The PROMIZING trial enrollment algorithm for early identification of patients ready for unassisted breathing

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Abstract

Background: Liberating patients from mechanical ventilation (MV) requires a systematic approach. In the context of a clinical trial, we developed a simple algorithm to identify patients who tolerate assisted ventilation but still require ongoing MV to be randomized. We report on the use of this algorithm to screen potential trial participants for enrollment and subsequent randomization in the Proportional Assist Ventilation for Minimizing the Duration of MV (PROMIZING) study.

Methods: The algorithm included five steps: enrollment criteria, pressure support ventilation (PSV) tolerance trial, weaning criteria, continuous positive airway pressure (CPAP) tolerance trial (0 cmH2O during 2 min) and spontaneous breathing trial (SBT): on fraction of inspired oxygen ($\text{FiO}_2$) 40% for 30–120 min. Patients who failed the weaning criteria, CPAP Zero trial, or SBT were randomized. We describe the characteristics of patients who were initially enrolled, but passed all steps in the algorithm and consequently were not randomized.

Results: Among the 374 enrolled patients, 93 (25%) patients passed all five steps. At time of enrollment, most patients were on PSV (87%) with a mean (± standard deviation) $\text{FiO}_2$ of 34 (± 6) %, PSV of 8.7 (± 2.9) cmH2O, and positive end-expiratory pressure of 6.1 (± 1.6) cmH2O. Minute ventilation was 9.0 (± 3.1) L/min with a respiratory rate of 17.4 (± 4.4) breaths/min. Patients were liberated from MV with a median [interquartile range] delay between initial screening and extubation of 5 [1–49] hours. Only 7 (8%) patients required reintubation.

Conclusion: The trial algorithm permitted identification of 93 (25%) patients who were ready to extubate, while their clinicians predicted a duration of ventilation higher than 24 h.

Keywords: Ventilator weaning, Extubation, Mechanical ventilation, Respiratory mechanics, Critical care

Background

Liberating critically ill patients from invasive mechanical ventilation (MV) at the earliest opportunity is essential to avoid the morbidity and mortality associated with prolonged ventilation [1, 2]. However, the process of discontinuing MV is complex. In the “acute phase” of acute respiratory failure and/or uncontrolled critical illness, patients generally receive full ventilator support.
We screened all critically ill patients who received invasive MV for more than 24 h, and who were not expected to be extubated in the next 24 h. Major exclusion criteria were an underlying medical condition likely to result in prolonged or chronic ventilator dependence such as a severe chronic obstructive pulmonary disease or a progressive neuromuscular disorder (the full lists of inclusion and exclusion criteria are provided in Additional file 1: Table E1). After enrollment, further screening tests were done in a step-by-step algorithm to identify patients who were eligible for randomization in the PROMIZING Study to receive either PSV or PAV+ (Fig. 1). The goal of this process was to ensure that patients who proceeded to randomization still required continued MV using objective criteria, to ensure that they would not dilute treatment effect (including shortening duration of MV).

Step 1—Enrollment criteria
Patients satisfying all screening criteria were followed daily until they met the enrollment criteria (see Additional file 2: Table E2). This step ensured (i) that patients were able to trigger ventilator breaths with a reasonable level of assistance, (ii) did not have severe impairment in gas exchange, and (iii) were not hemodynamically unstable. Patients who met enrollment criteria, or their substitute decision makers, were approached for consent. Upon obtaining consent, patients were considered enrolled in the PROMIZING study and ready to undergo further screening tests to determine eligibility for randomization.

Step 2—Pressure support ventilation tolerance trial
Patients meeting all enrollment criteria were immediately placed on PSV, if they were not already. The PSV tolerance trial (PSVTT) consisted in a pressure of 5–20 cmH₂O (the total pressure did not exceed 30 cmH₂O) for at least 30 min [11]. The positive end-expiratory pressure (PEEP) and the fraction of inspired oxygen (FiO₂) settings were similar to that before the PSVTT. If patients were unable to tolerate the PSV because of respiratory distress or clinical instability (see Additional file 3: Table E3), they were immediately returned to the prior ventilation mode. A new PSVTT was attempted at least once daily until patients passed the trial.

