=0.340) during the CWR test (Table 4). The main symptom that limited exercise tolerance reported by participants was leg discomfort (Table 4).

### 3.4. Thoracoabdominal volume regulation and breathing pattern

Out of the included 23 participants, two participants' (one in each group) OEP data were not analysed due to technical difficulties. Pre- and post-training values for  $V_E$ ,  $V_E/MVV$ , bf, and total  $V_T$  during CWR exercise isotime are shown in Table 4, and as percentages of exercise isotime (QB, 25, 50, 75, and 100%) in Figure 4 for the IMT and SHAM-IMT groups. No significant intervention x pre-post x time interactions were observed for  $V_E$  (p=0.371),  $V_E/MVV$  (p=0.371), bf (p=0.535), or total  $V_T$  (p=0.408).

Compartmental (RCp, RCa, and AB)  $V_T$  at QB and during CWR exercise isotime (25, 50, 75, and 100%) are shown in Figure 5 for the IMT and SHAM-IMT groups. No significant intervention x prepost x time interactions were observed for any compartmental  $V_T$  (RCp: p=0.316; RCa: p=0.847; AB: p=0.181). A significant intervention x pre-post interaction was found for RCa  $V_T$  only (Figure 5c), with the IMT group showing higher values compared to control (p=0.028).

No significant intervention x pre-post x time interactions in end-inspiratory and end-expiratory thoracoabdominal volumes ( $V_{EI}$  and  $V_{EE}$ , respectively) were observed within the total thoracoabdomen or any of its compartments when expressed as absolute values (supplementary material B) or as %FVC (supplementary material C). No significant intervention x pre-post interactions were observed for any of the aforementioned variables or total IC (p=0.487), however, the IMT group exhibited greater post-intervention changes in  $V_{RCa, EI}$  values compared to the control group, that fell short of statistical significance (p=0.059).

The association between changes ( $\Delta$ ) following IMT or SHAM-IMT in rib cage (RC V<sub>T</sub>) and total thoracoabdominal V<sub>T</sub>, along with the association between changes in abdominal (AB V<sub>T</sub>) and total thoracoabdominal V<sub>T</sub>, during CWR exercise are shown in Figure 6. A significant correlation between  $\Delta$ RC V<sub>T</sub> and  $\Delta$ total thoracoabdominal V<sub>T</sub> was observed in the IMT group (r=0.781, p=0.008) but not in the control group (r=0.119, p=0.727). Furthermore, a significant correlation was observed between

 $\Delta AB V_T$  and  $\Delta total thoracoabdominal V_T in the control group (r=0.893, p<0.001) but not in the IMT group (r=0.134, p=0.713).$ 

### 3.5. Physical activity levels

Significant intervention x pre-post interactions were observed for daily steps (p=0.012), movement intensity (VMU/min; p=0.005), sedentary time (p=0.018), and MVPA time (p=0.002; Table 3). These interactions were attributable to significant decreases following training within the SHAM-IMT group only for daily steps (p=0.013), VMU/min (p=0.016), and MVPA time (p<0.001), along with a significant decrease in sedentary time following training within the IMT group only (p=0.042).

### 3.6. Quality of life

No significant intervention x pre-post interactions were observed in any of the 8 dimensions of health (physical function: p=0.527; role physical: p=0.826; bodily pain: p=0.659; general health perception: 0.279; vitality: p=0.646; social function: p=0.307, role emotional: p=0.307; and mental health: p=0.443; Table 3). All dimensions remained unchanged following training in both the IMT and SHAM-IMT groups.

### 3.7. Balance

No significant intervention x pre-post interactions were observed in any of the mini-BEST domains (anticipatory: p=0.401; reactive: p=0.162; sensory: p=0.952; dynamic: p=0.822; Table 3). A significant increase from pre-intervention values following training was observed for reactive postural control within the IMT group (p<0.001) but not within the SHAM-IMT group (p=0.111). All other variables remained unchanged in both groups.

