# The effects of COVID-19 on respiratory muscle performance: making the case for respiratory muscle testing and training

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**SARS-CoV-2 infection itself may cause damage to the respiratory muscles and may contribute to the acute and persistent dyspnoea in patients with COVID-19. Respiratory muscle testing and training appears to be important for patients with COVID-19.** https://bit.ly/3vxwKGG

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## Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection results in multiorgan damage primarily mediated by viral infiltration *via* angiotensin-converting enzyme-2 receptors on the surface of cells. A primary symptom for many patients is exertional dyspnoea which may persist even beyond recovery from the viral infection. Respiratory muscle (RM) performance was hypothesised as a contributing factor to the severity of coronavirus disease 2019 (COVID-19) symptoms, such as dyspnoea, and outcomes. This was attributed to similarities between patient populations at elevated risk for severe COVID-19 symptoms and those with a greater likelihood of baseline RM weakness and the effects of prolonged mechanical ventilation. More recent evidence suggests that SARS-CoV-2 infection itself may cause damage to the RM, and many patients who have recovered report persistent dyspnoea despite having mild cases, normal lung function or undamaged lung parenchyma. These more recent findings suggest that the role of RM in the persistent dyspnoea due to COVID-19 may be more substantial than originally hypothesised. Therefore, screening for RM weakness and providing interventions to improve RM performance appears to be important for patients with COVID-19. This article will review the impact of SARS-CoV-2 infection on RM performance and provide clinical recommendations for screening RM performance and treatment interventions.

## Introduction

At the start of the coronavirus disease 2019 (COVID-19) pandemic, most attention was focused on the effects of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the lungs. This was because SARS-CoV-2 infiltrates the body through the mucosal membranes in the nasopharynx and larynx and coronaviruses typically affect the respiratory system [1, 2]. Additionally, many patients with severe COVID-19 developed acute respiratory distress syndrome (ARDS) and respiratory failure requiring mechanical ventilation (MV) [1]. It is now apparent that SARS-CoV-2 infection results in multiorgan damage primarily mediated by viral infiltration *via* angiotensin-converting enzyme-2 (ACE-2) receptors on the surface of cells [1, 3]. However, the extent of this damage to organs remains unclear, particularly in cases of COVID-19 not requiring hospitalisation [3].

What is consistent across many cases, irrespective of severity, are symptoms of exertional dyspnoea that persist beyond acute recovery from the viral infection. Approximately 82% of hospitalised patients and

38% of nonhospitalised patients with COVID-19 develop dyspnoea [4]. At 2 months post-hospitalisation it has been reported that 43% of patients with COVID-19 may still experience dyspnoea [5]. Symptoms of dyspnoea may persist even in nonhospitalised patients [5]. In patients with PCR-confirmed COVID-19, Bliddal *et al.* [6] found that 10% continued to report symptoms of dyspnoea at both 4 and 12 weeks following diagnosis. However, the prevalence of persistent dyspnoea in both mild and severe cases may be even greater. An online survey study by Goërtz *et al.* [7] found that over 71% of patients with COVID-19 who were never hospitalised reported experiencing dyspnoea 79 days post infection. Given the impact dyspnoea has on important clinical outcomes such as physical activity, psychological wellbeing and quality of life [4], identifying and addressing contributing factors is crucial for effective management of patients with COVID-19.

Early in the pandemic, respiratory muscle (RM) performance was hypothesised as a contributing factor to the severity of COVID-19 symptoms and outcomes [8]. The basis for this early hypothesis was that patients at risk for severe COVID-19 symptoms and poor outcomes are populations where RM weakness and increased demands of breathing are more prevalent [8]. A viral infection such as SARS-CoV-2, which causes inflammatory damage to the lung parenchyma and decreases lung compliance, may cause an even greater imbalance between the demands of breathing (Pibr) and RM force-generating capacity (Pimax) [8]. Additionally, patients with severe cases of COVID-19 requiring MV may experience rapid RM atrophy and weakness which may further compound this imbalance [8, 9]. More recent evidence suggests that SARS-CoV-2 infection itself may cause damage to the RM [9, 10], and many patients who have recovered from COVID-19 report persistent dyspnoea despite having mild cases [6, 7] normal lung function [11] or undamaged lung parenchyma [12]. This suggests that the role of the RM in the persistent dyspnoea reported by patients with COVID-19 may be more substantial than originally hypothesised. Therefore, screening for RM weakness and providing interventions to improve RM performance appears to be important for patients with COVID-19. This article will review the impact of COVID-19 infection on RM performance and provide clinical recommendations for screening RM performance and treatment interventions.

