Mechanical ventilation (MV) aims to support the failing ventilatory system. However, it is not always understood that MV has profound positive and negative effects on the cardiovascular system. In general, the haemodynamic effects of MV are decreased preload to the heart, increased right ventricle afterload but decreased left ventricle (LV) afterload. When considering MV effects, it is important to remember that the thorax acts as a pressure chamber; breathing in creates negative pressure that assists venous return.

The cardiovascular effects of MV include changes in lung volume and changes in intrathoracic pressure. Increased intrathoracic pressure associated with MV can increase external constraint and limit ventricular diastolic filling and, therefore, output. Even spontaneous ventilation during exercise is not without risk: it increases the preload and LV afterload, causes hypoxaemia and, in extreme circumstances, the high lung volumes and pressures can compress the heart. Intrathoracic pressure swings can lead to pulmonary oedema and where there is airway obstruction they can result in bleeding into the alveoli.

MV can severely affect venous return and left ventricle ejection. It is important to consider the concept of the ‘thoracic pump’ which is a determinant of venous return. In patients, low mean systemic filling pressure results in decreased venous return and reduced cardiac output. MV can also have an impact on pulmonary vascular mechanics. During both spontaneous and positive pressure MV, tidal changes in pleural pressure, transpulmonary pressure, and lung volume influence key components of haemodynamics: preload, afterload, heart rate, and myocardial contractility. It is important to titrate the mean airway pressure to optimise the balance between mean lung volume and ventricular function minimise pulmonary vascular resistance, and routinely monitor cardiorespiratory parameters closely.

Positive end expiratory pressure (PEEP) as an adjunct to MV can be beneficial in conditions including ARDS and acute cor pulmonale. PEEP can be increased when haemodynamic conditions permit it. The advantages of PEEP are decreased work of breathing, cardiac stress and LV afterload but disadvantageous are decreased preload and increased PVR and alveolar dead space. In moderate to severe ARDS, PEEP is used to drive pressure and oxygenation. Some limited data suggest that PEEP is safe for use and provides haemodynamic benefits in LV dysfunction/failure and cardiogenic shock.

Ventilator induced lung injury (VILI) is a suitable term for lung trauma seen in animal models but in patients it could be better termed ‘ventilator-associated’ or ‘healthcare-associated’ lung injury because it is not clear how much of the injury arises from the treatment or the disease. VILI arises as a result of various factors:

- Barotrauma (regional overdistension and gross air leaks)
- Volutrauma (damage caused by volume not pressure more subtle effects, oedema)
- Atelectrauma (low absolute lung volume, repetitive opening and closing)
- Biotrauma (secretion of cytokines attracting neutrophils leading to inflammation and tissue damage).

Several meta-analyses show that in patients without ARDS receiving MV there is an association between higher tidal volumes (6, 6–10 and ≥10 ml/kg) and worsened morbidity (pulmonary complications), mortality and longer duration of ventilation. Some of the studies reviewed, however, span long durations and in recent years tidal volumes used in MV have been generally decreasing.

To prevent LIVI it is necessary to prevent overdistension and recruit recruitable lung tissue. Therefore, low tidal volume is key. This was shown in a pivotal randomized trial of ARDS patients (n=821) in which 6 ml/kg PBW was associated with substantially improved survival and earlier liberation from ventilation than 12 ml/kg PBW. In the PreVENT study in ICU patients without ARDS (n=961), intermediate tidal volumes (8–10 ml/kg) were shown to be produce similar rates of survival, freedom from ventilation, ICU length of stay and hospitalisation as low tidal volumes (4–6 ml/kg PBW). The important message was that both low and intermediate volumes were equally safe in these patients.

Surgery is also associated with lung injury; various studies show...
that post-operative pulmonary complications (PPCs) are strongly associated with increased morbidity and mortality.\textsuperscript{15,16} The IMPROVE study (n=400) showed that low tidal volumes (6–8 ml/kg vs 10–12 ml/kg PBW) produced significantly fewer PPCs and shorter hospital stays (p=0.001).\textsuperscript{17}

Several studies in the past 20 years have shown that in prevention of atelectrauma, high PEEP does not improve outcomes in ICU patients with ARDS.\textsuperscript{18} A subsequent meta-analysis showed that high PEEP produces some reduction in mortality and time to unassisted breathing in patients with mild ARDS but these are increased in moderate to severe ARDS.\textsuperscript{19} Another large meta-analysis showed that higher PEEP overall seems not to benefit patients without ARDS and during surgery does not reduce PPCs.\textsuperscript{20} A further analysis showed that while higher tidal volume is associated with 30-day mortality, driving pressure is not.\textsuperscript{21} Overall, in the LUNG SAFE (ARDS), PROVENT (non-ARDS) and LAS VEGAS (post-operative) studies the tidal volumes were consistently 8 ml/kg PBW although some patients still receive higher volumes.\textsuperscript{22–24} LAS VEGAS study analyses revealed that females tend to receive higher tidal volumes than necessary and have consequently poorer outcomes. This results from body weight predictions that are inaccurate for smaller patients.

