



UNIVERSITY OF
GLOUCESTERSHIRE

This is a peer-reviewed, final published version of the following document and is licensed under Creative Commons: Attribution-Noncommercial-No Derivative Works 4.0 license:

Turner, Louise A ORCID logoORCID: <https://orcid.org/0000-0002-0153-7075> and Tiller, Nicholas B. (2023) Lung function responses to cold water ingestion: A randomised controlled crossover trial. *Respiratory Physiology and Neurobiology*, 318. Art 104161. doi:10.1016/j.resp.2023.104161

Official URL: <http://doi.org/10.1016/j.resp.2023.104161>

DOI: <http://dx.doi.org/10.1016/j.resp.2023.104161>

EPrint URI: <https://eprints.glos.ac.uk/id/eprint/13220>

Disclaimer

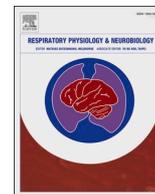
The University of Gloucestershire has obtained warranties from all depositors as to their title in the material deposited and as to their right to deposit such material.

The University of Gloucestershire makes no representation or warranties of commercial utility, title, or fitness for a particular purpose or any other warranty, express or implied in respect of any material deposited.

The University of Gloucestershire makes no representation that the use of the materials will not infringe any patent, copyright, trademark or other property or proprietary rights.

The University of Gloucestershire accepts no liability for any infringement of intellectual property rights in any material deposited but will remove such material from public view pending investigation in the event of an allegation of any such infringement.

PLEASE SCROLL DOWN FOR TEXT.



Lung function responses to cold water ingestion: A randomised controlled crossover trial

Louise A. Turner^{a,*}, Nicholas B. Tiller^b

^a School of Sport and Exercise, University of Gloucestershire, Gloucester, UK

^b Institute of Respiratory Medicine and Exercise Physiology, The Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center, Torrance, CA, USA

ARTICLE INFO

Edited by M. Dutschmann

Keywords:

Lung function
Pulmonary function
Cold drink
Beverage

ABSTRACT

This study tested the hypothesis that cold water ingestion would reduce lung function and thereby confound its measurement in a way that is mediated by both temperature and volume. In a randomised crossover trial, 10 healthy adults performed spirometry before and 5, 10, 15, and 30-minutes after consuming one-of-four drinks: 500 mL or 1000 mL refrigerated water (~2 °C); identical water volumes at ambient temperature (~18 °C). Ingesting 1000 mL cold water significantly reduced forced vital capacity (FVC) for at least 10 min (mean difference =0.28 L, $p < 0.05$, $d=1.19$) and forced expiratory volume in 1 s (FEV₁) for at least 15 min (0.20–0.30 L, $p < 0.05$, $d=1.01$). Ingesting 500 mL cold water reduced FEV₁ for 5 min (0.09 L, $p < 0.05$, $d=1.05$). Room-temperature water had no influence on lung function. To avoid confounding the measurement of lung function, we conclude that individuals should avoid drinking cold water, especially in large volumes, immediately prior to a given test.

1. Introduction

Spirometry is a pulmonary function test (PFT) commonly used for diagnosing and monitoring respiratory disorders (Graham et al., 2019; Miller et al., 2005). The test examines the competency with which patients inspire/expire air as a function of time by requiring them to perform forced vital capacity (FVC) maneuvers into a pneumotachograph, or other such flow/volume-measuring device. A variety of factors, external to the device, may confound the measurement including exercise (Price et al., 2013; Weiler et al., 2007), cigarette smoking (Unverdorben et al., 2010), and restrictive clothing (MacHose and Peper, 1991). Failing to account for these factors may lead to suboptimal and/or non-repeatable results. For instance, during spirometry, values for FVC and FEV₁ must be within 150 mL to be considered reproducible (Sylvester et al., 2020). In patients with obstructive lung disease, values that deviate from baseline by 100–140 mL, or 5–10 %, represent a clinically meaningful change (Jones et al., 2011). And exercise-induced bronchoconstriction (EIB) is diagnosed on the basis of a ≥ 10 % decline in FEV₁ following a bronchial provocation test (Parsons et al., 2013), such that a post-test decrease of 9 % is not considered abnormal. As such, the margin for error is slight, and even small perturbations in lung function may confound its clinical assessment. For these reasons, the

ATS/ERS taskforce recommend that patients wear loose-fitting clothing and abstain from vigorous exercise and smoking/vaping for 1 h before an assessment (Graham et al., 2019).

Limited data indicate that food and/or fluid ingestion may also confound the PFT measurement, via two potential mechanisms. First, abdominal distention has been shown to increase sympathetic outflow (Rossi et al., 1998), ribcage volumes, and intrathoracic pressures (Gilroy et al., 1985; Rossi et al., 1998). The degree of abdominal distention is also proportional to the volume of ingested substrate (Burri et al., 2013). Nevertheless, in healthy subjects, we observed significant decreases in FVC (2.6 ± 3.6 %) and FEV₁ (2.9 ± 3.1 %) following a large fluid bolus, but with no such changes following a volume-matched food bolus (Turner et al., 2015). As such, while the findings of our previous study suggest that the pulmonary function response to fluid ingestion may be volume-dependent, the mechanism by which fluid ingestion attenuates lung function is not exclusively dependent on fluid volume and gastric load.

Second, data show that fluid ingestion may have temperature-mediated effects on lung function. Patients with airway hyper-responsiveness exhibited significant lung function declines after ingesting small amounts of ice water (250 mL, 0–4 °C), but with no changes after ingesting warm water (Lin and Hsieh, 1997). Although the

* Corresponding author.

E-mail address: lturner14@glos.ac.uk (L.A. Turner).

<https://doi.org/10.1016/j.resp.2023.104161>

Received 3 July 2023; Received in revised form 31 August 2023; Accepted 10 September 2023

Available online 12 September 2023

1569-9048/© 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

precise mechanism for this response is not yet known, it is plausible that ingesting cold water may cool the upper airway, causing pro-inflammatory bronchoconstriction in a similar manner to breathing cold air (Cockcroft and Davis, 2006). Indeed, the trachea is in close anatomical proximity to the upper-gastrointestinal tract (the laryngopharynx and esophagus), and a decrease in airway temperature during an exercise challenge results in a decrease in esophageal temperature (Deal et al., 1979). The reciprocal may also be true, that a cold-water-mediated cooling of the oesophagus results in cooling of the airway (Lin and Hsieh, 1997), with the potential to evoke an obstructive pattern.