## Impact of MV on RM performance

The management of patients with severe cases of COVID-19 often requires MV to improve oxygenation, ventilation and reduce the work of breathing. While MV is a crucial lifesaving intervention for patients with critical illness, there are major physiological consequences that may ensue. One notable adverse consequence of MV that has been consistently reported is the profound and rapid atrophy and weakness of the RMs [13, 14]. This acute pathology to the RM during MV has classically been reported in the diaphragm and is referred to as ventilator-induced diaphragm dysfunction (VIDD) [13]. The prevalence of VIDD has been reported to be 79% when assessed over the course of an intensive care unit (ICU) stay [15] and may occur even within 18 h of initiating MV [13]. Grosu *et al.* [16] reported that patients under MV demonstrate a reduction of diaphragm muscle thickness at a rate of 6% per day. Jaber *et al.* [17] reported that 1 week of MV results in a 32% reduction RM strength assessed *via* twitch tracheal airway pressure. While these acute changes to the RM following MV have been primarily reported in the diaphragm, findings from more recent studies have demonstrated that changes to the extra-diaphragmatic RM may also occur. Nakanishi *et al.* [18] reported that 76% of patients with diaphragm atrophy following MV demonstrated concurrent reductions in intercostal muscle thickness. Interestingly, a subset of patients in that same cohort demonstrated changes to intercostal muscle thickness independent or in the opposite direction of changes to diaphragm muscle thickness. However, the majority of patients in that cohort demonstrated changes to both the diaphragm and intercostals in the same direction [18]. Additionally, pathology to the expiratory muscles has also been reported in patients with critical illness requiring MV and may also occur independently of changes to the diaphragm [19].

Multiple pathophysiological mechanisms have been attributed to these changes to the RM following MV, including but not limited to muscle proteolysis, dysfunction of the contractile elements, mitochondrial dysfunction and oxidative stress [14, 20–23]. It has been suggested that the underlying pathophysiological mechanism causing this is the inflammatory state of critical illness [21, 24]. However, several studies have demonstrated that VIDD, for example, can develop even in the absence of sepsis and does not require a systemic inflammatory state [13, 21]. One theory is that inactivity of the RM occurring under MV may be the major factor, especially under continuous mandatory ventilation [20, 21]. Partial-support MV, where some RM activity is preserved, has been shown to prevent muscle proteolysis of the diaphragm, which may help protect against the development of VIDD [14, 21].

While these acute reductions in RM strength can be profound and impair the ability of patients to be successfully weaned off MV, the demands of tidal breathing are generally far below the typical capacity of

the RM (Pibr/Pimax). Tidal breathing in healthy individuals only requires ~5–10 $cmH_2O$ and ~40 $cmH_2O$ to fully recruit the alveoli of a healthy lung [25–27]. The average maximal inspiratory pressure (MIP) generated by healthy adult males aged 18–29 years is 128 $cmH_2O$ (116.3–139.5 $cmH_2O$) and 97 $cmH_2O$ (88.6–105.4 $cmH_2O$) for females [28]. Therefore, even a hypothetical 50% reduction of peak RM strength caused by MV in a healthy adult would still place the demands of tidal breathing at less than 10% of their capacity. However, in patients with underlying RM weakness, the acute impairments resulting from MV may cause the demands of tidal breathing to approximate the peak capacity of the RM and may result in dyspnoea (figure 1). This relationship between underlying RM weakness and the acute effects of MV is supported by the association between lower diaphragm thickness at baseline and an increased risk of failing to wean off MV [29]. Many patients at risk of failure to wean off MV have been shown to possess RM weakness, especially those who are obese [8, 30]. Additionally, MIP, a measure of peak RM strength, is associated with MV weaning outcomes [30]. Further, previous research has indicated pre-operative RM training (RMT) improves RM strength and weaning outcomes following surgery [31].

