

# Expiratory Muscles of Respiration and Weaning Failure: What do We Know so Far?

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Successful weaning from mechanical ventilation involves a combination of factors, resolution of primary disease, the strength of the respiratory muscles, balance of load and respiratory muscle capacity, and intact central drive. The respiratory muscle pump comprises three groups of muscles: the diaphragm, accessory inspiratory, and expiratory muscles, and plays a pivotal role in the weaning and liberation of mechanical ventilation. Most research on respiratory failure has focused on the diaphragm and its weakness linked to adverse patient outcomes, including prolonged mechanical ventilation and mortality. However, the role of expiratory muscles, which are constituted of abdominal skeletal muscles like transversus abdominis, internal oblique, external oblique, and rectus abdominis, and rib cage muscles (internal oblique and transversus thoracic muscles) is mainly unexplored in the literature.

## ROLE OF ABDOMINAL EXPIRATORY MUSCLES IN RESPIRATION

Exhalation is passive during tidal respiration, and expiratory muscles are mainly inactive. Expiratory muscle activation occurs during an imbalance of capacity and demand (load) on inspiratory muscles. Expiratory abdominal muscles recruit hierarchically during an imbalance, with transverse abdominis being the first to activate, followed by internal and external obliques, and finally, rectus abdominis. Conditions like low pulmonary compliance, intrinsic positive end-expiratory pressure (iPEEP), and even exercise can produce high respiratory muscle load. Lower capacity of respiratory muscles is observed with respiratory muscle weakness, both inherent or acquired [e.g., ICU-acquired weakness (ICUAW)].<sup>1</sup>

In healthy individuals, the recruitment of abdominal muscles may help to overcome the increased demand. The increase in abdominal pressure, produced by muscle contraction, is transmitted across the diaphragm to pleural space and increases pleural pressure ( $P_{pl}$ ). Increasing pleural pressure decreases the expiratory transpulmonary pressure [ $P_{tp}$  = alveolar pressure ( $P_{alv}$ ) -  $P_{pl}$ ]. Lower  $P_{tp}$  during expiration helps in lung deflation and reduces lung strain. Moreover, abdominal muscle contraction also stimulates inspiration. The abdominal muscle contraction shifts the diaphragm cranially to a more favorable position for tension gradient. It also reduces expiratory lung volumes by increasing abdominal pressure, creating an elastic recoil before the next inspiration. Finally, expiratory muscles play an essential role in an effective cough. Expiratory muscle weakness has been linked to an

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increased risk of pneumonia or atelectasis because of its negative effect on the strength and peak flow velocity of cough.<sup>1,2</sup>

In critically ill patients with acute respiratory distress syndrome (ARDS) or atelectasis, increased pleural pressure may result in negative  $P_{tp}$ , causing cyclical alveolar and airway collapse. This may also increase the risk of ventilator-induced lung injury.<sup>3,4</sup> The benefit of neuromuscular blocker agents (NMBA) in patients with ARDS on mechanical ventilation may be explained partially by paralysis of the abdominal skeletal muscles. This was observed with significantly higher  $P_{tp}$  in the NMBA group compared with the control ( $1.4 \pm 2.7$  cm H<sub>2</sub>O vs  $-1.8 \pm 3.5$  cm H<sub>2</sub>O,  $p = 0.02$ ).<sup>5</sup> Dynamic airway closure during expiration also results in expiratory flow limitation and the development of iPEEP, especially in patients with obstructive airway disease.<sup>6</sup> Finally, expiratory muscle recruitment is observed during weaning from mechanical ventilation, where an imbalance exists between respiratory muscle capacity and load. In a cohort study of 20 patients, a significantly higher effort of expiratory muscles (as measured by expiratory gastric pressure time product) was observed in patients with weaning failure.<sup>7</sup> In another study of 37 patients, recruitment of expiratory muscles was associated with higher chances of failure of a spontaneous breathing trial.<sup>8</sup>

## RISK FACTORS FOR EXPIRATORY MUSCLE WEAKNESS IN CRITICALLY ILL PATIENTS

Sarcopenia is defined as a loss of muscle strength, mass, and function. Respiratory sarcopenia has been found to be a poor prognostic marker for mechanical ventilation-free days, ICU and hospital

length of stay, and mortality.<sup>9</sup> ICU-acquired weakness is usually associated with both peripheral and diaphragmatic weakness. Various risk factors are linked to ICUAW and weakness of the diaphragm. However, the impact of these risk factors on expiratory muscles is unknown.<sup>10</sup> In this issue of the journal, Vishwas et al., in a retrospective study, found nutrition status as an independent risk factor for loss of abdominal expiratory muscle mass. They evaluated nutrition through modified nutritional risk in critically ill (mNUTRIC) score and used ultrasound to measure muscle thickness.<sup>11</sup> A recent review by Shi et al., proposed sepsis, systemic inflammation, mechanical ventilation, chronic obstructive pulmonary disease (COPD), preexisting myopathies, drugs (like NMBA, corticosteroids, and sedatives), and intra-abdominal hypertension are other risk factors for expiratory muscle weakness.<sup>1</sup>

