# Long COVID

## Pathophysiology

### Exercise

* Lower VE/VCO2 slope (32.1 severe vs 32.9 normal; p = 0.068) (Cherneva et al., 2025)
* Lower max heart rate
  + (Contreras et al., 2023)
* Lower o2 delivery / utilization
  + Only 2 subjects demonstrated Respiratory Limitation (RL) (Baratto et al., 2021)
  + Lower A-V difference (Baratto et al., 2021)
  + Lower peripheral oxygen extraction (Baratto et al., 2021)
  + Lower SaO2 (Baratto et al., 2021)
  + 19.6 versus 17.1 (Baratto et al., 2021)
  + Lower A-VO2 difference with lower peripheral oxygen extraction, (Baratto et al., 2021)
  + Cardiac output
    - No difference in absolute values, but COVID has lower percentage of predicted values (Baratto et al., 2021)
  + Lower O2 pulse
    - 16% lower on Day 2 compared to Day 1 in PEM (Thomas et al., n.d.)
  + Low Cardiac and O2 pulse [@deBoerDecreasedFattyAcid]
  + No sign of ventilatory impairment, impaired o2 pulse and oxygen uptake capacity (Evers et al., 2022, p. 8)
* Earlier anaerobic threshold
  + Impaired fat metabolism from mitochondria 🡪 higher mean lactate [@deBoerDecreasedFattyAcid]
    - Not associated with COVID symptoms [@deBoerDecreasedFattyAcid]

### Cardiac

* No difference in LVEF
  + (Baratto et al., 2021)
* Mildly dilated right ventricle
  + 40 mm vs 35 mm diameter (Baratto et al., 2021)
* Abnormal left or right ventricular strain
  + 1/3 (Baratto et al., 2021)
* Higher cardiac output and PAP at rest, similar total pulmonary resistance (TPR) (Baratto et al., 2021)

### Autonomic Nervous System (ANS)

* No difference in resting heart rate
  + 78 vs 77 (Contreras et al., 2023)
  + (Santos-de-Araújo et al., 2024)

## Mediators

### Dyspnea

* Improvements in dyspnea are not associated with improvements in fatigue
  + r= 0.122 (insignificant) (Harenwall et al., 2022)

### Vascular

* Lower EQI (EQI < 2) is NOT associated with:
  + - Sleep (Charfeddine et al., 2021)

## SpO2

* SpO2 did not correlate with dyspnea severity
  + Long COVID (Paradowska-Nowakowska et al., 2023)

## Symptoms

### Fatigue

* Improvements in fatigue are associated with improvements in QOL
  + r = -0.371; p < 0.001 (Harenwall et al., 2022)

# Descriptive Statistics

## Age

* Age is associated with:
  + higher rates of fatigue
    - CFQ (Harenwall et al., 2022)
  + reduced activity tolerance
    - Borg scale (Paradowska-Nowakowska et al., 2023)
  + reduced FMD
    - [@riouReducedFlowMediatedDilatation2021]
  + more severe cognitive impairment
    - [@rabaiottiEffectsMultidisciplinaryRehabilitation2023]
    - less risk of cognitive impairment
      * (Bonner-Jackson et al., 2024)
* Age was not associated with:
  + Dyspnea
    - p = 0.372 (Paradowska-Nowakowska et al., 2023)
    - (Craparo et al., 2022)
  + Brain Fog
    - (Craparo et al., 2022)
  + Sensory Disorder

(Craparo et al., 2022)

## Gender

* Females are more likely to experience long COVID
  + [@charfeddineLongCOVID192021]
  + 63.6% (versus 41.1%) (Barbagelata et al., 2022)
  + Higher proportion of females (73.3%) versus controls (59.1%) (Bonner-Jackson et al., 2024)
  + Higher proportion of females (71%) versus controls (58%) (Contreras et al., 2023)
* Females are more likely to experience brain fog
  + (Orfei et al., 2022)
  + (Nordvig et al., 2023)
* Females are more likely to experience dyspnea
  + (Craparo et al., 2022)
* Females are more likely to experience more than 1 long COVID symptom
  + (Craparo et al., 2022)
* Males are more likely to experience brain fog
  + 42.3% of males (u = 6.45) versus 29.1% of females (u = 5.66) [@vyasMildCognitiveImpairment2022]
* Females have better respiratory values than men:
  + FEV1 / FVC
    - (Paradowska-Nowakowska et al., 2023)
* Females have better lung health than men
  + XRAYS/CT
    - (Paradowska-Nowakowska et al., 2023)
* Females have better exercise capacity
  + 6MWT
    - (Paradowska-Nowakowska et al., 2023)
* Females have worse exercise tolerance
  + Borg scale
    - (Paradowska-Nowakowska et al., 2023)
* Females have healthier hearts
  + LVEF
    - (Paradowska-Nowakowska et al., 2023)
* Females are more likely to report the following long COVID symptoms:
  + Myalgia
    - (Paradowska-Nowakowska et al., 2023)
  + Palpitations
    - (Paradowska-Nowakowska et al., 2023)
  + Increased or unstable blood pressure
    - (Paradowska-Nowakowska et al., 2023)
  + Impaired concentration
    - (Paradowska-Nowakowska et al., 2023)
  + Memory deterioration
    - (Paradowska-Nowakowska et al., 2023)
  + Worsened mood
    - (Paradowska-Nowakowska et al., 2023)
  + Sleep disorder
    - (Paradowska-Nowakowska et al., 2023)
  + Hair loss
    - (Paradowska-Nowakowska et al., 2023)
  + Dizziness
    - (Paradowska-Nowakowska et al., 2023)