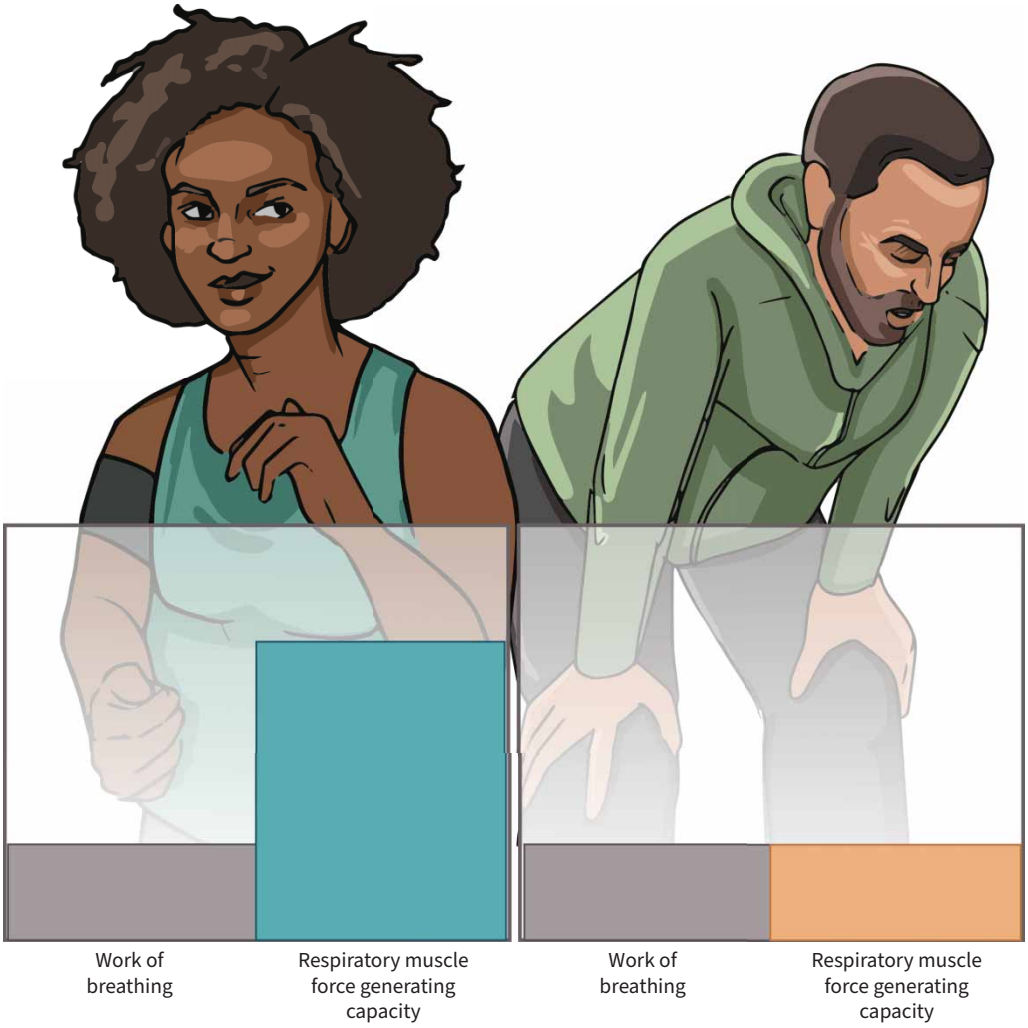


**FIGURE 1** The relationship between respiratory muscle strength and dyspnoea. Normally the respiratory muscles operate at a high efficiency rate where the work of breathing is far below the force-generating capacity of the respiratory muscles. This reserve of force-generating capacity of the respiratory muscles allows individuals to tolerate increases in the work of breathing such as during exercise without experiencing dyspnoea (patient on the left). However, when the work of breathing approximates the force-generating capacity of the respiratory muscles, patients may experience dyspnoea (patient on the right). This can be caused by an increase in the work of breathing (increased airway resistance or reduction in respiratory system compliance) or a reduction in the force-generating capacity of the respiratory muscles.

## Independent effects of COVID-19 on RM performance

There is growing evidence that COVID-19 infection may independently cause damage to the RM [3]. This hypothesis was introduced by Severin *et al.* [8], who proposed that RM may be an underappreciated factor contributing to COVID-19 outcomes, specifically noting poorer COVID-19 outcomes in patient populations known for possessing baseline RM weakness and increased demands of breathing. For example, in patients who are obese, the demands of breathing can increase threefold, and obesity is one of the strongest risk factors for severe COVID-19 symptoms and poor outcomes [8]. The hypothesised role of the RM in COVID-19 outcomes has gained further support as newer evidence has emerged.