It is plausible that fluid ingestion may reduce lung function by an amount that exceeds the minimal clinically important difference, and yet, the phenomenon has not been explored empirically. Moreover, the testing guidelines offer no guidance in this regard, other than recommending that “Drinking water should be available.” (Graham et al., 2019).

This study tested the hypothesis that fluid ingestion would diminish lung function in healthy subjects in both a volume- and temperature-mediated fashion. Such data may have implications for the standardization of lung function testing, the diagnosis of obstructive respiratory conditions (e.g., EIB), and for exercising individuals who regularly consume large fluid boluses before, during, and after exercise.

2. Methods

2.1. Participants

Ten healthy, recreationally-active adults (6 male/4 female) volunteered for the study (mean \pm SD age = 29 \pm 4 y; stature = 177 \pm 8 cm; mass = 72.2 \pm 11.9 kg; BMI = 23.1 \pm 3.3 kg·m²). Participants were non-smokers and free from known cardiorespiratory or metabolic disorders as determined by a self-reported medical questionnaire. Inclusion criteria were age between 18 and 40 y, BMI between 18.5 and 29.9 kg·m², and spirometry in the normal range (Quanjer et al., 2012). In the 24 h before each trial, participants recorded their evening meal, replicated their evening meal from the previous session, and abstained from strenuous exercise, alcohol, and caffeine. All female participants were tested during the early follicular phase of the menstrual cycle (3 – 6 d after day 1 of menses). Following approval from the institution Research Ethics Committee, each participant provided written, informed consent. Procedures were conducted in accordance with the Declaration of Helsinki.

2.2. Study design

This was a randomized, controlled, crossover trial that compared the effects of various fluid boluses on spirometric output. Participants visited the laboratory on five occasions, each separated by at least 2 d. Visit one allowed participants to become accustomed to procedures and perform baseline spirometry. Visits two through five were experimental trials wherein participants performed spirometry immediately before, and 5, 10, 15, and 30-min after ingesting one-of-four liquid drinks: (1) 500 mL refrigerated water at \sim 2 °C (Cold500); (2) 1000 mL refrigerated water at \sim 2 °C (Cold1000); (3) 500 mL ambient temperature water at \sim 18 °C (Ambient500); and (4) 1000 mL room-temperature water at \sim 18 °C (Ambient1000). Each test commenced at 0800 \pm 1 hr and was conducted under similar laboratory conditions. Subjects were given 10 min to fully consume each drink.

2.3. Pulmonary function

2.3.1. Spirometry

Using a calibrated, computerized spirometer with reusable turbine (MIR Minispiro® spirometer and Winspiro Pro® software, Roma, Italy, USA), each participant, with the nose occluded, performed between

three and eight spirometry tests for the determination of forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁), the ratio of FEV₁ to FVC (FEV₁/FVC), peak expiratory flow (PEF), and forced expiratory flow during 25–75 % of FVC (FEF_{25–75}). Maneuvers were performed according to the ATS/ERS guidelines (Miller et al., 2005), i.e., seated, in an upright position, and with verbal encouragement and feedback given to achieve correct and consistent efforts. The three largest values within 100 mL were recorded at each time-point, and the manoeuvre with the largest combined FVC and FEV₁ was used in the analysis. Changes in spirometric indices from baseline were expressed in absolute terms. FVC and FEV₁ were also expressed as the percentage change from baseline owing to the clinical importance of such values in diagnosing EIB (Parsons et al., 2013). To quantify the severity of airway obstruction during the 30 min post-ingestion period, FVC and FEV₁ were additionally assessed using the total area under the curve of the percentage change with time (AUC_{0–30}) (Hallstrand, 2014).

2.4. Sample size calculation

Using data from Turner et al. (2015) which assessed the change in FEV₁ before and after ingesting a large water bolus ($n = 20$, $d = 0.93$), an *a priori* power analysis was performed using G*Power version 3.1.9.6. With a Type 1 error rate of 5 % ($\alpha = 0.05$) and a statistical power of 0.80, eight participants were required to correctly detect a large and significant effect. Ten participants were recruited presently to account for possible attrition.

2.5. Statistical analysis

Jamovi statistical software (jamovi, Version 2.3) was used for all statistical analyses. Between-trial reproducibility of baseline measures was assessed via intraclass correlations (ICC), standard error of measurement (SEM), and coefficient of variation (CV). All data were normally distributed, as determined by the Shapiro-Wilk test. A two-way (condition \times time) repeated-measures ANOVA was used to assess changes in lung function (FVC, FEV₁, FEV₁/FVC, PEF, and FEF_{25–75}) within (pre- to post) and between conditions (Cold500, Cold1000, Ambient500, Ambient1000). Differences in AUC_{0–30}, and percentage change in FEV₁ and FVC between conditions were assessed using a one-way repeated measures ANOVA. Planned comparisons using Bonferroni correction were used to follow up significant main effects and interactions (post-ingestion versus baseline). Absolute values are reported as mean \pm SD and follow-up analyses are shown as mean difference with 95 % confidence intervals. Alpha level was set as < 0.05 . Effect size (Cohen’s d) was used to quantify the magnitude of the differences where $< 0.2 =$ small, $0.5 =$ medium, and $0.8 =$ large effect (Cohen, 1977).

3. Results

3.1. Spirometry

Baseline values. Baseline spirometry for the cohort is shown in Table 1. Values were within the normal range (Quanjer et al., 2012). There were no systematic differences in baseline lung function among

Table 1
Baseline pulmonary function.

| | Mean \pm SD | %Predicted | Range |
|---|-----------------|--------------|------------|
| FVC (L) | 4.97 \pm 0.96 | 98 \pm 9 | 3.65–6.60 |
| FEV ₁ (L) | 4.17 \pm 0.82 | 98 \pm 9 | 3.27–5.98 |
| FEV ₁ /FVC (%) | 84.2 \pm 4.6 | 100 \pm 4 | 78.6–92.3 |
| PEF (L·s ⁻¹) | 9.90 \pm 2.37 | 90 \pm 14 | 6.83–14.44 |
| FEF _{25–75} % (L·s ⁻¹) | 4.38 \pm 1.01 | 104 \pm 10 | 3.23–6.92 |

Means \pm SD, $n = 10$. FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 s; PEF = peak expiratory flow; FEF_{25–75} % = forced expiratory flow at 25–75 % of FVC.

the four experimental conditions (Table 2). Using baseline data from each visit, we showed between-trial reproducibility that is deemed acceptable for clinical measures (i.e., ICC >0.9 [(Portney and Watkins, 2009) and CV <5 % (Sylvester et al., 2020): FVC (ICC = 0.983; SEM = 0.121; CV = 2.6 %), FEV₁ (ICC = 0.983; SEM = 0.102; CV = 2.5 %), FEV₁/FVC (ICC = 0.911; SEM = 1.549; CV = 1.9 %), PEF (ICC = 0.963; SEM = 0.464; CV = 4.7 %) and FEF₂₅₋₇₅ % (ICC = 0.962; SEM = 0.203; CV = 5.1 %).