MV frequently harms the muscles of respiration, most notably, the diaphragm. Acute diaphragm failure often occurs soon after arrival in the ICU and results from sepsis, shock and systemic inflammatory response syndrome. Phrenic nerve stimulation studies show that 64% of patients show diaphragm weakness with 24 h of intubation.\textsuperscript{25} The key risk factors for this weakness were mainly disease severity and sepsis and it was associated with substantially increased ICU and in-hospital mortality.

Acquired diaphragm weakness tends to occur during MV as a result of diaphragm unloading and it increases with time of ventilation.\textsuperscript{26} This is supported by studies showing increasing degradation and reduction in the size of patient diaphragm muscle fibres, diaphragm thickness and contractile activity with time of MV.\textsuperscript{27,28} Diaphragm weakness also causes difficult and prolonged weaning of patients from ventilation, greater morbidity and mortality.\textsuperscript{29} There is, however, no apparent correlation between diaphragm and limb muscle weakness.\textsuperscript{30} Diaphragm dysfunction can be determined using sub-or intercostal ultrasound and thickness can be determined using high resolution ultrasound.

Other respiratory muscle groups can also be affected by MV. Recent studies show with weakening diaphragm there is corresponding thickening of intercostal muscles suggesting compensation by these muscles. Other studies show that intercostal muscle fraction thickening of >8% is indicative of weaning failure.\textsuperscript{31}

In addition to immediate adverse events, critical respiratory illness with MV often has long-term implications, complexities and morbidities that can profoundly affect quality of life. A study of ARDS survivors (n=109) found significant disability (distance walking and SF-36 scores of physical functioning) and weight loss (mostly due to muscle loss) up to 12 months after discharge.\textsuperscript{32} After 5 years, these patients still showed decreased walking and SF-36 scores that had plateaued below normal values.\textsuperscript{33} Other studies have shown fibrosis, myopathy and profound structural changes in muscle that may explain observed comorbidities.\textsuperscript{44} These are largely associated with sepsis, drug treatments and immobility.

MV is also associated with neurocognitive sequelae that affect processing speed (70% of patients), memory (60%), executive function (40%), attention (30%) and IQ (20%) and these functions usually do not return to normal.\textsuperscript{35} These effects are associated with MRI brain atrophy and white matter changes. A large-scale study of patients after critical illness (n=821) found that 40% of patients had cognitive dysfunction 1.5 SD below the mean and 26% were 2 SD below the mean.\textsuperscript{36} These changes were similar at 3 and 12 months and were not affected by patient age. The duration of delirium in the ICU correlated with the degree of subsequent cognitive dysfunction. In addition, many patients develop post-traumatic stress during and after their time on MV.\textsuperscript{37} Other common neuropsychological effects post ICU discharge include clinically significant depression (17%) and post-traumatic stress disorder (18–23%). Key risk factors for these conditions are morbidity before and during ICU, greater age, cognitive impairment, disease burden, organ dysfunction, duration of MV and severe sepsis. Despite awareness of these factors, it is not easy to modify patient outcomes and general health and vitality are substantially reduced even after 5 years.\textsuperscript{38}

After critical illness, patients are frequently left with various issues including lung/trachea damage, musculoskeletal problems, need for chronic dialysis, dysphagia, wound infections, vascular damage and hearing loss. The risk of these events and muscle injury generally increases with time on MV. It is also concerning that many patients deteriorate during the 12 months after discharge and substantial proportions remain out of work after 5 years.\textsuperscript{32,39} Long-term outcomes of MV are being investigated in the RECOVER Program (n=343) which has found that after 1 year, older patients are more likely to be hospitalised, readmitted to the ICU or be in rehabilitation than younger patients. This study also identified a significant burden of depression on caregivers during the year after patient discharge.\textsuperscript{39,40} This highlights the wider burden on caregivers that results in various conditions including psychiatric illness, PTSD, and reduced quality of life.

Overall, MV has both positive and negative cardiovascular effects resulting from decreased preload and LV afterload and increased RV afterload. The adverse haemodynamic effects of MV need to be recognised and minimised. LVI is a likely outcome of MV in all patients and results from different pathways of harm. It is particularly important to be aware of harm caused by volutrauma but also atelectrauma and biotrauma and that measures are taken to prevent them. Respiratory muscle dysfunction in MV is frequent and associated with poorer prognosis and inhibits recovery. Whilst this can be detected early, its prevention is a major challenge. MV causes multiple different comorbidities including neurocognitive effects that can last many years after discharge. These have long-term effects on ability to work and quality of life and create a heavy burden on carers. A seamless post-ICU care pathway is a substantial need that would improve outcomes for both patients and carers following MV treatment for critical illness.
References