	IMT		SHAM-IMT			
	Baseline	Post-intervention	Baseline	Post-intervention		
	Exercise capacity					
6MWD (m)	$588.7\pm56.4$	$607.5 \pm 48.0*$	$600.6\pm54.0$	$600.1\pm54.8$		
CWR cycling time (s)	$673.7\pm415.2$	$676.8\pm460.7$	$598.9\pm276.1$	$577.7\pm326.0$		
		Physical activity	levels (Actigrap	h)		
Daily steps	$9560\pm3175$	$9847 \pm 4262^\dagger$	$11942\pm2819$	$9128 \pm 3678*$		
VMU/min	$732.3 \pm 146.6$	$781.7\pm205.3^\dagger$	$808.7 \pm 138.8$	$759.1 \pm 114.3*$		
Sedentary (min/day)	$462.8\pm35.3$	$434.8\pm31.6^{*\dagger}$	$426.4\pm60.6$	$454.2\pm69.2$		
Light (min/day)	$266.2\pm56.2$	$245.7\pm59.3$	$247.2\pm64.6$	$239.5 \pm 78.6$		
MVPA (min/day)	$47.1\pm30.9$	$50.5\pm40.0^{\dagger}$	$72.1\pm24.8$	$41.0\pm25.0*$		
	Quality of life (SF-36)					
Physical function	$90.5\pm8.5$	92.3 ± 5.2	$93.3\pm6.9$	$93.3\pm6.5$		
Role physical	$95.5\pm15.1$	95.5 ± 15.1	$93.8 \pm 15.5$	$95.8 \pm 13.3$		
Bodily pain	$87.7 \pm 16.6$	$80.7 \pm 26.7$	$86.9 \pm 14.5$	$83.1 \pm 11.7$		
General health perception	$76.4\pm8.7$	$74.5\pm10.1$	$74.6\pm9.9$	$75.8\pm9.0$		
Vitality	$70.9\pm9.7$	$70.0 \pm 7.4$	$65.8\pm9.7$	$66.7\pm8.1$		
Social function	98.9 ± 3.8	$95.5 \pm 8.4$	$93.7 \pm 12.5$	$93.8 \pm 11.3$		
Role emotional	$93.9\pm20.1$	$100.0 \pm 0$	$97.2\pm9.6$	$97.2\pm9.6$		
Mental health	$78.2\pm7.0$	77.5 ± 7.6	$76.3\pm8.8$	$73.7\pm10.2$		
	Balance (mini-BEST)					
Anticipatory	$5.1 \pm 0.7$	$5.4 \pm 0.5$	$5.3\pm0.9$	$5.3\pm0.8$		
Reactive	$4.3 \pm 0.8$	$5.5 \pm 0.7*$	$4.0\pm4.6$	$4.6\pm1.8$		
Sensory	$5.8 \pm 0.4$	$5.9\pm0.3$	$5.9\pm0.3$	$6.0\pm0.0$		
Dynamic	$9.4 \pm 0.7$	$9.2 \pm 0.6$	$9.0 \pm 0.9$	$8.9 \pm 1.1$		

**Table 3.** Baseline and post-intervention values for exercise capacity, central haemodynamics, physical activity, quality of life, and balance variables.

Data presented as mean±SD. 6MWD, six-minute walk distance; CO, cardiac output; CWR, constant work rate; HR, heart rate; MVPA, moderate to vigorous physical activity; SV, stroke volume; VMU/min, vector magnitude units per minute; \*denote significant difference from pre-intervention; <sup>†</sup>significant intervention x pre-post interaction.

	IMT		SHAM-IMT	
	Baseline	Post-intervention	Baseline	Post-intervention
Work rate (W)	$85.4\pm21.1$		$90.6\pm22.7$	
Reason for termination (n [%])				
Dyspnoea	0 (0)	1 (9)	0 (0)	0 (0)
Leg discomfort	8 (73)	7 (64)	9 (75)	10 (83)
Combination	3 (27)	3 (27)	3 (25)	2 (17)
Other	0 (0)	0 (0)	0 (0)	0 (0)
Exercise time at isotime (s)	$620\pm396$		$522\pm252$	X
Dyspnoea (Borg units)	$5.6 \pm 1.6$	$5.1 \pm 1.2$	$4.9\pm1.7$	$4.4 \pm 1.2$
Leg discomfort (Borg units)	$6.9 \pm 1.8$	$5.8\pm2.0^{\ast}$	$6.0 \pm 1.6$	5.7 ± 1.3
CO (L/min)	$16.4\pm2.9$	$16.4\pm3.6$	$17.8\pm3.1$	$19.1\pm4.2$
SV (ml/min)	$113.7\pm26.6$	$109.8 \pm 18.3$	$132.8\pm24.3$	$145.8\pm43.6$
HR (beats/min)	$145 \pm 11$	$149 \pm 12$	$135 \pm 14$	$134\pm13$
V <sub>E</sub> (L/min)	$63.3\pm20.3$	$61.2\pm17.5$	$66.2\pm22.1$	$64.1 \pm 18.5$
V <sub>E</sub> /MVV (%)	$54.8 \pm 10.2$	$53.5 \pm 7.7$	$56.0\pm12.6$	$56.8 \pm 12.3$
bf (breaths/min)	$31.6\pm5.2$	$31.0\pm5.7$	$32.4\pm6.5$	$32.4\pm4.0$
Total V <sub>T</sub> (L)	$2.00\pm0.44$	$1.98 \pm 0.40$	$2.07\pm0.61$	$2.02\pm0.61$
$RCp V_T(L)$	$0.57\pm0.22$	$0.57\pm0.20$	$0.64\pm0.19$	$0.61\pm0.21$
RCa $V_T(L)$	$0.28\pm0.09$	$0.32\pm0.11$	$0.35\pm0.14$	$0.32\pm0.08$
AB $V_T(L)$	$1.15\pm0.45$	$1.09 \pm 0.40$	1.08 ±0.43	$1.09\pm0.47$

