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INVITED COMMENTARY

Should We Assess Diaphragmatic Function During Mechanical Ventilation Weaning in Guillain–Barré Syndrome and Myasthenia Gravis Patients?

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Acute respiratory failure is the main reason for the admission of Guillain–Barré syndrome (GBS) and myasthenia gravis (MG) patients to the ICU. About 30% of GBS patients and 10 to 30% of MG patients will require mechanical ventilation (MV) over their disease course [1–3]. Once the disease and eventually its triggering event are treated, time for weaning begins. Liberation from MV, i.e. extubation success, constitutes the final achievement of this process. Outside the scope of neurocritical care unit (NICU), patients are now sorted into four weaning groups [4] (Table 1): the group "no weaning", made of patients who never experienced any separation attempt; the group 1 (short weaning): the first attempt resulted in a termination of the weaning process within 1 day; the group 2 (difficult weaning): the weaning was completed after more than 1 day but in less than 1 week after the first separation attempt and the group 3 (prolonged weaning): weaning was still not terminated 7 days after the first separation attempt. Even if the original study including 2729 patients did not excluded specifically GBS or MG patients, their proportion was likely to be limited and no study have used this classification in these patients. However, between 26 [5] and 75% [6] of GBS or MG patients are still under MV at day 7 and most authors assume that extubation failure accounts for 30% in those patients [5, 7]. Whereas prolonged MV is associated with an increased risk of ventilator-associated pneumonia, premature liberation is associated with increased risk of extubation failure and increased risk of mortality and morbidity [5, 8]. Hence, determining the optimal timing for extubation is of major importance.

Several questions arise when the weaning process begins: (1) which ventilation mode should be preferred to enable the respiratory muscles to both rest and not to waste? [9]; (2) when to start spontaneous breathing trials (SBT)?; (3) should positive pressure support (PSV) or T-piece trials be used for SBT?; (4) which respiratory parameters should be used to predict successful extubation?; and finally (5) is there any place for non-invasive mechanical ventilation (NIV) or high-flow nasal oxygenation to increase extubation success rate?

Synchronized intermittent mandatory ventilation is now discouraged since this mode was associated with prolonged weaning [8, 10], and pressure support ventilation (PSV) should be preferred over assisted ventilation when weaning begins [8, 11, 12]. In general ICU, readiness criteria to start SBT and readiness criteria for extubation are widely accepted and should probably at least be applied to NICU patients (Table 1) [8, 11]. In GBS and MG patients, forced vital capacity and maximal inspiratory pressure are frequently added to these minimal criteria (Table 1) [5]. Whereas no difference has been found in SBT duration when ranging from 30 min to 2 h in general ICU [8], most neurointensivists performed "prolonged" SBT in GBS and MG patients going from one to several hours, up to 12–24 h, but this practice is

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Table 1 Weaning according to a new definition (WIND) classification and criteria for considering a spontaneous breathing trial (SBT) in general ICU and in neurocritical ICU

Weaning according to a new definition (WIND) classification
Group "no weaning": made of patients who never experienced any separation attempt
Group 1 (short weaning): the first attempt resulted in a termination of the weaning process within 1 day (successful separation or early death)
Group 2 (difficult weaning): the weaning was completed after more than 1 day but in less than 1 week after the first separation attempt (successful separation or death)
Group 3 (prolonged weaning): the weaning was still not terminated 7 days after the first separation attempt (by successful separation or death)
Group 3a prolonged weaning leading to a successful weaning after 7 days or more after the first attempt
Group 3b prolonged weaning without success
Criteria for considering SBT
General ICU
Resolution of the medical condition that led to MV
Hemodynamic stability (BPM < 135/min, 90 < systolic arterial pressure < 160 mmHg with no need for vasopressors)
Patient awake or easily aroused (RASS between 1 and − 2) and sedation stopped
Patient able to cough effectively
SpO_2 > 90% with F_IO_2 < 40% or PaO_2/F_IO_2 > 150 and PEEP < 8 cm H_2O
RR < 35/min
pH > 7.35
Neurocritical ICU, especially GBS and MG patients
Resolution of the medical condition that led to MV
Hemodynamic stability (BPM < 135/min, 90 < systolic arterial pressure < 160 mmHg with no need for vasopressors)
Patient awake or easily aroused (RASS between 1 and − 2) and sedation stopped
Patient able to cough effectively
Adequate secretion clearance (cough strength)
SpO_2 > 90% with FIO_2 < 40% or PaO_2/FIO_2 > 150 and PEEP < 8 cm H_2O
RR < 35/min
pH > 7.35
Normal blood gases
Forced vital capacity (FVC) > 10 mL/kg (or 15 or improvement of more than 4 mL/kg)
Maximal inspiratory pressure > − 20 cm H20
Maximal expiratory pressure > 40 cm H20