Step 3 – General weaning criteria
Patients who passed the PSVTT were immediately evaluated for general weaning criteria including (i) a peripheral oxygen saturation (SpO₂) ≥ 90% on FiO₂ ≤ 40% and a PEEP ≤ 8 cmH₂O, (ii) an arterial pH ≥ 7.32, and (iii) vasopressor requirement ≤ 0.1 µg/kg/min of norepinephrine equivalents. Patients who did not meet these three weaning criteria were randomized in the PROMIZING study (Not ready for...
weaning group). Patients who met these three criteria proceeded directly to a ZERO CPAP tolerance trial to assess their rapid shallow breathing index (RSBI) and capacity to undergo an SBT.

**Step 4 – Zero CPAP tolerance trial**
Patients were monitored during a two minute CPAP tolerance trial on their ventilator using a pressure level of 0 cmH₂O. We assessed the RSBI (as the ratio of respiratory rate to tidal volume, RR/Vₜ). Patients who failed this ZERO CPAP tolerance trial due to either a RR/Vₜ ratio > 100, or respiratory distress or clinical instability (see Additional file 4: Table E4) were randomized into the PROMIZING trial (ZERO CPAP tolerance failure group). Patients with a RR/Vₜ ratio ≤ 100 breaths/min/L and S_pO₂ ≥ 90% proceeded directly to a SBT.

**Step 5 – Spontaneous breathing trial on T-piece or CPAP 0**
Patients were monitored during a 30–120 min SBT on either T-piece or no assistance on the ventilator using CPAP with a pressure level of 0 cmH₂O as previously described, with F_O₂ 40% [5, 12]. Failure criteria included respiratory distress and clinical instability as for the PSVTT and the ZERO CPAP tolerance trial (see Additional file 4: Table E4). Patients were randomized into the PROMIZING trial if they failed the SBT (SBT failure group). Conversely, patients who passed the SBT were screened and non-randomized (SNR) because they were considered ready for extubation (SNR group).

**Statistical analysis**
Demographic, prognostic scores and respiratory parameters were collected before randomization. Continuous variables were expressed as the mean (± standard deviation, SD), or median [interquartile range, IQR]. Categorical variables were quoted as the frequency (percentage).
For comparing difference in groups’ characteristics, we used Chi-square test or a one-way analysis of variance (ANOVA) followed by a Tukey’s multiple comparisons post-test when appropriate. All statistical analyses were conducted using R Core Team software (version 4.1.1, R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/). Unadjusted p-values are provided to quantify the statistical evidence against equality among the groups in various baseline variables.

Results
Study population
Between September 2016 and February 2020, we enrolled (before randomization) 382 patients in the PROMIZING study. Eight patients could not be classified into one of the four groups as they did not complete the pre-randomization assessment or did not have complete data. The mean (±SD) age was 63 (±13) years and 65% were male. The mean delay between the first intubation and the enrollment was 5.9 (±5.0) days (Table 1).

Effect of the study algorithm on the mechanical ventilation process
Of the 374 patients, 139 (37%) were randomized because they did not meet general weaning criteria (Not ready for weaning group). Of the remaining 235 patients, 142 patients moved to the next steps: 101 (27%) met general weaning criteria but failed the ZERO CPAP tolerance trial (ZERO CPAP tolerance failure group subsequently randomized); 41 (11%) passed the 2-min CPAP but failed the SBT (SBT failure group subsequently randomized) and 93 (25%) initially screened patients were not randomized in the PROMIZING study, because they were considered already ready for the liberation phase (SNR group) (Fig. 1).

Distribution of patients in the mechanical ventilation process according to the mode of ventilation
At enrollment, 41 (11%) of the 374 patients analyzed were under assist-control ventilation (ACV). Among them, 19 (46%) progressed to the recovery phase (Not ready for weaning group), 11 (27%) progressed to the weaning phase (ZERO CPAP tolerance and SBT failure groups), and 11 (27%) progressed to the liberation phase (SNR group). Compared with patients with PSV at enrollment (325, 87%), there was no significant difference concerning the percentage of patients in the recovery (118, 36%), weaning (128, 40%) or liberation phase (79, 24%) (p = 0.211, p = 0.119, and p = 0.724; respectively) (Table 2).

Description of screened non-randomized patients
Of the 93 patients included in the SNR group, 59 (65%) were male and the mean (±SD) age was 65 (±13) years. The mean duration from intubation to enrollment was 4.5 (±4.1) days. The mean Richmond agitation-sedation scale (RASS) was -1.01 (±1.38) consistent with drowsy or light sedation (Table 1).

At the time of enrollment, a large majority of patients were under PSV (85%) with a mean FIO2 of 34 (±6) %, pressure support of 8.7 (±2.9) cmH2O, and PEEP of 6.1 (±1.6) cmH2O. The mean minute ventilation (VE) was 9.0 (±3.1) L/min with a RR of 17.4 (±4.4) breaths/min (Table 1).