Table 4. Measurements at constant work rate exercise isotime.

Data presented as mean $\pm$ SD. AB, abdomen; bf, breathing frequency; CO, cardiac output; HR, heart rate; MVV, maximal voluntary ventilation; RCa, abdominal rib cage; RCp, pulmonary rib cage; SV, stroke volume; V<sub>E</sub>, minute ventilation; V<sub>T</sub>, tidal volume; \*denote significant difference from pre-intervention.

# 4.0. Discussion

The main findings of this study were that, in healthy older adults, IMT resulted in significantly greater improvements in inspiratory muscle strength compared to SHAM-IMT. Furthermore, breathing discomfort was reduced during an IMT bout sustained at 50%  $PI_{max}$  at 4 and 8 weeks of training in the IMT group only. These improvements in the IMT group did not translate into significantly different changes in exercise capacity or dyspnoea during cycling between groups. No significant changes were observed following training in total thoracoabdominal volume regulation during CWR exercise;

however, greater changes in total  $V_T$  expansion were associated with greater changes in the rib cage  $V_T$  within the IMT group only. This is indicative of greater inspiratory rib cage expansion and greater diaphragmatic descent post-IMT. Furthermore, IMT resulted in a significant reduction in sedentary time; however, all other changes in physical activity variables were due to changes within the SHAM-IMT group only. Reactive postural control was significantly improved within the IMT group, whereas quality of life remained unchanged.

### 4.1. Inspiratory muscle strength

Improvements in inspiratory muscle strength (maximal inspiratory pressure;  $PI_{max}$ ) observed in this study following IMT (by ~20cmH<sub>2</sub>O) are in line with previous studies in healthy older adults (Manifield et al., 2021). The mechanisms explaining these improvements are likely increased inspiratory muscle strength, power output and speed of shortening (Romer & McConnell, 2003), and/or hypertrophy of inspiratory muscles (Mills et al., 2015; Souza et al., 2014). Furthermore, this study observed significantly reduced breathing discomfort following IMT during a bout of inspiratory muscle effort equivalent to 50% of  $PI_{max}$  compared to the SHAM-IMT group. This reduced effort perception may be explained by a combination of underlying mechanisms relating to structural and functional adaptations of the inspiratory muscles following IMT, including: 1) increased diaphragm thickness (Enright et al., 2006; Souza et al., 2014), 2) increased proportion of type I muscle fibres (Ramírez-Sarmiento et al., 2002), 3) increased oxidative capacity (Brown et al., 2012; Turner et al., 2012), 4) increased force-generating capacity (Romer et al., 2002), and/or 5) desensitised sensory input from the inspiratory muscles to the brain (El-Manshawi et al., 1986; Romer et al., 2002).

As no significant increases in inspiratory muscle strength variables were observed within the SHAM-IMT group, it is likely that the increased values within the IMT group can be explained by genuine increases in strength and not a placebo effect or improved technique of manoeuvres. Interestingly, the SHAM-IMT group showed a greater magnitude of change in  $PI_{max}$  when measured from FRC compared to RV. This is in contrast to previous studies which have shown increases in  $PI_{max}$  after IMT via

pressure-threshold loading predominately at lung volumes at which training was performed (Tzelepis et al., 1994; Van Hollebeke et al., 2020). Due to the length-tension of the respiratory muscles, the load trained at by the SHAM-IMT group (15%  $PI_{max}$  at RV) would be higher relative to  $PI_{max}$  at FRC (where there is less force-generating capacity of the inspiratory muscles (Rahn et al., 1946; Sheel & Romer, 2011)). This low intensity of training has been insufficient to elicit significant effect on  $PI_{max}$  at RV (Volianitis et al., 2001), however, due to the aforementioned mechanisms, it may be more likely to elicit greater, albeit non-significant, improvements in  $PI_{max}$  at higher lung volumes (i.e., FRC).