BPM beats per minute, *FVC* forced vital capacity, F_IO_2 inspired oxygen fraction, *GBS* Guillain–Barré syndrome, *MG* myasthenia gravis, *MV* mechanical ventilation, PaO_2 partial oxygen arterial pressure, *PEEP* positive end-expiratory pressure, *PSV* pressure support ventilation, *RASS* Richmond assessment sedation scale, *RR* respiratory rate, *SBT* spontaneous breathing trial, SpO_2 pulsed oxygen saturation

performed without supportive data [6, 13]. It has recently been shown that the use of PSV could be associated with an earlier liberation of MV compared to T-piece trials in intubated patients in general ICU [14], whereas these latter's could be preferred in patients with tracheotomy [8, 12].

Extubation success is classically predicted by clinical parameters at the end of the SBT, by blood gases if clinical parameters fail. In neuromuscular patients, they are of limited interest since inconsistent results have been found [5, 12, 15–17]. Some authors proposed to assess diaphragmatic performance in these patients and found that an increase in maximal transdiaphragmatic pressure was predictive of weaning success and was superior to inspiratory pressure [18]. Unfortunately, the technique used was not easily applicable in every patient. It should be noticed that in MG patients, residual bulbar weakness can be revealed in some cases only after extubation. This probably explains failure of these parameters to predict successful extubation. Limited data are available on strategies to increase success rate after extubation in GBS or MG patients. Rabinstein et al. presented however encouraging results for NIV after extubation in MG patients [19]. These strategies should be precised in neuromuscular patients, since in general ICU NIV have been proven to be effective if P_aCO_2 where higher then 45 mmHg and high-flow nasal oxygen associated to NIV was superior to high-flow nasal oxygen alone to prevent extubation failure [20].

In this issue of the journal, Krishnakumar et al. present original data on a dynamic evaluation of diaphragm function assessment during SBT in patients with neuromuscular diseases. This work suggests that new available tools could be valuable in these patients. Weaning failure is due to the imbalance between the mechanical load imposed on the diaphragm and the capacity of the respiratory system to cope with it. Based on that, the authors evaluated prospectively diaphragm functioning during SBT using diaphragm ultrasonography and diaphragm electrical activity (Edi peaks using neurally adjusted ventilatory assist (NAVA) catheter) every 30 min. Indeed, diaphragmatic thickening fraction (DTF) correlates with the diaphragm workload and electrical activity of the diaphragm (Edi) is a surrogate of respiratory drive. Eight patients with neuromuscular diseases (five GBS and three MG patients) on MV for more than 7 days could be evaluated. Their preliminary results suggest that over time as patients progress towards successful weaning Edi values and DTF stabilize over the SBT. Interestingly, neither respiratory rate nor End-tidal CO_2 ($EtCO_2$) did change over the weaning period. In the general ICU population, a recent study found that neither changes in DTF nor in diaphragmatic excursion was associated to extubation failure [21, 22]. Concerning Edi, a study performed in a NICU population including stroke and traumatic brain injury patients showed that an increase in Edi by 12% reflected patient exhaustion [23]. Concerning MG, a single-case report suggested its usefulness as an early marker of respiratory muscles recovery [24]. Some limitation should however be emphasized. A major limitation is the huge interindividual Edi variations [25] that explains that some authors proposed to use instead Edi/tidal volume ratio [26, 27]. The sample size was very limited, and it is not sure that GBS and MG behave exactly the same way. Thus, further studies should probably focus on a larger and more homogenous population. Edi values reported here were clearly lower than classically described. Is this as proposed by the authors solely due to the chronic muscle waste possibly present in this specific population? if this hypothesis could be easily proposed in MG, it is less evident in the acute setting of GBS. Another limitation is the feasibility of the ultrasonography of the diaphragm and the other extradiaphragmatic respiratory muscles [28, 29]. Patients with poor ultrasound window for diaphragm assessment were here excluded. Nevertheless, diaphragm ultrasonography is non-invasive and feasible at bedside in every NICU. Whereas Edi catheter placement is very close to the placement of a nasogastric tube, those catheters are not nowadays widely used.

To conclude, this paper addresses weaning strategies of patients with neuromuscular diseases, which is a major issue in NICU. It originally proposes to use dynamically new tools available at bedside to identify early diaphragmatic exhaustion and prevent SBT failure and its consequences. Nevertheless, the lack of consensus on the categorization of weaning groups and the absence of any uniform definition of extubation failure in neuromuscular patients preclude the improvement in weaning strategies in these patients. Bedside available tools are only half of the problem.

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Conflicts of Interest
Dr Nicolas Weiss received consultant fees from MedDay pharmaceuticals.

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