Comparison of baseline characteristics between non-randomized and randomized patients
Compared to the other groups, the SNR group contained a higher proportion of postoperative patients and had a higher P2O2/F1O2 ratio. The time from intubation to enrollment was shorter in the SNR group. Conversely, there was not strong evidence of differences among the groups in age, sex, and RASS. The sequential organ failure assessment (SOFA) on ICU admission was significantly higher in the SNR group, reflecting higher organ dysfunction, but this was not confirmed with other prognostic scores (Table 1).

Although the ventilation mode was similar between groups (see Additional file 5: Table E5), the initial ventilator settings slightly differed with a lower level of F1O2, pressure support and PEEP in the SNR group. These differences were significant when compared with the Not ready for weaning and ZERO CPAP tolerance failure groups, while they disappeared when compared with the SBT failure group. Likewise, the RR was lower in the SNR group compared to the Not ready for weaning group, leading to a significant decrease in VE (Table 1 and Fig. 2).

Discussion
The major findings of this study are as follow: first, the stepwise algorithm developed for screening and randomizing patients in the PROMIZING trial was helpful in identifying patients who were ready to be separated from the ventilator. Second, a surprisingly large proportion of patients (25% in the present study) for whom clinicians predicted a duration of ventilation higher than 24 h were ultimately determined by the algorithm to be
Table 1. Baseline (pre-randomization) characteristics comparisons

| Parameters                        | All patients n = 374 | Not ready for weaning group (Recovery phase) n = 139 | ZERO CPAP tolerance failure group (Weaning phase) n = 101 | SBT failure Group (Weaning phase) n = 41 | SNR Group (Recovery phase) n = 93 | p value |
|----------------------------------|----------------------|------------------------------------------------------|----------------------------------------------------------|----------------------------------------|---------------------------------|---------|
| Age, years                       | 63 ± 13              | 62 ± 13                                               | 63 ± 14                                                  | 63 ± 13                                | 65 ± 13                         | 0.326   |
| Male – n (%)                     | 242 (65)             | 95 (69)                                              | 58 (59)                                                  | 30 (75)                                | 59 (65)                         | 0.212   |
| BMI, Kg/m² – median [IQR]        | 27.8 [24.2–32.1]     | 28.9 [25.1–34.5]                                     | 27.0 [23.5–31.2]                                        | 25.9 [23.3–31.2]                      | 28.1 [24.9–32.0]                | 0.010   |
| RASS                             | –1.37 ± 1.65         | –1.59 ± 1.78                                         | –1.44 ± 1.67                                             | –1.22 ± 1.60                          | –1.01 ± 1.38                    | 0.062   |
| Postoperative – n (%)            | 74 (20)              | 17 (12)                                              | 19 (19)                                                  | 7 (17)                                 | 31 (33)                         | 0.001   |

**Parameters All patients** n = 374

- **Age, years**
  - 63 ± 13
- **Male – n (%)**
  - 242 (65)
- **BMI, Kg/m² – median [IQR]**
  - 27.8 [24.2–32.1]
- **RASS**
  - –1.37 ± 1.65
- **Postoperative – n (%)**
  - 74 (20)

**Parameters Not ready for weaning group (Recovery phase)** n = 139

- **Age, years**
  - 62 ± 13
- **Male – n (%)**
  - 95 (69)
- **BMI, Kg/m² – median [IQR]**
  - 28.9 [25.1–34.5]
- **RASS**
  - –1.59 ± 1.78
- **Postoperative – n (%)**
  - 17 (12)

**Parameters ZERO CPAP tolerance failure group (Weaning phase)** n = 101

- **Age, years**
  - 63 ± 14
- **Male – n (%)**
  - 58 (59)
- **BMI, Kg/m² – median [IQR]**
  - 27.0 [23.5–31.2]
- **RASS**
  - –1.44 ± 1.67
- **Postoperative – n (%)**
  - 19 (19)

**Parameters SBT failure Group (Weaning phase)** n = 41

- **Age, years**
  - 63 ± 13
- **Male – n (%)**
  - 30 (75)
- **BMI, Kg/m² – median [IQR]**
  - 25.9 [23.3–31.2]
- **RASS**
  - –1.22 ± 1.60
- **Postoperative – n (%)**
  - 7 (17)

