**Usefulness of parasternal intercostal muscle ultrasound during**

 **weaning from mechanical ventilation**

**Supplemental Digital Content**

**METHODS**

**Study B**

Decision to initiate pressure-support ventilation.

**Study C**

- Readiness criteria to undergo a first spontaneous breathing trial

- Contraindications to magnetic stimulation of the phrenic nerves

- Criteria defining failure of the spontaneous breathing trial

- Measurement: the phrenic nerve stimulation method

**RESULTS**

**Table SDC1.** Intra-class correlation – intra-observer variations of parasternal intercostal muscle ultrasound measurements in healthy subjects (study A) and patients (study C)

**Table SDC2.** Comparison of ROC curves of the four indices to predict spontaneous breathing trial failure

**Figure SDC1**.Changes in diaphragm thickening fraction (TFdi) and parasternal intercostal thickening fraction (TFic) under stepwise increase in pressure support (study B)

\* as compared to pressure support (PS) 7 and positive end expiratory pressure zero (ZEEP) for TFdi

# as compared to pressure support (PS) 7 and positive end expiratory pressure zero (ZEEP) for TFic

**Figure SDC2.** Receiver operating characteristics curves of endotracheal pressure induced by a bilateral phrenic nerve stimulation (**Ptr,stim**), diaphragm thickening fraction (**TFdi**), parasternal intercostal muscle thickening fraction (**TFic**) and **TFic/TFdi** **ratio** to predict failure of the spontaneous breathing trial.

**METHODS**

***Study B***

*Decision to initiate pressure-support ventilation.*

Patients were considered ready to be placed on pressure-support ventilation if they could sustain this mode for at least 1 hour with:1

1. pressure support ≤24 cmH2O
2. positive end-expiratory pressure ≤12 cmH2O
3. total level of inspiratory pressure <30 cmH2O
4. respiratory rate ≤24/min
5. tidal volume ≥5 ml/kg ideal body weight, without signs of labored breathing, as defined by retractions or recessions - sucking in of the skin around the ribs and the top of the sternum, or prominent use of accessory respiratory muscles.

***Study C***

*Readiness criteria to undergo a first spontaneous breathing trial*

The criteria used to assess the readiness for weaning were derived from the International Conference on Weaning:2

1. adequate oxygenation (SpO2 >90% on a fraction of inspired oxygen ≤40% and positive end expiratory pressure ≤8 cmH2O)
2. respiratory rate ≤35/min
3. a cooperative cognitive state
4. stable cardiovascular status (systolic arterial blood pressure of 90-160 mmHg without or minimal vasopressors and heart rate ≤140/min)

*Contraindications to magnetic stimulation of the phrenic nerves*

1. cardiac pacemaker or defibrillator
2. cervical implants
3. cervical spine injury
4. pregnancy

*Non-inclusion criteria for study C*

1. suspicion of underlying hemi-diaphragm paralysis (defined as an elevation of >2.5 cm of one hemi-diaphragm compared to the other on chest radiograph),
2. pre-existing neuromuscular disorders,
3. age <18 years and
4. decision to withhold life-sustaining treatment.

*Criteria defining failure of the spontaneous breathing trial*

The criteria of failure of the spontaneous breathing trial were derived from the International Conference on Weaning.2 The spontaneous breathing trial was considered to be a failure if at least one the following criteria was present:

1. blood oxygen saturation (SpO2) of < 90 % with a fraction of inspired oxygen (FiO2) ≥ 50 %;
2. acute respiratory distress (RR ≥ 40/min, agitation, cyanosis);
3. systolic arterial blood pressure of ≥ 180 mmHg;
4. cardiac arrhythmias;
5. respiratory acidosis [pH<7.32 with an arterial carbon dioxide tension (PaCO2) of ≥50 mmHg].

If none of these failure criteria was present, the spontaneous breathing trial was considered as successfully completed.

**Measurements**

*Parasternal intercostal muscle ultrasound.* Patients and subjects were studied in a semi-recumbent position. A 10-15 MHz linear array transducer (Sparq ultrasound system, Phillips, Philips Healthcare, Andover, MA, USA for patients and HFL-38xe, FUJIFILM Sonosite, Bothell, WA, USA for healthy subjects) was positioned perpendicular to the anterior thorax surface in the sagittal plane, at the level of the second right intercostal space, approximately 6-8 cm lateral to the sternal edge with a window visualising the 2nd and 3rd ribs. This intercostal space was chosen as the inspiratory effect of the external parasternal intercostal muscle is maximal at this location, compared to more caudal interspaces.3 The second right parasternal intercostal muscle was identified as a three-layered biconcave structure: two linear hyperechoic membranes respectively running from the anterior and posterior aspects of the adjoining ribs, and a medial portion with muscle echotexture (Figure 1). Considering that during inspiration the muscle fibers of the parasternal intercostal contract, displacing the rib cage cranially and anteriorly3 and that their mass remains constant, an increase in thickness of the muscular structure can be visualized using ultrasound. Using M-mode, the ultrasound beam was perpendicularly directed at the midsection of the muscle, where it is the thinnest at end-expiration. The thickness of the parasternal intercostal muscle was measured on frozen images at end-expiration (Tee) and at peak inspiration (Tei). TFic was defined as the percent change in muscle thickness between expiration and inspiration. This change in thickness determined the thickening fraction of the parasternal intercostal muscle (TFic = (Tei- Tee)/Tee). All measurements were repeated on at least three separate breaths and their average was reported. For the sack of feasibility, ultrasound was performed on the right parasternal intercostal muscle only. Ultrasound measurements were performed by MD, BPD and SV.

