Integrated Diaphragmatic Function, Chemosensitivity, and Endurance in Exercising Divers

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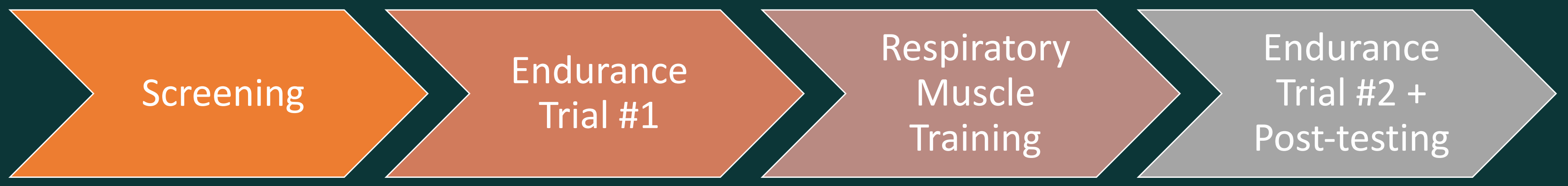
Introduction

While exercising underwater, divers experience increased ventilatory load due to increased gas density and airways resistance, which can predispose them to respiratory muscle fatigue and hypercapnia with increased risk of CO_2's narcotic effects or seizure (secondary to CNS oxygen toxicity). Hypercapnic ventilatory response (HCVR) is a highly variable measure of the physiological response to increased pCO_2, and a lower HCVR is associated with increased pCO_2 while diving. Respiratory muscle training (RMT) has been shown to augment endurance in divers and is also associated with increased HCVR in those with a low baseline HCVR. A prior study in our lab showed sub-toxic CO exposure has beneficial effects on skeletal muscle through upregulating mitochondrial biogenesis and GLUT4/aerobic metabolism. This study aimed to test the effects of RMT (with and without CO) on chemosensitivity (HCVR), integrated diaphragmatic function (IDF), and diving exercise endurance.