A *post mortem* study by Shi *et al.* [10] compared the RM tissue of patients admitted to the ICU with COVID-19 to those without this viral infection. They reported that ACE-2 was expressed in the myofibre membrane of the human diaphragm and found evidence of viral infiltration of SARS-CoV-2 in the diaphragm myofibres of a subset of patients (four out of 26) who died from COVID-19. Importantly, despite similar durations of MV usage and ICU stay, patients with COVID-19 demonstrated an increased expression of genes associated with fibrosis and a twofold increase in both epimysal and perimysal fibrosis compared to those without COVID-19 [10]. A prospective observational study by Farr *et al.* [9] used ultrasonography to compare the diaphragms of patients admitted to an inpatient rehabilitation hospital following MV for severe COVID-19 infection (n=21) to those following MV without COVID-19 (n=11). They found that 76% (16/21) of the patients recovered from COVID-19 had at least one sonographic abnormality of diaphragm muscle structure or function compared to 45% (5/11) in non-COVID-19 patients [9]. The mean thickening ratio (*i.e.* diaphragm thickness at end-inspiration/end-expiration) for patients recovered from COVID-19 (1.14±0.19) was also significantly lower than in patients who did not have the viral infection (1.53±0.46) (p=0.0278) [9]. Notably, there was no significant difference in the length of MV use or circulating biomarkers between the COVID-19 and non-COVID-19 groups [9]. A cross-sectional study by Hennigs *et al.* [32] of patients 5 months post COVID-19 infection reported RM weakness in 88% of all patients and in 65% of nonhospitalised patients. In summary, it has become apparent that COVID-19 may directly cause damage to the RM that may contribute to the persistent dyspnoea, especially during physical exertion, reported in this patient population.

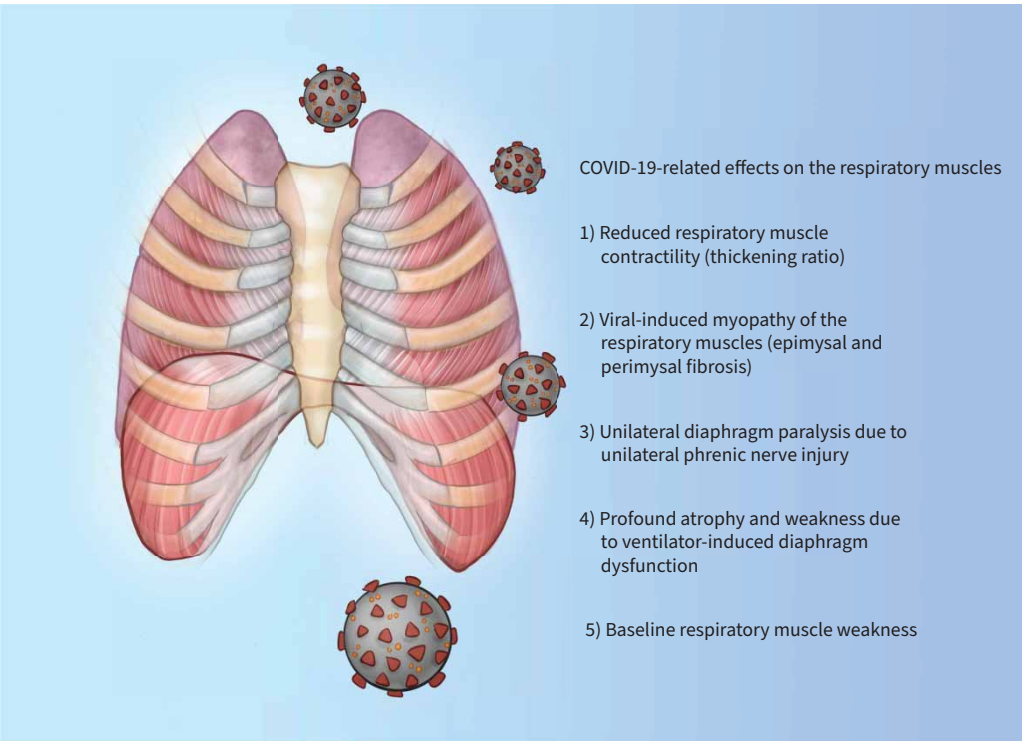


**FIGURE 2** Coronavirus disease 2019 (COVID-19)-related effects on the respiratory muscles. This figure highlights the effects of COVID-19 on respiratory muscles. Some of these effects are due to the fibrotic damage induced by the viral infection [9, 10], while others may be related to mechanical ventilation and baseline health status [7].