CPET

* Higher proportion of women in the O2 delivery / utilization group (62.5%) compared to dysfunctional breathing group (46.7%) or the respiratory limitation group (17.9%)

## Ethnicity

* Black race was associated with lower likelihood of cognitive impairment

(Bonner-Jackson et al., 2024)

# IMT

## Outcomes

### Cardiac

* IMT does not improve LVEF
  + (Trevizan et al., 2021)
* IMT does not improve BNP
  + (Trevizan et al., 2021)

### Respiratory

* + Reduced EMGdi / EMG dimax (Langer et al., 2018)
* No change in phrenic nerve conductance
  + [@schaefferEffectsInspiratoryMuscle2023]
* No change in diaphragm EMG [@schaefferEffectsInspiratoryMuscle2023]
* No change in diaphragm thickness
  + (Benli et al., 2024)
  + (Spiesshoefer et al., 2024)
* Dyspnea
* IMT reduces dyspnea
  + Long COVID (McNarry et al., 2022)
  + MRC, TDI (Langer et al., 2018)
  + TDI [@schaefferEffectsInspiratoryMuscle2023]
  + DSI [@abodonyaInspiratoryMuscleTraining2021]
  + Long COVID, improved mmRC (3 to 2) and CRQ dyspnea domain (Spiesshoefer et al., 2024)
  + CHF, mMRC (Tanriverdi et al., 2023)
  + (Katayıfçı et al., 2022)
  + COPD meta-analysis SGRQ, TDI total, mMRC (Ammous et al., 2023)
* IMT does not reduce dyspnea
  + mMRC (Jimeno-Almazán et al., 2023) ## Inhalation
* IMT improves MIP
  + (Katayıfçı et al., 2022)
  + (Alwohayeb et al., 2018)
  + (Freeberg et al., 2023)
  + CKD (Campos et al., 2018)
  + CHF (Trevizan et al., 2021)
  + (Chen et al., 2023)
  + Long COVID (McNarry et al., 2022)
  + (Langer et al., 2018)
  + [@azeredoInspiratoryMuscleTraining2022]
  + (Del Corral et al., 2023), p. 5)
  + mean change: 21.43 meta-analysis [@chenCanInspiratoryMuscle2023]
  + [@schaefferEffectsInspiratoryMuscle2023]
  + CHF (Tanriverdi et al., 2023)
  + Long COVID, +79.4 versus +17.3 (Palau et al., 2022)
* IMT improves inspiratory muscle endurance
  + (Del Corral et al., 2023), p. 5)
  + CHF, ITL (Tanriverdi et al., 2023)
* IMT improves MIP but not above the MCID
  + COPD meta-analysis Mean: 14.57 cmH20 (Ammous et al., 2023)
* IMT improves S-index
  + (Yáñez-Sepúlveda et al., 2022)
* IMT improves SMIP
  + Long COVID (McNarry et al., 2022)
* IMT improves Fatigue Index Time (FIT)
  + Long COVID (McNarry et al., 2022)
* IMT does not improve TLC
  + RMT (Bisconti et al., 2018)
  + Long COVID (Spiesshoefer et al., 2024)

### Oxygen Saturation

* No improvement in SaO2 at nadir or baseline

[@krause-sorioInspiratoryMuscleTraining2021]

* IMT does not improve spO2

CKD (Campos et al., 2018)

### Autonomic

* No change in LF/HF (Bisconti et al., 2018)
* IMT improves resting heart rate
  + (∆: −2.6 ± 2.9 bpm) (Yáñez-Sepúlveda et al., 2022)
  + CKD (Campos et al., 2018)
  + Long COVID (75 to 68) (Edgell et al., 2025)
* IMT does not improve HRV
  + RMT (Bisconti et al., 2018)

### Strength

* IMT improves LE strength
  + (Katayıfçı et al., 2022)
  + 60 second sit-to-stand (Del Corral et al., 2023), p. 5)
  + CHF, quad strength dynamometry (Tanriverdi et al., 2023)
* IMT does not improve UE strength
  + Grip HHDT (Del Corral et al., 2023), p. 5)
  + Bench 1RM and Grip HHDDT (Jimeno-Almazán et al., 2023)
* IMT does not improve LE strength
  + (Jimeno-Almazán et al., 2023)

### Vascular

* IMT does not improve PWV
  + No acute change in response to single session (Tavoian et al., 2023)
  + [@Craighead2019InspiratoryMuscleStrength]
* No change in absolute % change, but significant improvement in shear rate (SR) and FMD normalized for shear (%FMD/SR) (Bisconti et al., 2018)
* Increased Diameter peak (Bisconti et al., 2018)
* Blood flow AUC response is 29% lower following RMT training (Bisconti et al., 2018)

## Duration

* 12 weeks
  + (Miozzo et al., 2018)
  + (Sadek et al., 2022)
  + improvements initially became apparent at week 3 and continued to increase through week 12 (Winkelmann et al., 2009)
  + (Elshafey & Alsakhawi, 2022)
  + (Dos Santos et al., 2019)
  + [@azeredoInspiratoryMuscleTraining2022]
  + (Palau et al., 2022)
* 4 months
  + (Trevizan et al., 2021)
* 6 months
  + [@schaefferEffectsInspiratoryMuscle2023]
* 4 weeks
  + (Alwohayeb et al., 2018)
  + (Bhatnagar et al., 2021)
* 8 weeks
  + (Del Corral et al., 2023)
  + [@ahmadnezhadInspiratoryMuscleTraining2020]
  + (Langer et al., 2018)
  + (Campos et al., 2018)
  + (Tanriverdi et al., 2023)
* 5 days
  + (Benli et al., 2024)
* 2 weeks
  + [@abodonyaInspiratoryMuscleTraining2021]