Methods

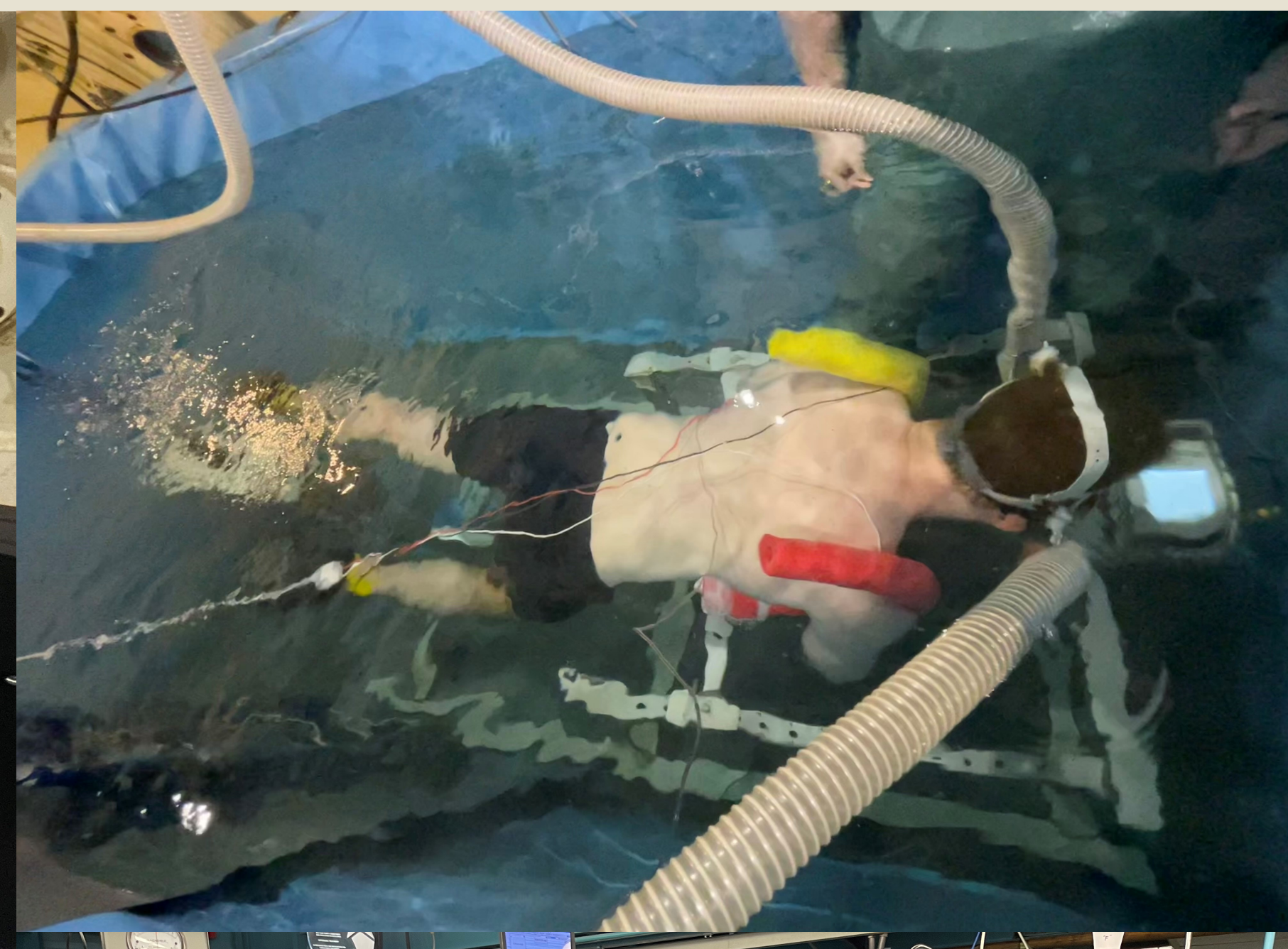
Fit male and female subjects (VO_2 peak ≥ 35 mL*kg^{-1}*min^{-1} and 30 mL*kg^{-1}*min^{-1} respectively) were recruited. Baseline spirometry, HCVR, VO_2peak (dry and wet), submersed (depth = 55 feet of seawater, fsw) bicycle exercise endurance at 85% VO_2peak with intermittent ABG, lactate, and pyruvate sampling, IDF, and transdiaphragmatic pressure were assessed. Subjects then completed twenty 30-minute RMT sessions over one month breathing either air or 200 ppm CO (double-blinded) with a starting inspiratory and expiratory pressure of 50 cmH_2O that is increased by 5 cmH_2O per week. Blood samples have been analyzed for stopped-flow analysis of O_2 offloading from hemoglobin (Hb). The same battery of tests was performed upon completion of RMT.

Variable	Analysis	Interpretation
Chemosensitivity (HCVR)	Pet CO_2 vs Ventilation (V_E, L/min), slope = HCVR	↑ HCVR from low baseline→ attenuated exercise hypercapnia
Submersed exercise endurance and breathing pattern	Time to exhaustion, V_E from metabolic cartridge and mass spectroscopy, and respiration rate (RR)	↑ time to exhaustion, steadier V_E & RR→ improved RMF
Arterial pH and PCO_2	ABG analysis (baseline, every 15 min during exercise, at end exercise, and 10 min post-exercise)	↓PCO_2→ improved chemosensitivity and RMF
Lactate and Pyruvate	Measured before, during, and after exercise	↓ lactate and L/P→greater training effect
Integrated Diaphragmatic Function (IDF)	Max Inspiratory & Expiratory Pressures (MIP & MEP) + Max Voluntary Ventilation (MVV)--(Pulmonary function testing) Diaphragm thickness (via ultrasound)	↑ IDF→ supports increased mitochondrial mass & aerobic glycolysis


Screening
Endurance Trial #1
Respiratory Muscle Training
Endurance Trial #2 + Post-testing

Hypotheses tested:

1. RMT will improve HCVR on individual with a low baseline HCVR.
2. RMT will lead to lower arterial PCO_2 during submersed exercise due to increased HCVR.
3. Exercise endurance and diaphragmatic function will improve more with RMT with low dose CO compared to RMT with air.
4. Submersed exercise endurance is limited by respiratory muscle fatigue and will improve with RMT with low dose CO.
5. Exercise capacity and arterial PCO_2 will be positively influenced by increased O_2 offloading from erythrocytes and RBC gas-channel expression.