**Parameters SNR Group (Recovery phase)** n = 93

- **Age, years**
  - 65 ± 13
- **Male – n (%)**
  - 59 (65)
- **BMI, Kg/m² – median [IQR]**
  - 28.1 [24.9–32.0]
- **RASS**
  - –1.01 ± 1.38
- **Postoperative – n (%)**
  - 31 (33)

Pairwise comparisons between groups by Tukey Honest Significant Difference Test where \( p = 0.05 \) was taken as a threshold for these post-hoc comparisons:

- **ACV**: assist control ventilation, APACHE: acute physiology and chronic health evaluation, BMI: body mass index, CPAP: continuous positive airway pressure, SNR: screened and non-randomized,  \( F_\text{O}_2 \): fraction of inspired oxygen, IQR: interquartile range, MV: mechanical ventilation, NA: not available, PAV +: proportional assist ventilation, PEEP: positive end-expiratory pressure, PSV: pressure support ventilation, RASS: Richmond agitation and sedation scale, RR: respiratory rate, SBT: spontaneous breathing trial, SOFA: sequential organ failure assessment, VE: minute ventilation, Vt: tidal volume

*Difference \( (p < 0.05) \) between Not ready for weaning group vs. SNR group
† Difference \( (p < 0.05) \) between ZERO CPAP tolerance failure group vs. SNR group
§ Difference \( (p < 0.05) \) between SBT failure group vs. SNR group

Table 2. Distribution of patients in the mechanical ventilation process according to the mode of ventilation at enrollment

| Study algorithm Group                  | Mechanical ventilation phase | Patients with ACV n (%) | Patients with PSV n (%) | p value |
|---------------------------------------|------------------------------|-------------------------|-------------------------|---------|
| Not ready for weaning group           | Recovery                     | 19 (46)                 | 118 (36)                | 0.211   |
| ZERO CPAP tolerance and SBT failure groups | Weaning                  | 11 (27)                 | 128 (40)                | 0.119   |
| SNR Group                             | Liberation                  | 11 (27)                 | 79 (24)                 | 0.724   |

ACV: assist control ventilation, CPAP: continuous positive airway pressure, PSV: pressure support ventilation, SBT: spontaneous breathing trial, SNR: screened and non-randomized
ready for liberation from MV. These patients were extubated within a median delay of 5 h from time of enrollment, and only 7 (8%) required reintubation. This low reintubation rate confirmed that the algorithm was safe [13]. Compared to patients not ready for extubation, they had a slightly lower PSV, PEEP and $V_E$. In contrast, the mode of ventilation at enrollment and the level of sedation were similar.

It is difficult for clinicians to determine when a patient is ready to advance from the acute phase of critical illness (requiring full ventilatory support) to the recovery phase (partial ventilatory support) and ultimately, the weaning phase. Several factors could explain this observation such as the absence of simple bedside parameters (e.g., $P_AO_2/F_iO_2$ ratio or respiratory system compliance) to predict with certainty the safety and tolerability of allowing patients to share the work of breathing and subsequently start SBTs. Furthermore, the risk of post-extubation respiratory failure requiring reintubation (occurring in up to 15% of cases) is associated with a high mortality rate [13, 14]. Consequently, clinicians frequently tend to underestimate the capacity of patients to be successfully weaned and breathe without assistance, leading to a risk of delayed extubation and exposing patients to unnecessary discomfort and complications (e.g., ventilation-acquired pneumonia) [1]. To avoid delays in the weaning process, international guidelines suggested the implementation of a ventilator liberation protocol to identify patients ready for extubation [3, 15, 16]. To date, guidelines have focused on the weaning phase of MV by proposing a daily interruption of sedation and performing a SBT (PSV with low support pressure, CPAP or T-piece trial) as soon as possible [17]. Because the absence of clear guidance concerning the recovery phase (i.e., when to switch the ventilator from a controlled mode to an assisted mode, and perform these tests) and a lack of objective criteria for deciding if a patient is ready for extubation, our algorithm might add substantial improvements to the current recommendations.