## EXPIRATORY MUSCLE THICKNESS ON LIBERATION FROM MECHANICAL VENTILATION

Mechanical ventilation is commonly associated with diaphragmatic deconditioning and weakness. However, the effect of mechanical ventilation on expiratory muscles is unknown. A recent ultrasound study in children showed loss of thickness of expiratory abdominal wall muscles in patients on mechanical ventilation. Moreover, there was a rapid thickness loss (by more than 10%) in 44% of children within 4 days of mechanical ventilation.<sup>12</sup>

In another recent retrospective study, patients with prolonged weaning had lower muscle mass of expiratory abdominal skeletal muscles compared with simple weaning.<sup>13</sup> However, there was no correlation found between expiratory muscle and diaphragm thickness.<sup>12,13</sup> Another ultrasound-based study showed time-dependent loss of muscle thickness in 22% of patients on mechanical ventilation. Increased muscle thickness was also observed in another 12% of patients and resulting from increased interparietal fascia thickness.<sup>14</sup>

Patients failing tracheal extubation were found to have lower maximum expiratory pressure (MEP) compared with those with successful extubation. Maximum expiratory pressure surrogates the activity of expiratory muscles. Hence, expiratory muscle weakness is a predictor of weaning failure.<sup>15</sup> The pathophysiology of weaning and extubation failure with expiratory muscle weakness is, however, an area of ongoing research. Proposed mechanisms include inadequate cough and secretions clearance, decreased contractility of the diaphragm, or inadequate reduction of iPEEP.<sup>16</sup>

## ASSESSMENT OF EXPIRATORY MUSCLE IN A CRITICALLY ILL PATIENTS

Measurement of muscle mass is challenging in critically ill patients. Reference standard tools for measuring muscle mass, such as dual-energy X-ray absorptiometry (DXA), are rarely feasible in critically ill patients because of the risk for transfer out of ICU, costs, and radiation exposure.<sup>16</sup>

CT and MRI are other measuring tools that may offer precise, accurate, and reliable measurements like muscle cross-sectional area and volume. However, the risk of transfer, radiation, and inability to follow-up examination are some limitations. Bioelectrical impedance analysis (BIA) is another imaging methodology evaluated in muscle thickness analysis. However, BIA may be challenging in ICU patients owing to considerable fluid shifts and peripheral edema.<sup>17</sup>

Ultrasonography is a safe, easy, reproducible, and noninvasive bedside tool increasingly becoming popular in ICUs to assess various organ systems. Ultrasound-guided diaphragmatic excursion assessment in critically ill patients is widely used during weaning. However, ultrasound has a few limitations and challenges for skeletal muscle assessment. There is insufficient data to define weakness based on any cutoff values of respiratory muscle mass. The training and competency of ultrasonography need to be standardized. There is also a lack of standardization of landmarks, reporting methods, reliability testing, measurements (cross-sectional area vs muscle thickness), and muscle site. Finally, small measurement errors (technically or physiologically) can substantially change the interpretation of results.<sup>18</sup>

The measurement of the strength of expiratory muscles involves the measurement of MEP. Recruitment of abdominal pressure will increase intrabdominal pressure, which can be measured by gastric balloon or urinary bladder catheter. The gastric balloon can be used to calculate gastric-pressure amplitude and gastric-pressure product, which surrogates the expiratory muscle effort.<sup>7</sup> Cough test, a simple bedside manoeuvre, can also evaluate expiratory muscle weakness. Peak expiratory flow rate in nonventilated or ventilated patients at the endotracheal tube is also used as a surrogate to expiratory muscle strength.<sup>1</sup>

## STRATEGIES TO IMPROVE EXPIRATORY MUSCLE STRENGTH

Being a skeletal muscle, abdominal expiratory muscles are likely to regain strength from nutrition and physical activity interventions. Nutritional strategies like a high-protein diet, including essential amino acids or their metabolites (such as leukine), have been found to stimulate muscle protein synthesis. The primary goal of nutrition therapy is to gain and preserve muscle mass lost during the acute phase of illness. There are ongoing studies on the effect of neuromuscular electrical stimulation of the expiratory muscles to prevent atrophy.

In conclusion, expiratory muscles are essential for maintaining alveolar ventilation during higher respiratory effort, effective cough, and prevention of atelectasis. Weakness of the expiratory muscles is linked to weaning failure and a higher risk of reintubation. Although both the diaphragm and the expiratory abdominal wall muscles are essential to the respiratory muscle pump, future studies may confirm the exact role of expiratory muscles during mechanical ventilation and critical illness. Ultrasound is an emerging tool for bedside assessment of change in muscle mass. However, there is a need for standardization of ultrasound measurements for comparison and research.

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