In addition to COVID-19-induced myopathic damage to the RM, there is emerging evidence suggesting that COVID-19 may infiltrate and affect structures involved in the neural control of breathing [16, 33, 34]. Three case studies have reported unilateral diaphragm paralysis following COVID-19 infection which were unrelated to MV or iatrogenic injury to the neck [34, 35]. In each case, the patients reported severe dyspnoea post resolution of the COVID-19 infection, but the lung parenchyma were normal on computed tomography images [34, 35]. FRANZ *et al.* [36] reports a case series of 32 survivors of severe COVID-19 who suffered peripheral nerve injuries and identified five patients with unilateral phrenic nerve injury. It is quite possible that many other cases of phrenic neuritis post-COVID have been missed since not even all academic centres have access to sonographers with protocols and experience scanning the phrenic nerve and/or diaphragm [37], which has been reported to be both highly sensitive and specific for the diagnosis of phrenic nerve injuries [38]. Another *post mortem* analysis by BULFAMANTE *et al.* [39] of two patients with severe COVID-19 demonstrated histological evidence of viral infiltration and pathology to the respiratory control centre. Altogether, these reports suggest that the effects of COVID-19 on RM performance and subsequent dyspnoea is perhaps neuromuscular in nature. More studies will be needed to further explore the aetiology and impact of COVID-19 on RM performance and clinical outcomes.

The available evidence for RM performance playing a substantial role in the symptomology and clinical outcomes in patients with COVID-19 is compelling (figure 2). As described previously, COVID-19 infection alone appears to induce myopathic damage to the RM that can be compounded by acute RM weakness if a patient requires MV. Additionally, patients at the highest risk for severe COVID-19 are populations where baseline RM weakness is more frequently encountered [8]. The combination of these different factors may explain why certain patient demographics are associated with a higher risk of severe cases and poorer outcomes following COVID-19 infection [8]. This may also explain the clinical phenotype of patients with COVID-19-related ARDS that had relatively normal lung compliance [1, 40, 41]. They may also explain the persistent dyspnoea reported in COVID-19 survivors despite the lung parenchyma remaining undamaged.

It is the opinion of the authors that RM performance testing should be strongly considered by clinicians to screen patients at increased risk for severe COVID-19 outcomes and when examining patients with persistent dyspnoea following acute COVID infection. Unfortunately, assessing RM function and RMT remains underappreciated and underutilised in clinical practice and is rarely performed [8]. There are also limited studies investigating the role of RMT in patients with COVID-19. Fortunately, assessments of RM function and RMT are easy to perform [42, 43], practice guidelines and normative values are available [28, 42], and the devices needed for assessment and training are fairly inexpensive [8, 28].

## RMT

To adequately prescribe RMT, a baseline assessment of RM function must be performed. Both in clinical practice and research, noninvasive handheld manometers are most frequently used to measure RM strength [28, 42]. These devices possess excellent reliability in addition to being affordable and accessible [8, 28, 42]. For patients without use of their mouth for breathing, measurements can be taken using a nasal probe for sniff pressure [28]. The most widely utilised measure of RM performance is MIP, which is a measure of peak inspiratory muscle strength [28, 42]. To assess MIP, patients are instructed to fully expire and then perform a maximal inspiratory effort for at least 1.5 s. The peak negative pressure sustained for at least 1 s during that inspiratory manoeuvre is considered the MIP. A minimum of three trials and a maximum of eight are performed with 1 min of rest between trials [28]. Each trial result should be within 10% of each other to be considered acceptable, and the highest value recorded during testing is then used for the MIP [28, 42].

In addition to measurements of peak static inspiratory muscle strength such as MIP, measures of endurance can also be performed [28, 42]. Two of the more commonly used testing protocols are constant load and incremental load [28, 42]. Constant load testing requires the patient to breathe against a submaximal constant load at a set cadence until task failure [28, 42]. The load is selected based on the MIP and it is recommended that it should be sufficient for the patient to attain task failure after 5–10 min of testing [28, 42]. The primary outcomes are time until fatigue and the total work performed during the test (testing time×testing load). Incremental load testing requires the patient to breathe against a load that is increased by a set amount (*i.e.* 10 $cmH_2O$) at regular intervals (time or number of breaths) until task failure [28, 42]. The primary outcomes are the pressure of the last completed step and time to task failure [28, 42]. For further details on MIP and other forms of RM testing, including expiratory muscle testing, we recommend referring to the European Respiratory Society statement on RM testing [28].