### 4.2. Exercise capacity

An increased 6MWD of 18.8m was observed in the IMT group following the 8-week intervention compared to -0.5m in the SHAM-IMT group. This change, however, did not reach statistical significance (p=0.114) and falls just short of the minimum clinically important difference (MCID) of 20m in this population (Perera et al., 2006). This is in contrast to previous literature exploring the effects of IMT on 6MWD in older adults summarised by our group in a previous meta-analysis (Manifield et al., 2021), which showed a small MCID (albeit non-significant) improvement of 24.7m.

No significant change in 6MWD was also observed in Mills et al. (2015) who suggested that this was due to the higher predicted baseline values (102-103%), calculated from previously published prediction models (Troosters et al., 1999), compared to the lower values (~90%) of studies that did observe significant improvements such as Huang et al. (2011). In the present study, the participants also had high predicted baseline values (~98%) which could explain the lack of significant change in this outcome measure.

No significant change in CWR exercise endurance time following IMT was observed within this study. To the authors knowledge, this is the first study to investigate the effects of IMT on sub-maximal cycling exercise tolerance in healthy older adults, however, these findings contrast with previous literature reporting increased endurance exercise time in COPD (Langer et al., 2018; Petrovic et al., 2012) and healthy younger individuals (Bailey et al., 2010; Edwards & Cooke, 2004). As there was a

relatively low ventilatory load ( $V_E/MVV$ : ~55%) at peak exercise and dyspnoea was not the main limiting factor (peak dyspnoea scores: ~5), it is unlikely that there were significant respiratory muscle load-capacity disturbances during exercise in this population. This may possibly explain why the significant improvements in PI<sub>max</sub> did not translate into improved cycling endurance time.

### 4.3. Breathing pattern and thoracoabdominal volume regulation

In the present study, no significant changes were observed in  $V_E$  during CWR exercise following IMT or SHAM-IMT. The findings presented for breathing pattern and thoracoabdominal volume regulation can, therefore, be presented as fractions of exercise isotime and relative to nearly identical minute ventilation (ventilatory requirement) pre- and post-training (i.e., isoventilation). Previous studies in COPD patients have reported changes in breathing pattern, specifically decreased breathing frequency and increased V<sub>T</sub>, during exercise following respiratory muscle training interventions (Charususin et al., 2016; Koppers et al., 2006; Petrovic et al., 2012; Wanke et al., 1994). The advantage of such modified breathing pattern, reported by Koppers et al. (2006), includes decreased ratio of dead space to V<sub>T</sub>, leading to an increase in effective alveolar ventilation, reduced work of breathing (Nici, 2000), and 3) delayed respiratory muscle fatigue (Larson & Kim, 1987). In the present study, no significant change in breathing pattern was observed in healthy older adults. This is in line with the studies conducted by Langer et al. (2018) and Ramsook et al. (2017) who did not observe changes in breathing pattern or operational lung volumes in COPD patients or healthy young adults respectively.

One potential reason for the lack of breathing pattern change in the present study is the nearly-identical ventilatory requirement observed pre- and post-training in both groups. This is due to ventilation being predominately dictated by the metabolic demand of the principal muscles of cycling (i.e., the lower limb muscles) during the CWR test, which were not trained over the course of the intervention and therefore, IMT did not elicit any metabolic adaptations within these muscles. Furthermore, no evidence of dynamic hyperinflation was observed over the course of the CWR at baseline in our participants (see

supplementary figures), suggesting an already optimised breathing pattern during exercise compared to COPD populations (Petrovic et al., 2012).