Forced vital capacity (FVC). Changes in FVC following ingestion of each drink are shown in Table 2. There was a significant main effect for time and a significant interaction (condition × time) effect, but no main effect for condition. Follow-up analyses revealed that, relative to baseline, Cold1000 significantly decreased FVC at 5 min (mean difference [MD] = 0.24 L, 95 % CI 0.00 – 0.39, *p* = 0.02, *d* = 1.15) and 10 min post ingestion (MD = 0.28 L, 95 % CI 0.11 – 0.44, *p* = 0.016, *d* = 1.19) (Fig. 1a). There were no significant changes in lung function following ingestion of Cold500, Ambient500, or Ambient1000. There was no effect of condition on AUC₀₋₃₀ (*p* = 0.066, η^2 = 0.230) or peak percentage change following ingestion (*p* = 0.066, η^2 = 0.230), as shown in Fig. 2a and b.

Forced expiratory volume in 1 s (FEV₁). Changes in FEV₁ following ingestion of each drink are shown in Table 2. There was a significant main effect for time and condition and a significant interaction (condition × time) effect (Table 2). Follow-up analyses revealed that, relative to baseline, Cold1000 significantly decreased FEV₁ at 5 min (MD = 0.30 L, 95 % CI 0.17–0.43, *p* < 0.01, *d* = 1.63), 10 min (MD = 0.28 L, 95 % CI 1.6 – 0.41, *p* < 0.01, *d* = 1.60), and 15 min post ingestion (MD = 0.20 L, 95 % CI 0.07 – 0.32, *p* = 0.028, *d* = 1.105), but not 30 min (MD = 0.19 L, 95 % CI 0.04 – 0.33, *p* = 0.068, *d* = 0.92). Relative to baseline, decreases in FEV₁ were also observed following ingestion of Cold500 at 5 min (MD = 0.09 L, 95 % CI 0.03 – 0.15, *p* = 0.036, *d* = 1.05). No other condition evoked changes in FEV₁ from baseline. A one-way repeated measures ANOVA revealed a significant effect of condition on FEV₁ AUC₀₋₃₀ (*p* = 0.04, η^2 = 0.384) in which Cold1000 was significantly lower than both Cold500 (MD = 93.0, 95 % CI 26.7–159, *p* = 0.044, *d* = 1.00) and Ambient1000 (MD = 76.4, 95 % CI 33.6–119, *p* = 0.012, *d* =

1.28), as shown in Fig. 2c. Following a significant condition effect for peak percentage change in FEV₁, Bonferroni correction revealed that Cold1000 (−8 ± 4 %) was significantly lower than Ambient1000 (−4 ± 4 %) (MD = 3.83, 95 % CI 1.55 – 6.12, *p* = 0.024, *d* = 1.20) and Ambient500 (−3 ± 3 %) (MD = −5.08, 95 % CI 1.69 – 8.47, *p* = 0.048, *d* = 1.07) as shown in Fig. 2d.

FEV₁/FVC. Changes in FEV₁/FVC following the ingestion of cold- and room-temperature water are shown in Table 2 and Fig. 1c. There was no significant interaction or main effect for trial or time on FEV₁/FVC.

Peak expiratory flow (PEF). Changes in PEF following ingestion of each drink are shown in Table 2. There were main effects for condition and time but no interaction effect. Follow up analysis revealed a significant decrease in PEF following the ingestion of a drink (main effect of time) compared to baseline at 5 min (MD = 0.50 L·s^{−1}, 95 % CI 0.31 – 0.69, *p* = 0.016, *d* = 1.83), 10 min (MD = 0.41 L·s^{−1}, 95 % CI 0.18 – 0.64, *p* = 0.024, *d* = 0.57), and 15 min (MD = 0.12 L·s^{−1}, 95 % CI 0.12 – 0.64, *p* = 0.048, *d* = 1.05), but not 30 min (MD = 0.24 L·s^{−1}, 95 % CI 0.11 – 0.60, *p* = 0.068 *d* = 0.19). Follow up analyses of the main effect for condition revealed that Cold1000 significantly decreased PEF compared to Ambient500 (*p* = 0.032) and Cold500 (*p* = 0.12).

Forced expiratory flow during 25–75 % of FVC (FEF₂₅₋₇₅). Changes in FEF₂₅₋₇₅ following ingestion of each drink are shown in Table 2 and Fig. 1d. There was no significant main effect for time or significant interaction. There was a main effect of condition. Follow-up analyses revealed no significant differences among trials.

4. Discussion

This study investigated the independent effects of fluid volume- and temperature on spirometric indices of lung function in healthy adults. We made several observations: i) ingesting cold water significantly reduced expiratory capacities and flows below baseline to an extent that is considered clinically meaningful; ii) the cold-mediated deterioration in lung function was further impaired and sustained for at least 10–15 min with a large fluid volume; iii) no equivalent observations were made following the ingestion of ambient-temperature water. Our

Table 2
Lung function following the ingestion of 500 and 1000 mL, cold- and ambient -temperature water.