We developed a step-by-step algorithm for patient recruitment in the PROMIZING trial, which could accelerate the weaning from MV. By different ways, it allowed to easily select patients potentially ready to be extubated. First, our algorithm screened early in the MV process, from the acute phase of their illness, when some patients were still in ACV. We proposed simple criteria to switch from ACV to PSV such as adequate gas exchange (with $F_iO_2 \leq 60\%$ and PEEP $\leq 15$ cmH$_2$O) and no hemodynamic instability. Thus, we encouraged a PSVT as soon as the patient’s condition shows early signs of improvement, but even before patients were seen to trigger the ventilator or before sedatives were weaned or vasopressors were discontinued. Among our 41 patients with ACV at enrollment, our algorithm detected that 19 patients were ready
to progress to the recovery (i.e., switch on PSV) phase, and 11 to the weaning phase (i.e., SBT). Moreover, 11 patients successively passed all phases of our algorithm and were ready for extubation. Of note, patients with ACV and PSV at enrollment had a similar extubation rate (27 vs. 24%; p = 0.724). This strategy to transfer the breathing workload as soon as possible might limit the development of diaphragm weakness and atrophy, which can occur during the first days of MV [18]. Several studies found a relationship between the diaphragm thickness and weaning failure, delays in liberation of MV or risk of reintubation [19–22].

Second, our protocol might shorten the length of MV, because we used pragmatic criteria to progress from the recovery phase to the weaning phase. Currently, the list of weaning criteria proposed by Boles et al. includes clinical assessment (e.g., adequate cough and no excessive tracheobronchial secretion) and hemodynamic and respiratory measurements [1]. However, some patients who do not meet all the criteria could successfully pass the SBT. In contrast, we moved patients to the weaning phase if they met only three simple criteria: adequate oxygenation ($\text{FiO}_2 \geq 90\%$ on $\text{FiO}_2 \leq 40\%$ and $\text{PEEP} \leq 8 \text{ cmH}_2\text{O}$), no severe acidosis ($\text{pH} \geq 7.32$), and low-dose of vasopressors. Although the discontinuation of vasopressors has been a precondition for SBT in clinical trials and guidelines, other studies have not found significant differences between patients extubated on and off vasopressors concerning the success of extubation, at least with low doses [23, 24]. In addition, previous studies have shown that patients extubated on vasopressors had a significant decrease in the ICU length of stay [24, 25]. Finally, we conducted the SBT regardless of the PSV or PEEP level (i.e., a gradual withdrawal of assistance was not necessary as long as the pressure support was between 5 and 20 cmH$_2$O). Thereby, the duration of the recovery phase could be very short in some of our patients, because they met the general weaning criteria immediately after passing the 30 min PSVT.

Third, our algorithm defined and separated the different phases of the MV process (i.e., acute, recovery, weaning and liberation phases), and proposed criteria for identifying patients in each phase (see Additional file 6: Fig. E1). In this way, the diagnosis of a possible liberation from MV could be assessed over a few hours. Currently, there is no consensus in the definition of the different phases, often leading to confusion [26]. Using our algorithm, the acute phase corresponded to a non-controlled underlying disease, when patients may need full ventilator support (i.e., ACV). The recovery phase began with the switch to PSV (or proportional ventilation mode), allowing the patient to share the work of breathing. Moving to the weaning phase required meeting the general weaning criteria including a 2-min CPAP trial to assess the RSBI (conducted on zero PEEP) followed by a SBT if the ZERO CPAP tolerance trial was successful. Recently, Burns et al. showed a large heterogeneity of SBT techniques across the world [8]. Our protocol proposed to perform an 30–120 min SBT on T-piece or CPAP at zero PEEP on the ventilator rather than a PSV using low level of pressure support in order to better simulate the physiologic conditions after extubation [5]. Because usual criteria of successful SBT were subjective and depended on the clinician’s interpretation, we provided easy to use criteria to define failure of each PSV, CPAP and T-piece trials [27].

Several limitations of this study need to be discussed. We did not record data regarding the cumulative dose and duration of sedative drugs received or the patient’s fluid balance, which may influence the weaning process [28, 29]. Moreover, our algorithm did not include additional physiologic measurements, such as the airway occlusion pressure ($P_{0.1}$). Finally, in spite of broad and easy-to-assess enrollment criteria (especially concerning oxygenation: $P_{O_2} \geq 60 \text{ mmHg}$ on $\text{FiO}_2 \leq 60\%$ and $\text{PEEP} \leq 15 \text{ cmH}_2\text{O}$), the delay between intubation and the enrollment remained long (around 6 days). This finding may also represent an opportunity for improvement as patients could be enrolled earlier in the acute phase. Because a criterion to enroll patients in PROMIZING was an expected need of ventilation of at least 24 h, it is unlikely that clinicians would have conducted a weaning trial independent from the study screening protocol on the same day, suggesting that application of the screening algorithm assisted in identifying patients ready for weaning earlier than the clinicians suspected.