The regression analysis within the current study (Figure 6) implies that any perturbations in total  $V_T$ during sub-maximal exercise following training were associated with increased rib cage volume and not increased abdominal volume in the IMT group. Previous studies that have utilised measures of inspiratory muscle electromyography (EMG) have observed significantly greater activation of extradiaphragmatic muscles, such as the sternocleidomastoid, during  $PI_{max}$  manoeuvres post-IMT compared to a control group (Ando et al., 2020). As the estimated shear modulus of the diaphragm increased in both IMT and control groups within the study by Ando et al. (2020), the authors concluded that the increased EMG amplitudes, and thus improved neural factors, of the sternocleidomastoid could be one of the main mechanisms behind the greater improvement in PI<sub>max</sub> observed within the IMT group. Furthermore, no changes in the EMG amplitude of the intercostal muscles were observed following IMT, with the authors suggesting that this may be either due to the length of the training programme (6 weeks) or the signal-to-noise ratio of measurements (Ando et al., 2020). Despite these findings, previous studies have reported no significant changes in extradiaphragmatic contribution during exercise following IMT in healthy young men (Ramsook et al., 2017). Furthermore, IMT has been found to reduce diaphragm activation (EMGdi) expressed relative to its maximum (EMGdi/EMGdi<sub>max</sub>) in COPD patients (Langer et al., 2018). No significant changes in the respiratory muscle recruitment index were reported however, leading the authors to conclude that the reduced EMGdi amplitude was not related to increased rib cage and accessory inspiratory muscle contribution resulting in diaphragm sparing (Langer et al., 2018).

The use of OEP to determine compartmental thoracoabdominal volume regulation following IMT has previously been reported at rest (Hoffman et al., 2021; Medeiros et al., 2019). The first of these studies (Medeiros et al., 2019) was conducted in chronic kidney disease patients, and involved an experimental group training at 50%  $PI_{max}$  for 8 weeks, with a control (sham) group training at the minimum device load (5 cmH<sub>2</sub>O). The authors observed a significant increase of 0.1 L in pulmonary rib cage volume of the experimental group during inspiratory capacity manoeuvres following IMT compared to the control

group. No difference, however, was observed during quiet breathing between groups. It was concluded that IMT was adequate to modify the volume of the chest cavity by directing the volume to the pulmonary rib cage compartment, altering the naturally restrictive pattern in chronic kidney disease patients (Medeiros et al., 2019). In the present study, a significant intervention x pre-post interaction was observed in the abdominal rib cage compartment only when resting and all exercise time-points were combined, suggesting greater mobility of the lower rib cage, and potentially increased diaphragmatic descent. The significant association between changes in rib cage volume and changes in total  $V_T$  suggest concurrent training adaptations of both the rib cage muscles and the diaphragm.

## 4.4. Physical activity, balance, and quality of life

Sedentary time was reduced following IMT compared to the SHAM-IMT group, with all other postintervention changes in physical activity outcomes (daily steps, movement intensity, and MVPA) being attributed to decreased values within the SHAM-IMT group. Research into the effect of IMT on physical activity levels in healthy older adults remains inconclusive. Aznar-Lain et al. (2007) reported an increase (~60%) in the levels of moderate to vigorous physical activity following IMT in in older adults, alongside a decrease (~38%) within the control group. No other changes in physical activity measures, such as sedentary time, were observed, leading the authors to suggest that IMT may not increase the total quantity of physical activity but perhaps increase the quality (or intensity) of activities performed (Aznar-Lain et al., 2007). Furthermore, when measured via self-reported questionnaires (physical activity scale for the elderly), Mills et al. (2015) did not observe any changes in physical activity levels following IMT.

The improvement in reactive postural control following IMT in healthy older adults observed in the present study is supported by previous research that reported the greatest improvements within this domain of the mini-BEST measures (Ferraro et al., 2019). An increase in anticipatory postural adjustments, sensory orientation, and dynamic balance during gait was also reported in the study by Ferraro et al. (2019), however, this was not observed in the present study. The activation of the

diaphragm during rapid limb movements (which challenges trunk stability) has previously been reported (Hodges & Gandevia, 2000a). This diaphragm activation assists with the mechanical stabilisation of the spine due to increased intra-abdominal pressure (Hodges & Gandevia, 2000b). Increased strength of the diaphragm (reflected by an increased  $PI_{max}$ ) therefore, likely had a positive effect on reactive postural control (Ferraro et al., 2019).

No significant change in quality of life was observed in the present study. This is in contrast to the findings of (Huang et al., 2011) who found that a 6-week IMT intervention significantly improved five domains of the SF-36 (physical function, bodily pain, general health perception, vitality, and social function). This may be due to a ceiling effect within the present study as baseline scores were higher than those reported by Huang et al. (2011) in most of these domains (physical function: 90.5 vs 83.3; bodily pain: 87.7 vs 76.0; general health perception: 76.4 vs 70.2; and social function: 98.9 vs 75.0).