| Drink Condition | | Time | FVC (L) | FEV ₁ (L) | FEV ₁ /FVC (%) | PEF (L·s ^{−1}) | FEF ₂₅₋₇₅ (L·s ^{−1}) | |
|-------------------------|--------------------|---------------------------|--------------------|----------------------|---------------------------|--------------------------|---|-------|
| Volume | Temperature | | | | | | | |
| 500 mL | Cold (2 °C) | Baseline | 4.81 ± 0.98 | 4.07 ± 0.81 | 84.9 ± 6.1 | 10.10 ± 2.70 | 4.22 ± 1.03 | |
| | | 5 min | 4.73 ± 0.90 | 3.98 ± 0.79 | 84.2 ± 4.2 | 9.70 ± 2.42 | 4.21 ± 1.06 | |
| | | 10 min | 4.71 ± 0.93 | 4.00 ± 0.80 | 84.9 ± 3.9 | 9.79 ± 2.36 | 4.26 ± 1.01 | |
| | | 15 min | 4.73 ± 0.96 | 3.98 ± 0.78 | 84.3 ± 4.4 | 9.83 ± 2.55 | 4.11 ± 0.92 | |
| | | 30 min | 4.72 ± 0.88 | 3.97 ± 0.72 | 84.3 ± 3.8 | 9.75 ± 2.27 | 4.18 ± 0.89 | |
| | | Baseline | 4.85 ± 0.89 | 4.08 ± 0.77 | 84.4 ± 4.8 | 10.10 ± 2.55 | 4.31 ± 1.03 | |
| | Ambient (18 °C) | 5 min | 4.87 ± 0.89 | 4.06 ± 0.79 | 83.5 ± 5.6 | 9.44 ± 2.30 | 4.19 ± 1.13 | |
| | | 10 min | 4.82 ± 0.91 | 4.02 ± 0.79 | 83.6 ± 5.1 | 9.72 ± 2.47 | 4.08 ± 0.96 | |
| | | 15 min | 4.78 ± 0.89 | 3.98 ± 0.74 | 83.3 ± 5.6 | 9.55 ± 2.42 | 4.10 ± 0.98 | |
| | | 30 min | 4.76 ± 0.88 | 4.05 ± 0.76 | 85.3 ± 4.5 | 9.87 ± 2.56 | 4.35 ± 1.04 | |
| | | Baseline | 4.84 ± 0.92 | 4.05 ± 0.87 | 84.4 ± 5.6 | 9.58 ± 2.27 | 4.20 ± 1.10 | |
| | | 5 min | 4.60 ± 0.79 | 3.75 ± 0.69 | 81.7 ± 6.1 | 9.04 ± 2.20 | 3.74 ± 1.03 | |
| 1000 mL | Cold (2 °C) | 10 min | 4.56 ± 0.82 | 3.76 ± 0.68 | 82.7 ± 4.8 | 9.06 ± 2.15 | 3.84 ± 0.92 | |
| | | 15 min | 4.67 ± 0.80 | 3.85 ± 0.70 | 82.5 ± 4.6 | 9.35 ± 2.22 | 3.86 ± 0.93 | |
| | | 30 min | 4.66 ± 0.84 | 3.86 ± 0.73 | 83.0 ± 4.6 | 9.38 ± 2.10 | 4.00 ± 0.95 | |
| | | Baseline | 4.78 ± 0.94 | 4.04 ± 0.81 | 84.9 ± 5.4 | 9.93 ± 2.40 | 4.21 ± 1.09 | |
| | | 5 min | 4.70 ± 0.86 | 3.92 ± 0.74 | 82.5 ± 5.9 | 9.52 ± 2.32 | 4.07 ± 0.99 | |
| | | 10 min | 4.70 ± 0.81 | 3.92 ± 0.72 | 83.5 ± 5.1 | 9.49 ± 2.31 | 4.08 ± 0.98 | |
| | Ambient (18 °C) | 15 min | 4.66 ± 0.82 | 3.90 ± 0.70 | 84.0 ± 5.2 | 9.74 ± 2.36 | 4.08 ± 0.87 | |
| | | 30 min | 4.68 ± 0.87 | 3.96 ± 0.76 | 84.6 ± 4.2 | 9.54 ± 2.20 | 4.18 ± 1.01 | |
| | | Interaction Effect | <i>p</i> | <0.001 ^a | <0.001 ^a | 0.404 | 0.779 | 0.099 |
| | | η^2 | 0.260 | 0.275 | 0.105 | 0.069 | 0.152 | |
| | | Time Effect | <i>p</i> | <0.001 ^b | <0.001 ^b | 0.093 | <0.001 ^b | 0.074 |
| | | η^2 | 0.395 | 0.537 | 0.194 | 0.516 | 0.206 | |
| Condition Effect | <i>p</i> | 0.053 | 0.003 ^c | 0.167 | 0.004 ^c | 0.024 ^c | | |
| | η^2 | 0.244 | 0.400 | 0.168 | 0.379 | 0.291 | | |

Means ± SD, n = 10. FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 s; PEF = peak expiratory flow; FEF₂₅₋₇₅ % = forced expiratory flow at 25–75 % of FVC. a, significant interaction effect; b, significant main effect for time; c, significant main effect for condition (*p* < 0.05).