*Phrenic nerve stimulation method*

Diaphragm pressure generating capacity was assessed in terms of changes in endotracheal tube pressure induced by bilateral phrenic nerve stimulation during airway occlusion (Ptr,stim). Phrenic nerve stimulation was performed by bilateral anterior magnetic stimulation. In brief, two figure-of-eight coils connected to a pair of Magstim® 200 stimulators (The Magstim Company, Dyfed, UK) were positioned immediately posterior to the sternomastoid muscles at the level of the cricoid cartilage. Stimulations were delivered at the maximum output intensity of the stimulator (100%) that is known to consistently result in supramaximal phrenic contraction.4–7 Patients were studied in a standardized semi-recumbent position, as follows: end-expiratory pressure was set to zero and the patient was allowed to exhale during an end-expiratory pause. Intrinsic positive end expiratory pressure was found when at relaxed end-expiration, the endotracheal pressure could not reach the zero baseline while the endotracheal tube was disconnected from the ventilator, manually occluded and by checking the absence of respiratory effort. While the endotracheal tube was manually occluded, bilateral anterolateral magnetic stimulation was performed. The absence of active respiratory efforts in response to stimulation was determined by checking the stability of the airway pressure signal. Two operators were required to achieve both stimulation and measurements. After determining the optimal position of the coils, at least three stimulations were performed at 100% of maximal output allowed by the stimulator. Stimulations were separated by at least 60-sec to avoid superposition. The average of the three measures was taken into account for analysis. Ptr,stim was defined as the amplitude of the negative pressure wave following stimulation, taken from baseline to peak. It was measured at the proximal external end of the endotracheal tube, using a linear differential pressure transducer (MP45 ±100 cmH2O, Validyne, Northridge, Calif., USA). The pressure signal was sampled and digitized at 128 Hz (MP30, Biopac Systems, Santa Barbara, Calif., USA or Powerlab, AD Instruments, Bella Vista, Australia) for subsequent data analysis.

**References**

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**Tables**

**Table E1.** Intra-class correlation – intra-observer variations of parasternal intercostal muscle ultrasound measurements in healthy subjects (study A) and patients (study C)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Intra-Observer #1** |  | **Intra-Observer #2** |  | **Inter-Observer** |
|  | ICC | 95% CI |  | ICC | 95% CI |  | ICC | 95% CI |
| **Study A** | Tee | 0.97 | 0.94 to 0.99 |  | 0.97 | 0.94 to 0.99 |  | 0.92 | 0.82 to 0.96 |
| Tei | 0.97 | 0.94 to 0.99 |  | 0.97 | 0.92 to 0.99 |  | 0.92 | 0.82 to 0.96 |
| TFic | 0.86 | 0.68 to 0.94 |  | 0.52 | 0.12 to 0.77 |  | 0.77 | 0.53 to 0.89 |
| **Study C** | Tee | 0.79 | 0.48 to 0.92 |  | 0.97 | 0.92 to 0.99 |  | 0.84 | 0.60 to 0.94 |
| Tei | 0.91 | 0.77 to 0.97 |  | 0.97 | 0.93 to 0.99 |  | 0.95 | 0.88 to 0.98 |
| TFic | 0.92 | 0.78 to 0.97 |  | 0.92 | 0.77 to 0.97 |  | 0.92 | 0.78 to 0.97 |

Tee: parasternal intercostal end-expiratory thickness; Tei: parasternal intercostal end-inspiratory thickness; TFic: parasternal intercostal muscle thickening fraction; ICC: intra-class correlation coefficient; CI: confidence interval

**Table E2.** Comparison of ROC curves of the four indices to predict spontaneous breathing trial failure

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | AUC | 95% CI | Comparison with |
| Ptr,stim |  | TFdi |  | TFic |  |  | TFic/TFdi |
| Ptr,stim | 0.91 | 0.80 to 0.97 | - |  | p = 0.472 |  | p = 0.415 |  |  | p = 0.851 |
| TFdi | 0.88 | 0.76 to 0.97 | - |  | - |  | p = 0.932 |  |  | p = 0.402 |
| TFic | 0.89 | 0.76 to 0.95 | - |  | - |  | - |  |  | p = 0.130 |
| TFic/TFdi | 0.92 | 0.81 to 0.96 | - |  | - |  | - |  |  | - |

Ptr,stim: endotracheal pressure induced by a bilateral phrenic nerve stimulation, TFdi: diaphragm thickening fraction; TFic: parasternal intercostal muscle thickening fraction; AUC: area under the receiver operating characteristics curves; CI: confidence interval

**Figures**

**Figure E1**

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**Figure E2**