**Conclusion**

The process to liberate patients from MV accounts for a significant duration of the ventilation time. Finding strategies to minimize this duration is desirable. We developed a comprehensive step-by-step algorithm for enrollment and randomization of patients in the PROMIZING study, which compares two spontaneous modes of MV. Surprisingly, our algorithm allowed an easy and early identification of patients ready to extubate, and might decrease the duration of MV. In our study, 25% of our patients, who were in need of ventilator assistance for at least 24 h according to their clinicians in charge, passed the whole process (recovery, weaning, and liberation) and were safely removed from the ventilator and extubated.

**Abbreviations**

ACV: Assist-control ventilation; ANOVA: Analysis of variance; CPAP: Continuous positive airway pressure; SNR: Screened and non-randomized; $\text{FiO}_2$: Fraction
of inspired oxygen; ICU: Intensive care unit; IQR: Interquartile range; MV: Mechanical ventilation; P0.1: Airway occlusion pressure; P0.2: Partial pressure of oxygen; PAV−P: Proportional assist ventilation with load-adjustable gain factors; PEEP: Positive end-expiratory pressure; PROMIZING: Proportional assist ventilation for minimizing the duration of mechanical ventilation study; PSV: Pressure support ventilation; RASS: Richmond agitation-sedation scale; RR/RR/τ: Ratio of respiratory rate to tidal volume; SBT: Spontaneous breathing trials; SD: Standard deviation; SOFA: Sequential organ failure assessment; S0.2: Peripheral oxygen saturation; Vτ: Minute ventilation.

Supplementary Information
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Additional file 1 Screening inclusion and exclusion criteria of the PROMIZING study. Step 1 to 5 refer to the algorithm for enrollment of patients in the PROMIZING study. ACV: assist-control ventilation; CPAP: continuous positive airway pressure; PAV: proportional assist ventilation; PROMIZING: Proportional assist ventilation for minimizing the duration of mechanical ventilation study; PSV: pressure support ventilation; SBT: spontaneous breathing trials.

Additional file 2 Enrolment inclusion, deferral and exclusion criteria of the PROMIZING study. CPAP: continuous positive airway pressure, ECMO: extracorporeal membrane oxygenation, PaO2: Arterial partial pressure of oxygen, PAV: proportional assist ventilation, PEEP: positive end-expiratory pressure, PROMIZING: Proportional assist ventilation for minimizing the duration of mechanical ventilation study, SpO2: peripheral oxygen saturation.

Additional file 3 Pressure support ventilation tolerance trial inclusion, deferral and exclusion criteria of the PROMIZING study. PROMIZING: Proportional assist ventilation for minimizing the duration of mechanical ventilation study.

Additional file 4 Definition of respiratory distress and clinical instability. RASS: Richmond agitation-sedation scale, SBP: systolic blood pressure, SpO2: peripheral oxygen saturation.

Additional file 5 Mode of ventilation at baseline (pre-randomization). CPAP: continuous positive airway pressure, SBT: spontaneous breathing trial, SNR: screened and non-randomized.

Additional file 6 Principles and objectives of each phases of the mechanical ventilation process in the PROMIZING study. Step 1 to 5 refer to the algorithm for enrollment of patients in the PROMIZING study. ACV: assist-control ventilation; CPAP: continuous positive airway pressure, PAV: proportional assist ventilation; PROMIZING: Proportional assist ventilation for minimizing the duration of mechanical ventilation study, PSV: pressure support ventilation, SBT: spontaneous breathing trials.

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Author contributions
LB and KJB designed the work. JM, JSM, TB, KB, TP, FL, PAB, EC, GC, TM, GB, AM, YS, FZ, LB, and KJB collected the data. CB, MLR, and KT analyzed the data. CB, JM, LB, and KJB wrote the manuscript. JM, LB, and KJB critically reviewed the manuscript. All authors approved the final version of the manuscript. All authors are agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Availability of data and materials
The raw data supporting the conclusions of this article will be made available by the authors, on reasonable request.

Declarations

Ethics approval and consent to participate: No animal studies are presented in this manuscript. No potentially identifiable human images or data are presented in this study. This study was reviewed and approved by the Western University Research Ethics Board and the Clinical Trials Ontario (project identifier: 0733).

Consent for publication
Informed consent was obtained from the patient or the substitute decision maker at time of enrollment. This early consent allowed to collect minimal information for the screened and non-randomized patients described here. We do not report any outcome of the randomized patients.

Competing interests
Not applicable.

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