## 4.5. Study limitations and future directions

The relatively small sample size in the present study highlights the need for larger studies to be conducted in order to confirm the present findings. The difference in  $PI_{max}$  following IMT in older adults reported by Watsford and Murphy (2008) was used within the sample size calculation to consider changes in thoracoabdominal volume regulation arising due to improved inspiratory muscle strength, however, due to one drop-out, this study may have been underpowered.

The lack of an incremental cardiopulmonary exercise test meant that we were unable to measure peak work rate. The use of previously published equations to predict peak work rate (and subsequently 75% of this for the constant work rate test) may have introduced some degree of error. As cycling is highly dependent on leg effort, the endurance shuttle walk test (Revill et al., 1999) may have been a more appropriate test to assess the effects of IMT on breathing effort during exercise in this population.

Simultaneous measurements of EMGdi via multipair oesophageal catheters, as outlined previously (Jolley et al., 2009), or EMG of extradiaphragm muscles via surface EMG, were unavailable for the present study, meaning that respiratory muscle activation patterns could only be indirectly assessed via

OEP. These measurements would have provided the opportunity to investigate  $EMGdi/EMGdi_{max}$  as an index of neural respiratory drive, which has previously been found to decrease following IMT in COPD patients (Langer et al., 2018).

## 5.0. Conclusion

This study has provided more evidence that IMT can significantly improve inspiratory muscle strength (as shown in the meta-analysis published by our group; Manifield et al., 2021), but this did not translate into improved exercise capacity in this population. Furthermore, this study observed significantly reduced breathing discomfort during inspiratory muscle effort, which, along with the increased respiratory muscle strength suggests enduring physiological adaptations with IMT. In terms of thoracoabdominal volume regulation, an increased rib cage and diaphragmatic contribution to  $V_T$  expansion during exercise was observed, suggesting a less restrictive effect on thoracic expansion, and increased diaphragmatic power generation.

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### **Declarations of interest**

None.

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**Figure 1.** Average weekly training session intensity (expressed as percentage baseline  $PI_{max}$ ; (*a*) and breathing discomfort (expressed as Borg scale ratings; (*b*) within the IMT (*open symbols*) and SHAM-IMT groups (*closed symbols*). Data presented as mean  $\pm$  SD.



**Figure 2.** Breathing discomfort (Borg ratings) measured at baseline (0 weeks), mid-intervention (4-weeks), and post-intervention (8-weeks) for the IMT (a) and SHAM-IMT groups (b). \* denote significant difference from pre-intervention.



**Figure 3.** The association between baseline maximal inspiratory pressure ( $PI_{max}$ ) and change ( $\Delta$ )  $PI_{max}$  within the IMT group expressed as absolute values (cmH<sub>2</sub>O; [a]) and percentage predicted (% pred; [b]).



**Figure 4.** Minute ventilation ( $V_E$ ; *a and b*), breathing frequency (bf; *c and d*), and total tidal volume ( $V_T$ ; *e and f*) at quiet breathing (QB) and during constant work rate exercise before (closed symbols) and after (open symbols) IMT in the experimental group (*left panels*) and SHAM-IMT in the control group (*right panels*). Data presented as mean ± SEM.



**Figure 5.** Compartmental (pulmonary rib cage [RCp], *a and b*; abdominal rib cage [RCa], *c and d*; and abdomen [AB], *e and f*) thoracoabdominal tidal volumes ( $V_T$ ) at quiet breathing (QB) and during constant work rate exercise before (closed symbols) and after (open symbols) IMT in the experimental group (*left panels*) and SHAM-IMT in the control group (*right panels*). Data presented as mean ± SEM.



**Figure 6.** The association between post-intervention/sham changes ( $\Delta$ ) in rib cage (RC) tidal volume (V<sub>T</sub>) and total thoracoabdominal V<sub>T</sub> (*a and b*), and between abdomen (AB) V<sub>T</sub> and total thoracoabdominal V<sub>T</sub> (*c and d*) within the IMT (*left panels*) and SHAM-IMT (*right panels*) groups. Each data point represents the combined average values over exercise isotime (25, 50, 75, and 100%) for each participant.

## Highlights

- IMT improves inspiratory muscle strength and reduces breathing discomfort during inspiratory loading
- This did not translate into significantly improved exercise capacity compared to SHAM-IMT
- During constant-load cycling, IMT induces greater inspiratory rib cage expansion