Another option to measure to assess RM performance is the test of incremental respiratory endurance (TIRE) [44]. The TIRE also requires the patient to breathe in maximally through the manometer from

residual volume to total lung capacity [44]. However, unlike MIP, during the TIRE the patient also sustains that maximal inspiration for as long as possible and inspiratory pressure measurements are continuously recorded [44]. Due to the format of this test, the TIRE provides MIP and several other measurements of RM performance [44]. Inspiratory duration, which is measured in seconds, represents the duration of the maximal sustained inhalation and is considered a measurement of RM endurance [44]. Sustained maximal inspiratory pressure (SMIP) is the area under the curve of the plot of inspiratory pressure measured over time. SMIP is expressed in pressure time units or joules and represents single-breath work capacity [44]. Lastly, the slope of the SMIP plot can also be measured and the result reflects the fatiguability of the RM (higher slopes indicating greater fatiguability) [45–47]. An example of a recording from the TIRE and the testing data provided is given in figure 3. The use of these additional measurements provided by the TIRE offers a more robust assessment of RM performance. The results may also identify different characteristics of RM performance that may be missed when only measuring MIP [46, 47]. Normative data has been published for the TIRE in healthy populations [45].

## Practical considerations for RMT

The broad and complex symptom profile of patients recovering from COVID-19 highlighted earlier in this article outlines the need for individualised approaches to address multidimensional symptomology [3]. The role and efficacy of RMT interventions has been outlined extensively in the literature. However, special consideration should be given to the approach, volume, intensity and frequency of RMT to optimise efficacy and outcomes.

### *Adherence and tolerance*

Clinicians must consider the ability for patients with COVID-19 to consistently participate in an RMT protocol. The goal should be to select an evidence-based intervention that incorporates the perspectives of the patient [48]. The authors have experience adopting such an approach in the first RMT protocol used in patients discharged from hospital with community-acquired pneumonia, where adherence was high (99.4%) [49]. It is also important to ensure that RMT protocols are well tolerated by patients, which may be influenced by disease status and symptom severity. Patients demonstrating significant reductions in RM strength and reporting more severe dyspnoea will demonstrate lower tolerance to RMT. Therefore, adjusting to the patient's status is likely to be more effective than traditional RMT protocols.

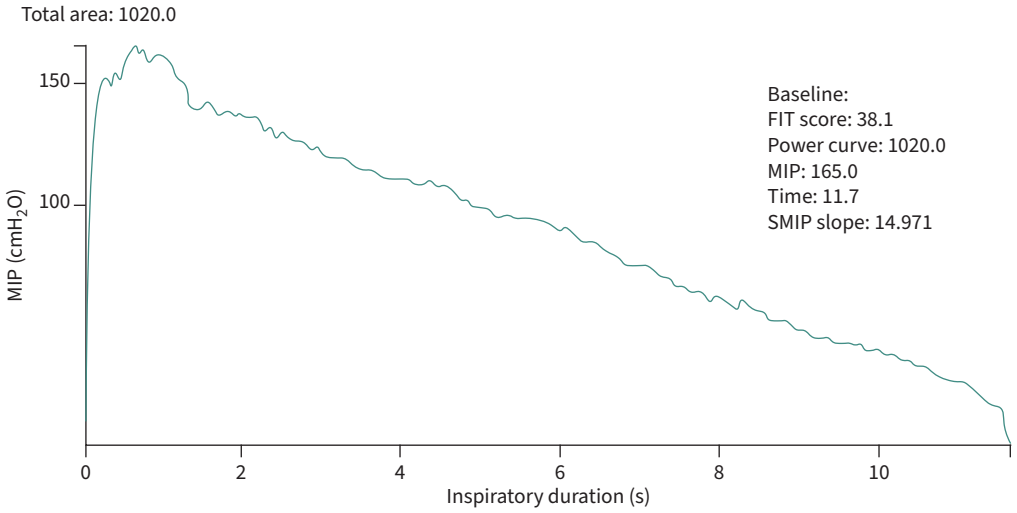


**FIGURE 3** Example report from the test of incremental respiratory endurance (TIRE). The TIRE provides a comprehensive assessment of the respiratory muscles. Participants perform a maximal and sustained inspiratory effort following a full expiration. Several measurements of respiratory performance are provided: 1) strength – maximal inspiratory pressure (MIP), the peak static inspiratory pressure generated which is provided in centimetres of water ($cmH_2O$); 2) endurance – inspiratory duration, the duration of the maximal breath in which is provided in seconds; 3) single breath work capacity – sustained maximal inspiratory pressure (SMIP) the area under the curve of pressure over time which is provided in pressure time units; 4) fatiguability – the slope of the SMIP plot (SMIP slope). FIT: fatigue index test.