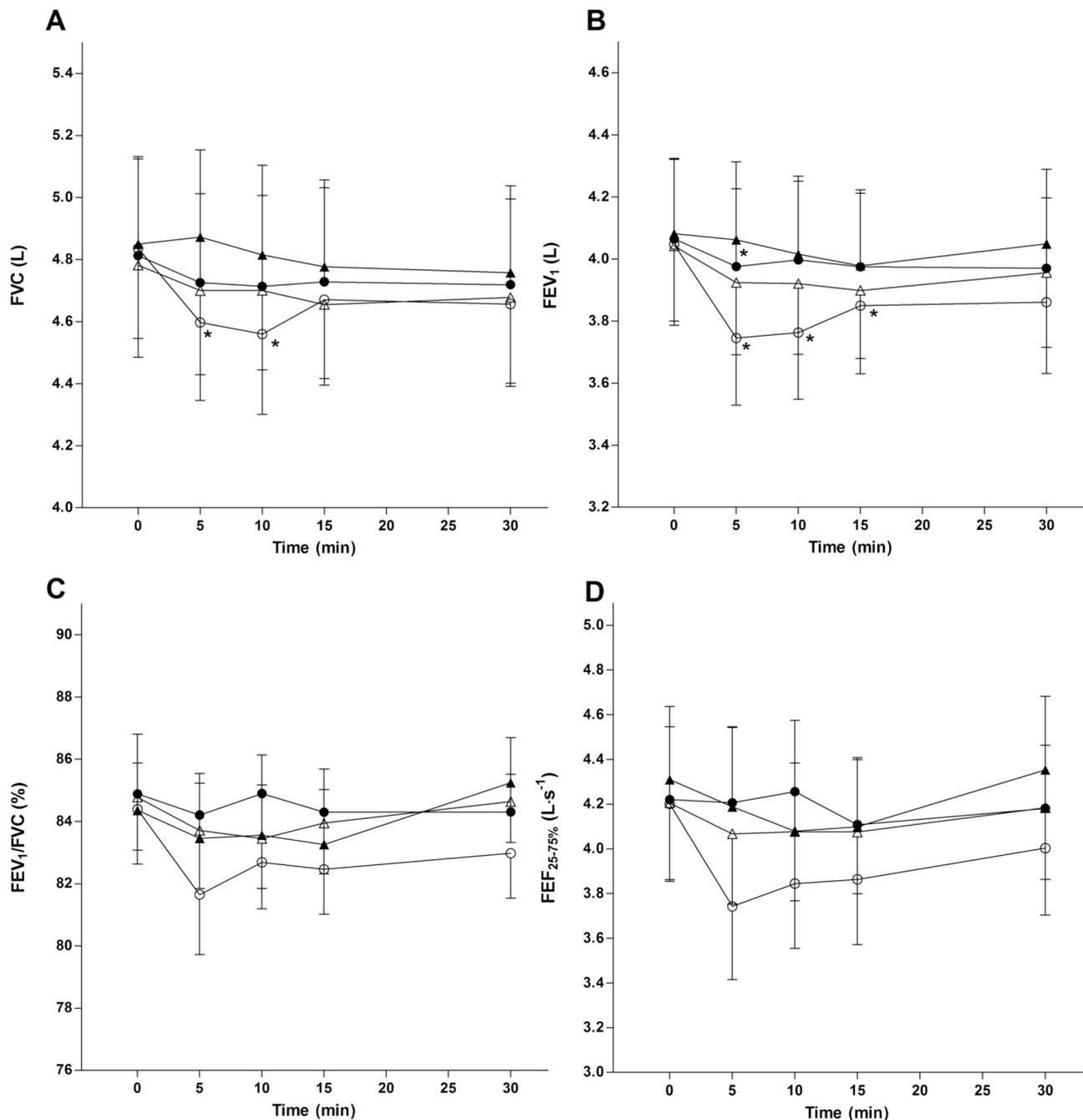


Fig. 1. Group mean (\pm SEM) responses in FEV₁ (A), FVC (B), FEV₁/FVC (C), and FEF_{25-75%} (D) post-drink ingestion for the Cold500 (●), Cold1000 (○), Ambient500 (▲), and Ambient1000 (△) conditions. * denotes significant difference from pre- to post- ingestion within a given trial at the timepoint indicated ($p < 0.05$). SEM is used in place of SD for visual clarity.

data confirm decreases in lung function following fluid ingestion, primarily mediated by temperature but with a secondary influence of volume.

4.1. Temperature effects

We have previously shown that a large fluid bolus (~ 750 mL) caused a significant and sustained decrease in FVC and FEV₁ of $\sim 3\%$ (Turner et al., 2015). Presently, our study design allowed us to distinguish between volume- and temperature-mediated effects of fluid ingestion. With a large cold-water bolus (1000 mL), we observed significant post-ingestion decreases in FVC (5%) and FEV₁ (7%) (Table 2; Fig. 1). There was a smaller (2%) decrease in FEV₁ with 500 mL cold water, but

no changes following equivalent volumes of water at room temperature. We determined therefore that decreases in FEV₁ with fluid ingestion are primarily mediated by temperature.

Interestingly, we observed no apparent change in airflow measured along the “effort independent” portion of expiration, quantified using FEF_{25-75%}. Although this metric has been proposed as a measure of small airway function, values for FEF_{25-75%} are highly dependent on the FVC, such that decreases in FVC, as observed presently, cause FEF_{25-75%} to be measured at a different lung volume, thereby altering its measurement accuracy. Indeed, the CV for FEF_{25-75%} was 5.1%, more than double that observed for FEV₁. We presently opted therefore to assess airway obstruction as changes in FEV₁.