Left: Taylor collecting arterial blood samples during exercise
Top Right: Subject performing submerged exercise
Bottom Right: Hyperbaric chamber control panel

Results

A total of 30 subjects completed all phases. Results show RMT increasing HCVR for those with low baselines (Fig. 1) and endurance duration (Fig. 2). Post-RMT, subjects had increased diaphragm thickness (Fig. 3) and higher mean arterial pCO_2 while exercising (Fig. 4) with no change in ventilation (56.37 L*min^{-1} compared to 58.85 L*min^{-1} pre-RMT, p=0.0967). Subjects also had more negative MIP indicating improved IDF/respiratory muscle static pressure (Fig. 5). Preliminary data supports significant differences in human vs. murine erythrocyte oxygen kinetics (without individual human differences) and a greater enhancement of endurance duration for subjects receiving CO.

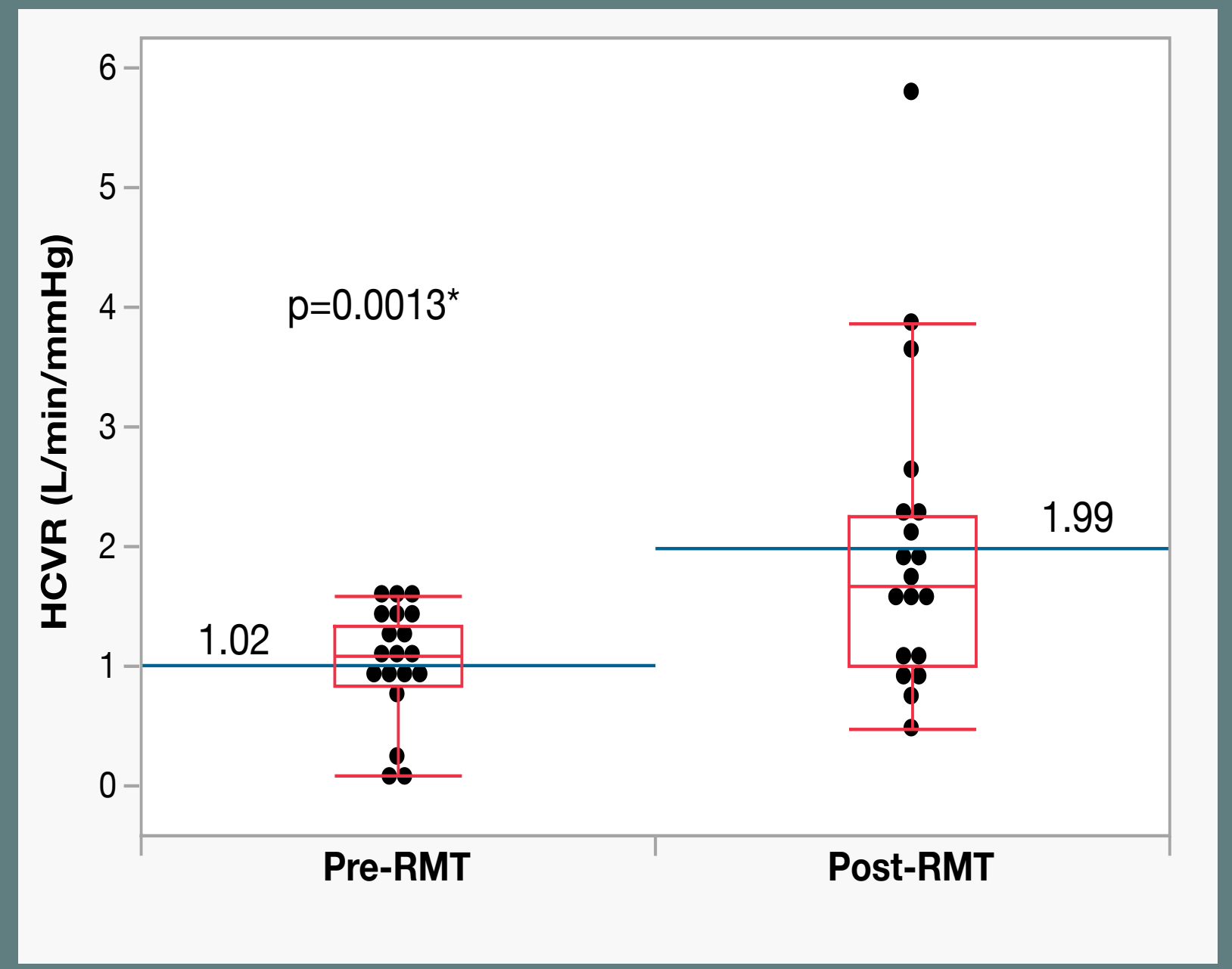