### *Frequency, intensity and volume*

Manipulation of variables to increase muscular strength and endurance are well documented throughout strength-training literature and are directly related to RMT approaches [50]. While methodological approaches vary, the use of pressure threshold loading (PTL) techniques are commonplace in athletic and clinical studies due to their ability to increase RM strength and endurance, ease of use, acceptance in clinical and sporting domains, and the ability to conduct sessions independent of research and clinical settings [51]. PTL techniques require participants to produce a negative pressure that is sufficient to overcome a pre-set threshold that loads the respiratory musculature. The efficacy of RMT interventions that use PTL techniques has been demonstrated in numerous clinical groups, using intensities ranging from 40 to 80% of MIP [51]. The debate surrounding the optimal training intensity for RMT interventions is longstanding, but evidence indicates that 40–50% of MIP is most effective [8]. However, it is important to consider the tolerability of conducting sessions >50% of MIP. Acute respiratory infections present a complex clinical picture where baseline RM strength could be altered by fluctuating physiologic status and symptomology. Therefore, the use of variable-resistance approaches that account for within- and between-day changes in RM strength may optimise training stimuli and outcomes.

Training volume and frequency are also subject to variation within the available literature and further research is needed to determine the most effective approach for clinical groups. Observations within the current literature highlight that training twice daily, five to seven times a week is common and continually demonstrates improved strength and endurance [51]. Similarly, training volume is still heavily debated. Traditional RMT protocols, such as 30 breaths per session performed twice per day, could hinder session tolerability and adherence. Recent pilot work demonstrated an incremental approach to build session volume in patients discharged with community-acquired pneumonia [49]. This approach could provide an alternative approach to increasing training volume to optimal levels in patients with COVID-19.

## The effects of RMT

Previous work has reported the effects of RMT in improving weaning off MV [52], physical function and balance [53]. These aspects led to extensive research and the use of RMT in clinical practices [53]. Additional studies have demonstrated that RMT results in improvements of quality of life, respiratory symptoms, activity tolerance and the ability to carry out activities of daily living [54]. The efficiency of RMT in improving such clinical outcomes has been demonstrated in several clinical populations with RM weakness including but not limited to asthma, heart failure, chronic obstructive pulmonary disease (COPD) and patients with neuromuscular disorders [55]. It is then possible to consider the potential use of RMT in COVID-19 rehabilitation. McNarry *et al.* [56] reported clinically meaningful improvements in RM strength, dyspnoea and other respiratory symptoms in patients 4 months post COVID following 8 weeks of home-based RMT. In addition, Abodonya *et al.* [57] demonstrated improvements in pulmonary function, dyspnoea, functional performance and quality of life in recovered ICU COVID-19 patients with only 2 weeks of RMT. However, more studies are warranted to investigate the reliability and feasibility of RMT as a standalone intervention as well as in combination with rehabilitative strategies for patients with COVID-19.

### *Alleviating fatigue and dyspnoea*

Deconditioning of the RM system is prominent in people living with acute and chronic respiratory conditions [8], including patients recovering from COVID-19 [57]. In addition, reductions in RM strength and dyspnoea have been heavily reported in the post-acute COVID-19 phase [58]. Owing to its prevalence, debilitating properties and broader implications for quality-of-life, dyspnoea is a common primary outcome in RMT studies in respiratory populations and is inherently linked to RM weakness [59]. RM deconditioning leads to an increased incidence of RM fatigue and elevated perceptual responses including dyspnoea and whole-body exertion during light exercise and activities of daily living [60, 61]. RMT approaches have been continuously demonstrated to be well tolerated and acceptable to clinical populations [55]. RMT is well documented to reduce perceptions of exertion, limb discomfort and dyspnoea responses [62]. Improved RM strength following RMT leads to a reduction in the relative work done by the respiratory musculature during exercise and physical activity [62, 63].