We can conceive several potential mechanisms to explain the

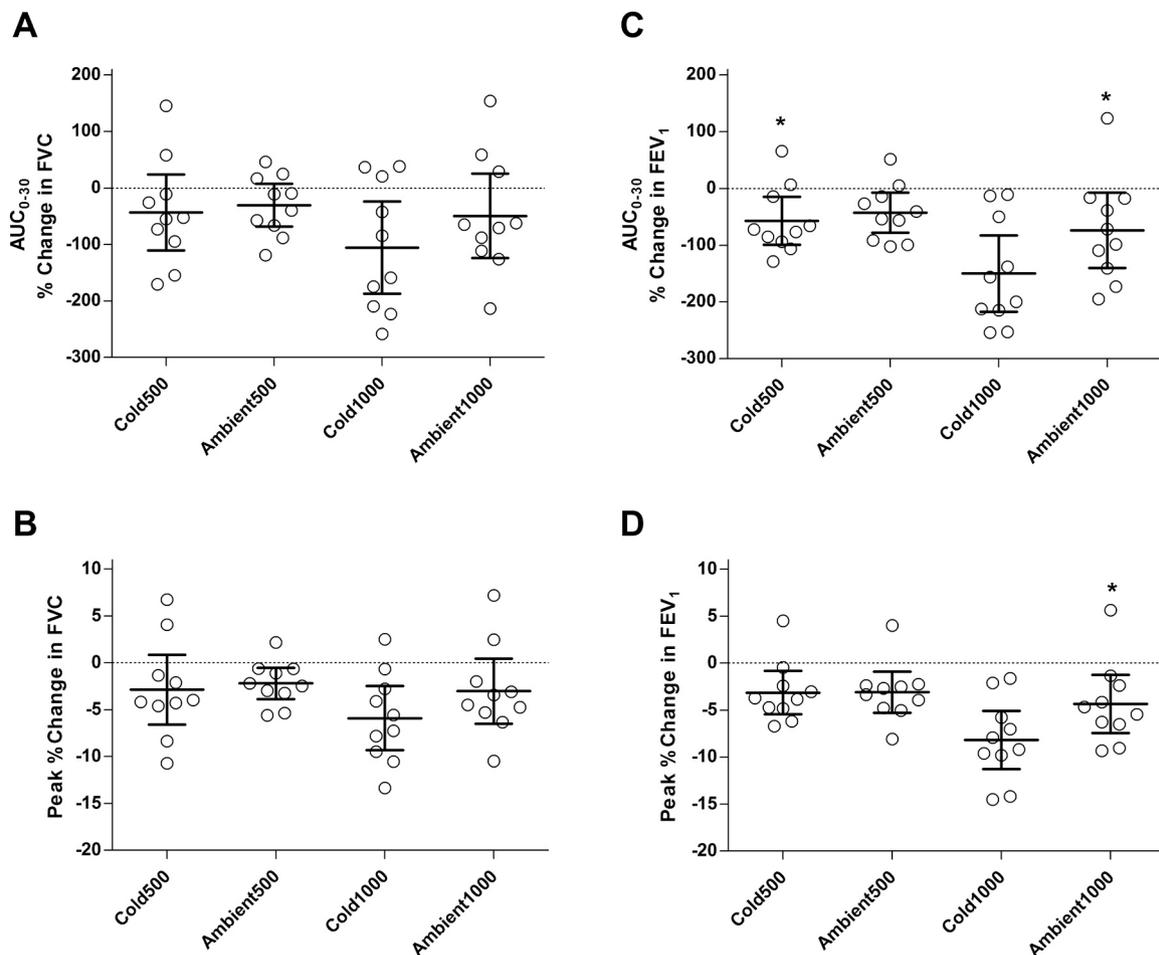


Fig. 2. AUC_{0-30} for FEV_1 (A) and FVC (B). Peak % change in FEV_1 (C) and FVC (D) from pre-ingestion. Values are means (95 % CI) (horizontal lines) and individual responses (○). * denotes significant difference from Cold1000 ($p < 0.05$).

observed decreases in FEV_1 following cold-water ingestion. First, it is well established that parasympathetic activity regulates airway smooth muscle, causing constriction and relaxation of the airways via acetylcholine and noncholinergic neurotransmitters, respectively (Canning et al., 2012). Ingesting ice-water has been shown to increase vagal tone, likely via vagal receptors located in the oesophagus (Siddanagoudra et al., 2015) resulting in vagally-mediated bronchoconstriction. There is also evidence to suggest that bronchospasm, stimulated by gastro-oesophageal reflux or airway obstruction, can be abolished by anticholinergics (Canning et al., 2012). It is therefore plausible that changes in airway function may relate to a temperature-mediated change in vagal tone. Second, the oesophagus and trachea share close anatomical proximity, separated by just a thin muscular layer. Cold water may have a direct cooling effect on the upper gastrointestinal tract, including the larynx, in turn cooling the upper airway (trachea). A pro-inflammatory airway hyperresponsiveness, and subsequent bronchospasm, may therefore result from cold-water ingestion and airway cooling, as observed in susceptible groups when ventilating cold air (Cockcroft and Davis, 2006; Nuutinen et al., 2007). In fact, exposure to a cold-stimulus (e.g., swimming in cold water, eating and drinking cold food/drinks) can cause cold urticaria (hives)—a pro-inflammatory response predominantly initiated through mast-cell activation (Nuutinen et al., 2007). Third, there is evidence that body temperature influences contractility of bronchiolar smooth muscle, whereby deviations of normal body temperature evoke contraction of the airway smooth muscle. This might be causative in bronchoconstriction (Mustafa, 2019). Therefore, airway obstruction, second to vagally-mediated bronchoconstriction and/or pro-inflammatory airway hyperresponsiveness, may

underpin a change in lung function associated with cold-water ingestion.

4.2. Volume effects

In addition to the cold-mediated decline in FVC and FEV_1 , our data suggest that fluid volume has an important effect on lung function. Specifically, the magnitude of peak percentage change in FEV_1 was larger with Cold1000 (~7 %) versus Cold500 (~3 %), and both 500 mL and 1000 mL conditions (independent of temperature) evoked prolonged decreases in PEF below baseline (~4 %). We also observed a significant decrease in FVC (and concomitant preservation of FEV_1 /FVC) with Cold1000, but not with Cold500.

Previous research has shown that abdominal distention raises resting intrathoracic pressures and increases ribcage volumes (Gilroy et al., 1985). Given that an FVC manoeuvre causes large increases in intrathoracic pressures that may reach ~75 % of maximum (Tiller and Simpson, 2018), we expected the large fluid bolus to attenuate FVC and/or FEV_1 , independent of temperature. However, while the volume-dependant changes in FEV_1 and FVC were observed between Cold500 and Cold1000, we did not observe decreases in pulmonary capacities or flows with Ambient1000. Based on these findings, we can largely discount abdominal distention, and any subsequent effects on respiratory mechanics, as causative in lung function decline in this instance.

Indeed, while a greater reduction in lung volumes observed with Cold1000 compared to Cold500 may suggest a potential mechanistic interaction between volume and temperature, these changes are likely

to be the result of greater airway cooling due to more exposure to cold water or may be an indirect result of reduced body temperature with the larger bolus. Body temperature has been shown to influence respiratory mechanics, where higher body temperatures increase respiratory system compliance and reduce airway resistance. Therefore, it is plausible that ingestion of a large volume of cold water could be sufficient to decrease body temperature, thereby impairing the elastic mechanical properties of the airways and reducing FVC (Rubini, 2011). These mechanisms and their interactions require further exploration.

4.3. Technical considerations and implications

There are several considerations that should predicate the interpretation of our data. First, the postprandial decreases in lung function ranged from 0 % to 14 %. Thus, an ability to detect a “real” change is an important consideration. We show excellent reproducibility of spirometry data (i.e., all CV <5 % and all ICC >0.91), and 8/10 subjects exhibited an FEV₁ decline with Cold1000 that exceeded the CV of ~2.5 %. Values are in line with our earlier research in which we assessed reproducibility using similar procedures and equipment (Tiller et al., 2019). We are therefore confident in the accuracy and reliability of our measures.

Second, although none of our subjects displayed spirometry values that fell below the lower limits of normal, the average FEV₁ decline with Cold1000 was 7 % at 5 min post-ingestion. Values that fall by 5–10 % are considered clinically meaningful in respiratory patients (Cazzola et al., 2008) and an FEV₁ decrease of ≥ 10 % is diagnostic in exercise-induced bronchoconstriction (Parsons et al., 2013). Thus, a 7 % decline is not trivial, and is more than sufficient to affect the accuracy and reliability of lung function measurements. Note that our data were recorded in healthy subjects with normal baseline lung function. However, we did not assess subjects for airway hyperresponsiveness. Given that patients with pre-existing respiratory disease or airway hyperresponsiveness may be more sensitive to cold water ingestion, perhaps experiencing unpleasant respiratory symptoms (Lin & Hsieh), further studies should replicate our findings in these populations.

Readers should also note that, while no adverse effects of fluid ingestion were reported in this study, some at-risk populations may experience aggressive coughing and vomiting with high fluid intakes. These symptoms could influence patient comfort (Cooper, 2011), measurement accuracy (Graham et al., 2019), and increase the risk of respiratory complications (i.e. aspiration) (Ulas et al., 2022). Thus, there may be safety concerns as well as technical ones associated with the ingestion of large fluid volumes.