Figure 1. Change in HCVR Post-RMT for those with low Baseline HCVR

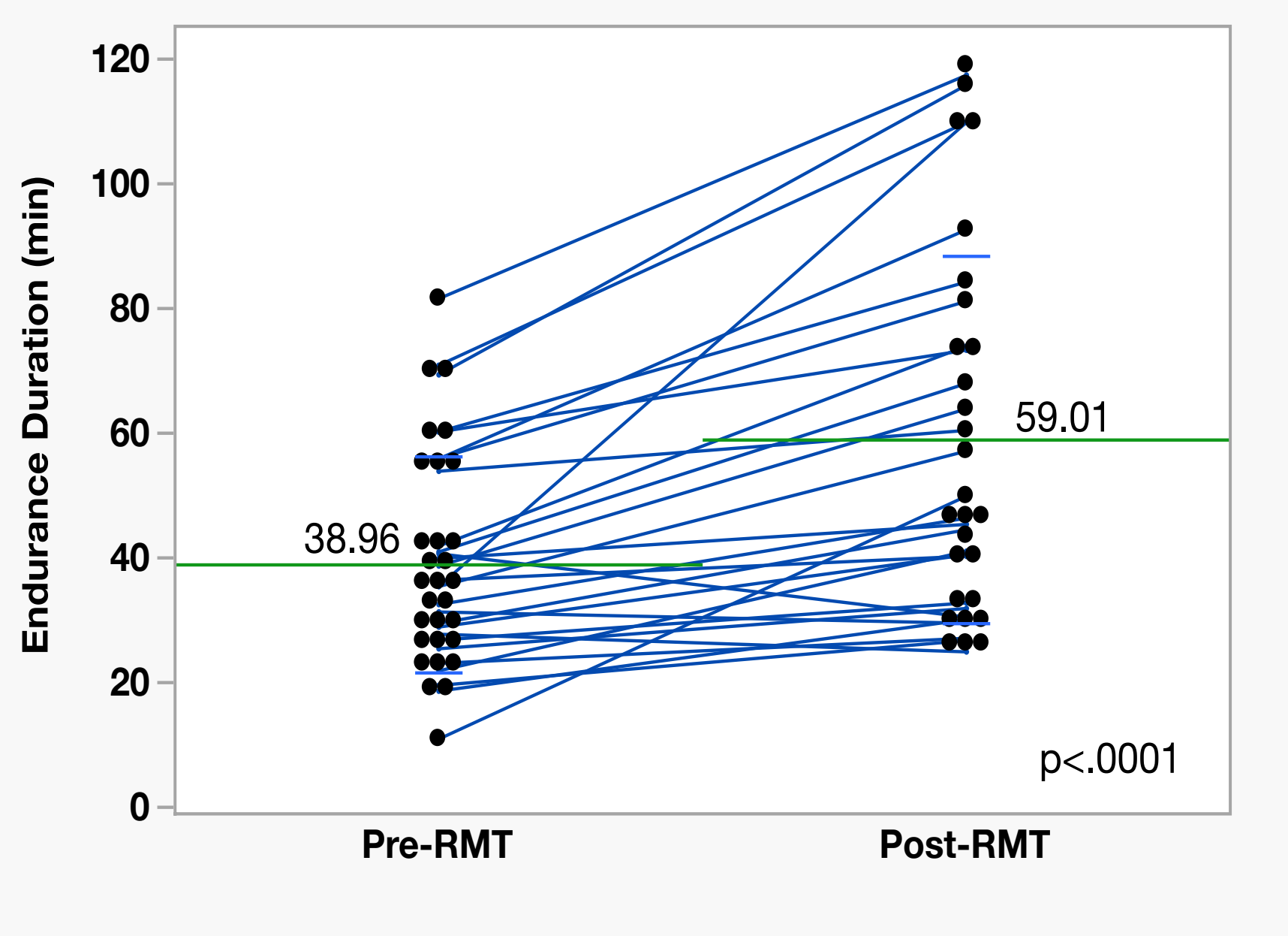


Figure 2. Endurance time during submersed exercise at 55 fsw

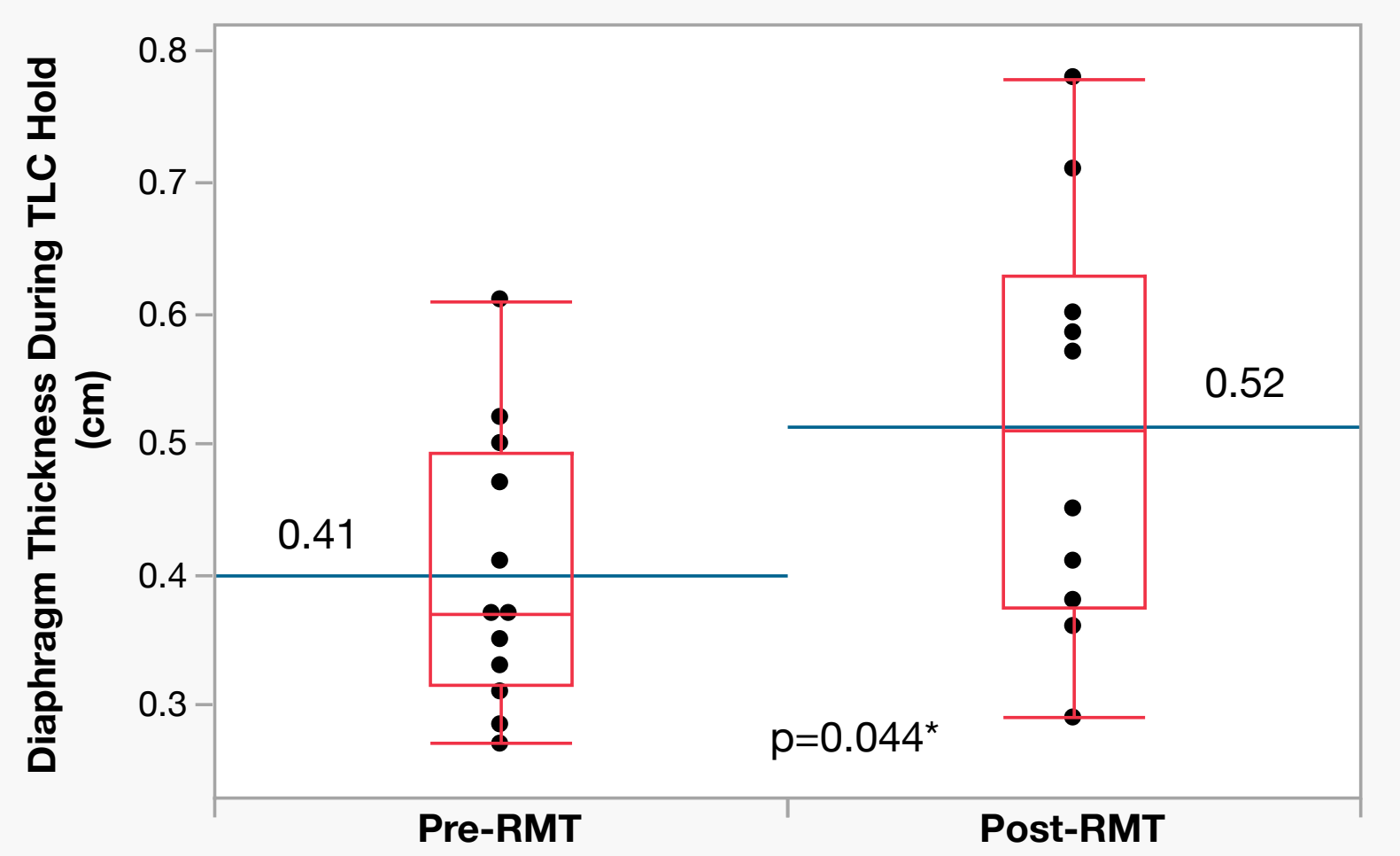


Figure 3. Diaphragm thickness Pre- vs Post-RMT

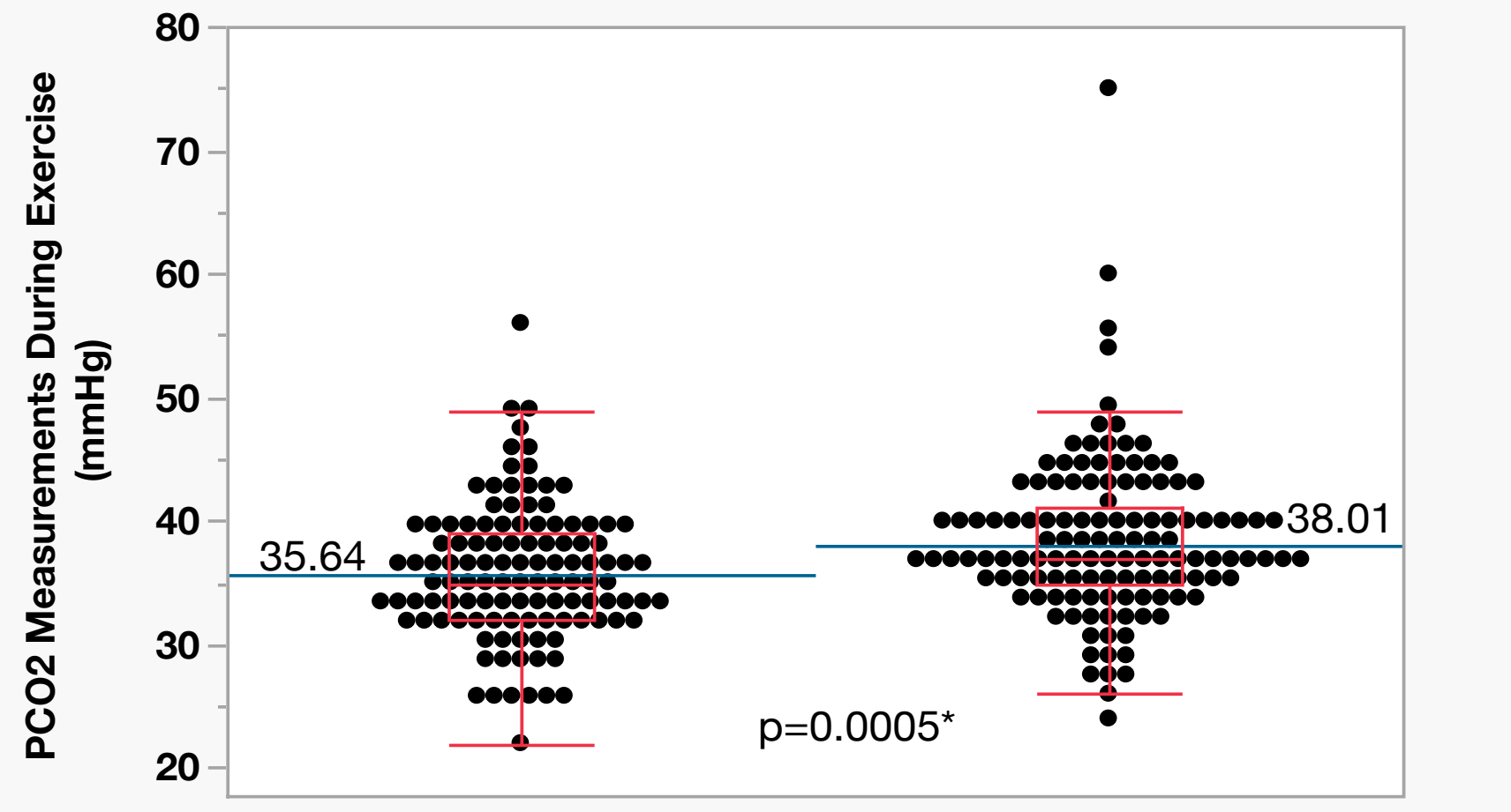


Figure 4. Mean $PaCO_2$ during submerged exercise at 55 fsw

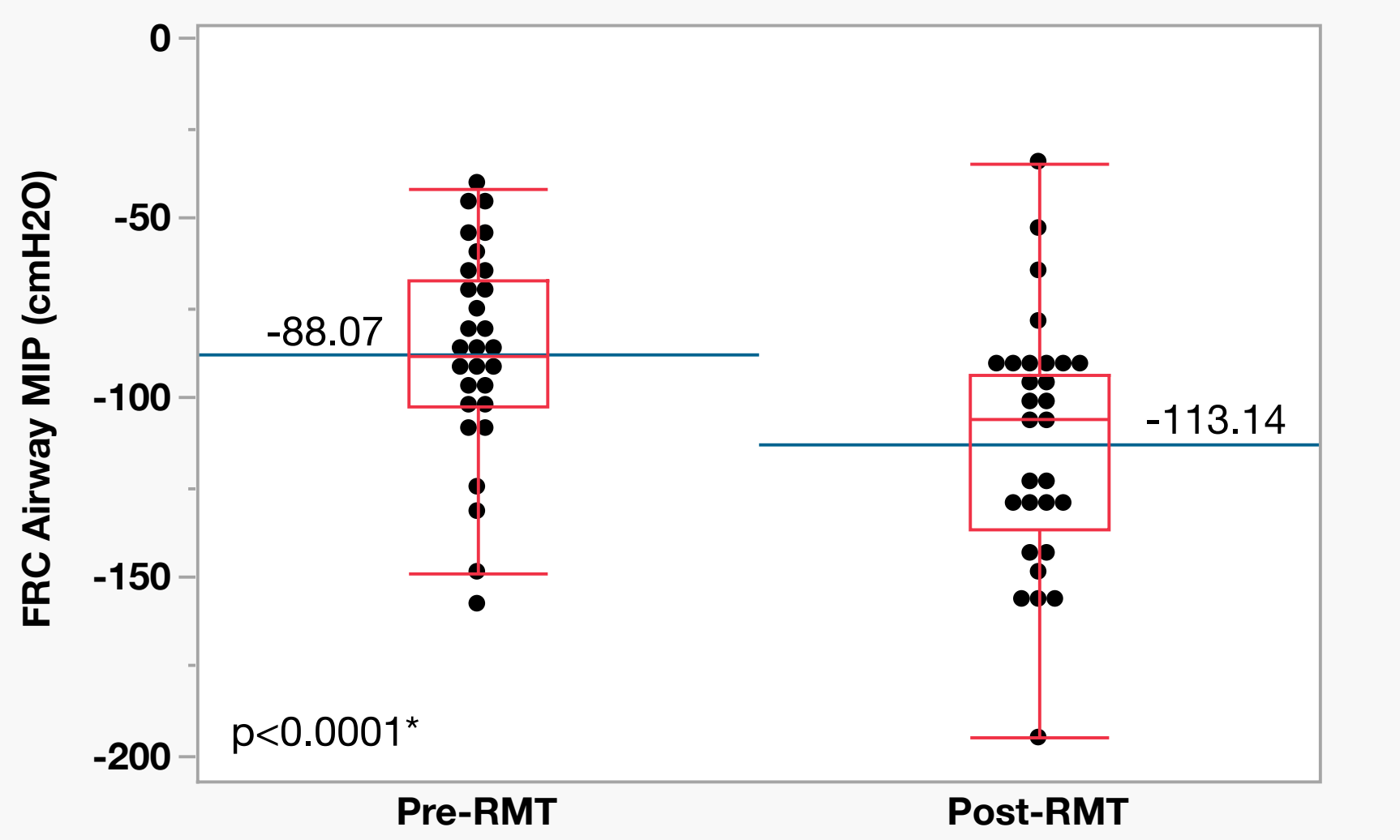


Figure 5. Maximum Inspiratory Pressure Before and After RMT

Conclusions

As predicted, RMT has a beneficial effect for divers and was able to improve chemosensitivity, integrated diaphragmatic function, and exercise endurance at depth with preliminary results supporting greater benefit when used with subtoxic CO instead of air. Surprisingly, mean pCO_2 increased with no change in ventilation following RMT. RMT benefits are possibly due to changes in chemosensitivity, IDF, and skeletal/respiratory muscle enhancement. The paradoxical changes in mean $PaCO_2$ and minute ventilation are still under investigation and will be further explored by assessing factors such as changes to respiratory dead space, time point during exercise, and the effect of baseline HCVR. Since the study was recently unblinded, the effect of CO is pending. Analysis of other variables such as diaphragm thickness, lactate/pyruvate, erythrocyte/Hg parameters, and breathing pattern are ongoing.