Mechanistically, the modulation of dyspnoea and perception of exertion following RMT interventions is likely the result of reduced afferent discharge frequency [64]. The respiratory musculature, specifically the diaphragm, comprises a complex network of group III and IV afferent nerve endings that project into the sensorimotor cortex *via* the dorsal horn to regulate ventilatory and circulatory responses and act as a continuous feedback mechanism between the central and peripheral nervous systems [65]. Repeated bouts of RMT increase the capacity of the RMs and whole-body performance through reductions in perceptual strain during exercise tasks occurring *via* an altered discharge frequency of the mechano-sensitive type III

and IV nerve afferents [65]. Due to increased capacity, exercise tasks are completed with reduced mechanical demand on the RM, which in turn reduces afferent feedback for a given workload and the perception of effort and breathing discomfort [64]. During relatively high-intensity exercise in patients with RM weakness, the RM metaboreflex may be induced which results in reduced locomotor muscle perfusion in order to preserve diaphragmatic blood flow [66–68]. This RM fatigue induced metaboreflex has been attributed to the leg fatigue and exercise intolerance most notably encountered in patients with heart failure [66–68]. However, recent work has also demonstrated that high-intensity exercise impairs perfusion in the extradiaphragmatic RMs (intercostal, scalene and abdominal) in patients with COPD, which is related to greater effort perceptions [69]. These blood flow changes to both muscle groups have been reported following RMT [70, 71].

### *Improving physical function*

Physical function is defined as an objective performance measure in which an individual is asked to perform a specific task and is evaluated in an objective, uniform manner using pre-determined criteria, which may include counting of repetitions or timing of the activity as appropriate [72]. In patients with COPD, significant improvements in 6-min walk test (6MWT) performance have been reported in several studies following 6–8 weeks of RMT [72]. Similar results have been reported in patients with chronic heart failure [73]. Further studies are now emerging that combine standard rehabilitative intervention (*e.g.* the Otago exercise programme) with RMT, named functional inspiratory muscle training, for patients with COPD showing significant improvements in physical function (*i.e.* 6MWT) and balance (*i.e.* the Berg balance scale) outcomes [74]. The effects of RMT on physical function have been widely documented. A study by Ferraro *et al.* [75] demonstrated the potential use of RMT as a standalone intervention to improve physical function and balance outcomes (mini balance evaluation test and timed up and go) in healthy older adults (aged 76–85 years old). Considering the low physical function documented in COVID-19-discharged patients [76], and the positive effect on balance and physical function reported after 6–8 weeks of RMT, it is possible to conceive a potential use of RMT as a standalone intervention or in combination with current rehabilitative practices for COVID-19-discharged patients. Indeed, similar interventions have been already introduced, where the improvements in the 6MWT appear to be significant after just 2 weeks of RMT [57]. The advantages of using RMT as an intervention to improve balance and physical function are its pragmatism as it is self-managed, with low costs and low risks. However, further studies are necessary to produce a tailored intervention that clinicians and health workers can adopt to enhance COVID-19 rehabilitative strategies worldwide.

**Points for clinical practice**

- SARS-CoV-2 infection itself may cause damage to the RMs.
- This viral infection mediated damage to the RMs may contribute to the acute and persistent dyspnoea in patients with COVID-19, especially in combination with VIDD and impairments in RM performance at baseline.
- RM testing and training appears to be an important component of the management of patients with COVID-19.

**Questions for future research**

- What is the efficacy of RMT for improving dyspnoea of patients with post-acute COVID-19 across different levels of severity?
- What is the ideal time to safely initiate RMT?
- To what extent is the viral-mediated damage to the RMs reversable with respiratory training?

## Conclusion

In addition to other organ systems, the available evidence suggests that SARS-CoV2 infection may result in specific damage to the RM. This acute pathology to the RM in patients with COVID-19 is likely further compounded by underlying health conditions, effects of MV and other COVID-19 pathology that impairs RM performance and increases the work of breathing. These factors combined may explain both the acute and persistent dyspnoea and other functional limitations demonstrated in patients with COVID-19. The role and efficacy of RMT in improving dyspnoea and other key functional outcomes are well established for patients across multiple health conditions. Due to the direct impact of SARS-CoV2 infection on RM performance it is becoming apparent that RM testing and RMT will play a key role in the rehabilitation of patients with COVID-19. However, evidence for the role of RM testing and RMT in the rehabilitation of patients with COVID-19 is still emerging. Further research is needed to determine the most appropriate RM testing and RMT protocols for patients with COVID-19 and the effect of RMT on key functional outcomes.

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