Third, we have proposed several physiological explanations for our findings. A non-physiological explanation may relate to cooling of the upper airway causing a decrease in exhaled breath temperature (EBT) and a subsequent effect on spirometer measurement (Miller and Sigaard, 1994). The pneumotachograph is the most common means of assessing lung function in the laboratory (de Jongh, 2008), although turbines and flow-measuring devices are also used. Measuring spirometry is somewhat dependent on gas viscosity which increases with temperature (Miller et al., 2005). As a result, a cold-water-mediated decrease in the EBT may alter airflow dynamics and disrupt the flow-pressure relationship on which the output is based. We have recently modelled this phenomenon in a pneumotachograph using computational fluid dynamics following the ingestion of cold- and room-temperature water in healthy subjects, finding that, although EBT fell by ~2.1 °C following cold-water ingestion, the effect on flow calculations was negligible (< 1 %) (Tiller et al., 2021). The effect would be expected to be similarly negligible (although not identical) with the use of a volume-measuring turbine such as that used presently. We are confident therefore that the present observations have a physiological explanation.

Fourth, while the current study was not designed to investigate sex-mediated disparities in the pulmonary function response to fluid

ingestion, it is plausible that males and females may respond differently. Females have smaller lungs and airways relative to males, even when corrected for age and stature, resulting in lower maximal flows (Harms and Rosenkranz, 2008). Additionally, independent of lung anatomy, females may exhibit greater airway hyperresponsiveness than males (Leynaert et al., 1997). Females may therefore be more sensitive to cold-water-induced decreases in lung function. Given the small number of females in our study (n = 4), it was not appropriate to assess sex-based differences, but the hypothesis warrants further study.

A final consideration is that exercisers regularly consume large fluid boluses before, during, and after training and competition in order to rehydrate (Sawka et al., 2007). Cold fluids are preferred by exercisers, especially in the heat, and are consumed in greater *ad libitum* volumes when compared to fluids at room temperature (Mundel et al., 2006). We show that consuming between 500 mL and 1000 mL of cold water over a 10 min period is sufficient to significantly diminish resting lung function. Notwithstanding the possible consequences on exercise performance, which remain speculative, rehydration strategies have the potential to confound lung function measurement when performed as part of applied research or health screening in athletic competition. For these reasons, greater consideration of the influence of fluid ingestion on lung function is warranted.

5. Conclusions

Cold water ingestion causes significant reductions in pulmonary capacities and flows in healthy subjects. The effects are primarily mediated by temperature but with a secondary, cumulative effect of fluid volume. To avoid erroneous results, individuals should abstain from drinking cold water, especially in large volumes, immediately prior to a lung function test. Further studies are needed to explore the phenomenon in patients with respiratory disease and airway hypersensitivity and to elucidate the precise mechanisms connecting fluid ingestion to acute lung function decline.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

There are no competing financial interests associated with this research.

References

- Burri, E., Cisternas, D., Villoria, A., Accarino, A., Soldevilla, A., Malagelada, J.R., Azpiroz, F., 2013. Abdominal accommodation induced by meal ingestion: differential responses to gastric and colonic volume loads. *Neurogastroenterol. Motil.* 25, 339–e253.
- Canning, B.J., Woo, A., Mazzone, S.B., 2012. Neuronal modulation of airway and vascular tone and their influence on nonspecific airways responsiveness in asthma. *J. Allergy (Cairo)* 2012, 108149.
- Cazzola, M., MacNee, W., Martinez, F.J., Rabe, K.F., Franciosi, L.G., Barnes, P.J., Brusasco, V., Burge, P.S., Calverley, P.M., Celli, B.R., Jones, P.W., Mahler, D.A., Make, B., Miravittles, M., Page, C.P., Palange, P., Parr, D., Pistolesi, M., Rennard, S.I., Rutten-van Molken, M.P., Stockley, R., Sullivan, S.D., Wedzicha, J.A., Wouters, E.F., American Thoracic, S., European Respiratory Society Task Force on outcomes of, C., 2008. Outcomes for COPD pharmacological trials: from lung function to biomarkers. *Eur. Respir. J.* 31, 416–469.
- Cockcroft, D.W., Davis, B.E., 2006. Mechanisms of airway hyperresponsiveness. *J. Allergy Clin. Immunol.* 118, 551–559 quiz 560–551.
- Cohen, J., 1977. *Statistical Power Analysis for the Behavioral Sciences*, Rev. ed. Academic Press, New York.
- Cooper, B.G., 2011. An update on contraindications for lung function testing. *Thorax* 66, 714–723.
- de Jongh, F., 2008. Spirometers. *Breathe* 4 (3), 251–254.
- Deal, E.C., Jr, McFadden, E.R., Jr, Ingram, R.H., Jr, Jaeger, J.J., 1979. Esophageal temperature during exercise in asthmatic and nonasthmatic subjects. *J. Appl. Physiol. Respir. Environ. Exerc. Physiol.* 46, 484–490.

- Gilroy, R.J., Lavietes, M.H., Loring, S.H., Mangura, B.T., Mead, J., 1985. Respiratory mechanical effects of abdominal distension. *J. Appl. Physiol.* 58, 1997–2003.
- Graham, B.L., Steenbruggen, I., Miller, M.R., Barjaktarevic, I.Z., Cooper, B.G., Hall, G.L., Hallstrand, T.S., Kaminsky, D.A., McCarthy, K., McCormack, M.C., Oropez, C.E., Rosenfeld, M., Stanojevic, S., Swanney, M.P., Thompson, B.R., 2019. Standardization of spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am. J. Respir. Crit. Care Med.* 200, e70–e88.
- Hallstrand, T.S., 2014. Approach to the patient with exercise-induced bronchoconstriction*. In: Adkinson, N.F., Bochner, B.S., Burks, A.W., Busse, W.W., Holgate, S.T., Lemanske, R.F., O’Hehir, R.E. (Eds.), *Middleton’s Allergy*, Eighth edition. W.B. Saunders, London, pp. 938–950.
- Harms, C.A., Rosenkranz, S., 2008. Sex differences in pulmonary function during exercise. *Med. Sci. Sports Exerc.* 40, 664–668.
- Jones, P.W., Donohue, J.F., Nedelman, J., Pascoe, S., Pinault, G., Lassen, C., 2011. Correlating changes in lung function with patient outcomes in chronic obstructive pulmonary disease: a pooled analysis. *Respir. Res.* 12, 161.
- Leynaert, B., Bousquet, J., Henry, C., Liard, R., Neukirch, F., 1997. Is bronchial hyperresponsiveness more frequent in women than in men? A population-based study. *Am. J. Respir. Crit. Care Med.* 156, 1413–1420.
- Lin, Y.Z., Hsieh, K.H., 1997. Asthma induced by ice water ingestion in ethnic Chinese asthmatic children: a challenge. *Pedia Allergy Immunol.* 8, 11–16.
- MacHose, M., Peper, E., 1991. The effect of clothing on inhalation volume. *Biofeedback Self Regul.* 16, 261–265.
- Miller, M.R., Sigsgaard, T., 1994. Prevention of thermal and condensation errors in pneumotachographic recordings of the maximal forced expiratory manoeuvre. *Eur. Respir. J.* 7 (1), 198–201.
- Miller, M.R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Crapo, R., Enright, P., van der Grinten, C.P., Gustafsson, P., Jensen, R., Johnson, D.C., MacIntyre, N., McKay, R., Navajas, D., Pedersen, O.F., Pellegrino, R., Viegi, G., Wanger, J., Force, A.E.T., 2005. Standardisation of spirometry. *Eur. Respir. J.* 26, 319–338.
- Mundel, T., King, J., Collacott, E., Jones, D.A., 2006. Drink temperature influences fluid intake and endurance capacity in men during exercise in a hot, dry environment. *Exp. Physiol.* 91, 925–933.
- Mustafa, S., 2019. Heating-induced contraction in airways smooth muscle: A possible causative factor of exercise-induced bronchoconstriction. *Respir. Physiol. Neurobiol.* 259, 162–165.
- Nuutinen, P., Harvima, I.T., Ackermann, L., 2007. Histamine, but not leukotriene C4, is an essential mediator in cold urticaria wheals. *Acta Derm. Venereol.* 87, 9–13.
- Parsons, J.P., Hallstrand, T.S., Mastrorade, J.G., Kaminsky, D.A., Rundell, K.W., Hull, J. H., Storms, W.W., Weiler, J.M., Cheek, F.M., Wilson, K.C., Anderson, S.D., American Thoracic Society Subcommittee on Exercise-induced, B, 2013. An official American Thoracic Society clinical practice guideline: exercise-induced bronchoconstriction. *Am. J. Respir. Crit. Care Med.* 187, 1016–1027.
- Portney, L.G., Watkins, M.P., 2009. *Foundations of Clinical Research: Applications to Practice*, 3rd ed. Pearson/Prentice Hall, Upper Saddle River, N.J.
- Price, O.J., Ansley, L., Menzies-Gow, A., Cullinan, P., Hull, J.H., 2013. Airway dysfunction in elite athletes—an occupational lung disease? *Allergy* 68, 1343–1352.
- Quanjer, P.H., Stanojevic, S., Cole, T.J., Baur, X., Hall, G.L., Culver, B.H., Enright, P.L., Hankinson, J.L., Ip, M.S.M., Zheng, J., Stocks, J., Initiative, E.R.S.G.L.F., 2012. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. *Eur. Respir. J.* 40, 1324–1343.
- Rossi, P., Andriess, G.I., Oey, P.L., Wieneke, G.H., Roelofs, J.M.M., Akkermans, L.M.A., 1998. Stomach distension increases efferent muscle sympathetic nerve activity and blood pressure in healthy humans. *J. Neurol. Sci.* 161, 148–155.
- Rubini, A., 2011. The effect of body warming on respiratory mechanics in rats. *Respir. Physiol. Neurobiol.* 175, 255–260.
- Sawka, M.N., Burke, L.M., Eichner, E.R., Maughan, R.J., Montain, S.J., Stachenfeld, N.S., 2007. American College of Sports Medicine position stand. Exercise and fluid replacement. *Med. Sci. Sports Exerc.* 39, 377–390.
- Siddanagoudra, S., Priya, S.A., Nallulwar, S., 2015. Ice Water Ingestion and Sympathovagal Balance in Healthy Subjects: Importance of time-domain heart rate variability. *J. Clin. Prev. Cardiol.* 2, 27–31.
- Sylvester, K.P., Clayton, N., Cliff, L., Hepple, M., Kendrick, A., Kirkby, J., Miller, M., Moore, A., Rafferty, G.F., O’Reilly, L., Shakespeare, J., Smith, L., Watts, T., Bucknall, M., Butterfield, K., 2020. ARTP statement on pulmonary function testing 2020. *BMJ Open Respir. Res.* 7.
- Tiller, N.B., Simpson, A.J., 2018. Effect of spirometry on intra-thoracic pressures. *BMC Res. Notes* 11, 110.
- Tiller, N.B., Turner, L.A., Taylor, B.J., 2019. Pulmonary and respiratory muscle function in response to 10 marathons in 10 days. *Eur. J. Appl. Physiol.* 119, 509–518.
- Tiller, N.B., Turner, L.A., Hart, J., Casaburi, R., 2021. Airflow dynamics and exhaled-breath temperature following cold-water ingestion. *Respir. Physiol. Neurobiol.* 284, 103564.
- Turner, L.A., Gonzalez, J.T., Rumbold, P.L., Green, B., Brown, M., Mickleborough, T.D., Stevenson, E., 2015. The influence of drink and meal ingestion on resting pulmonary function in active individuals: 2683 May 29, 2: 00 PM - 2: 15 PM. *Med. Sci. Sports Exerc.* 47, 723.
- Ulas, A.B., Aydin, Y., Eroglu, A., 2022. Foreign body aspirations in children and adults. *Am. J. Surg.* 224, 1168–1173.
- Unverdorben, M., Mostert, A., Munjal, S., van der Bijl, A., Potgieter, L., Venter, C., Liang, Q., Meyer, B., Roethig, H.J., 2010. Acute effects of cigarette smoking on pulmonary function. *Regul. Toxicol. Pharm.* 57, 241–246.
- Weiler, J.M., Bonini, S., Coifman, R., Craig, T., Delgado, L., Capao-Filipe, M., Passali, D., Randolph, C., Storms, W., Ad Hoc Committee of Sports Medicine Committee of American Academy of Allergy, A., Immunology, 2007. American Academy of Allergy, Asthma & Immunology Work Group report: exercise-induced asthma. *J. Allergy Clin. Immunol.* 119, 1349–1358.