ELECTRONIC SUPPLEMENTARY MATERIAL

INTENSIVE CARE MEDICINE

Prevalence and time course of patient-ventilator asynchronies during invasive mechanical ventilation

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METHODS

Detection of inspiration

Inspiratory trigger was set sensitive enough to minimize patient's efforts and to prevent autotriggering by the attending clinicians at the time MV was initiated. To detect inspiration, the software searches for a positive flow value of at least 12 L/min. This relatively high threshold minimizes the rate of false positives and false negatives (data not shown). However, flow does not usually reach 12 L/min until several milliseconds after the beginning of inspiration. To find the exact point in which inspiration begins, the software applies an algorithm that steps backward from this threshold using the first derivative of the flow wave. This backward stepping process identifies the point in which the airflow slope starts to change (Figure S3).

Detection of expiration

The recommended standard cycling off criteria were an inspiratory time less than 1 second in VCV and PCV and 25% of peak inspiratory flow in PSV set by the attending clinicians at the time MV was initiated. To detect expiration, the software searches for a negative flow value of at least 5 L/min that remains negative for at least 25 ms. This criterion is also achieved later than the true beginning of expiration. To find the exact point in which expiration begins, the software applies an algorithm that steps backward using the first derivative of the flow wave. This backward stepping process identifies the point in which the flow wave reaches zero or flow remains constant for at least 10 ms.

Short cycling and Prolonged Cycling

When a patient is in PSV and the mode detection algorithm identifies the mode as PSV, the algorithm to detect short and prolonged cycling is enabled. The software classifies as short cycles PSV breaths in which machine inspiratory time is less than half the mean inspiratory time (running mean of 20 consecutive breaths) [1-4]. The software classifies as prolonged cycles PSV breaths in which the ventilator inspiratory time doubles the mean inspiratory time (running mean of 20 consecutive breaths) [1-4]. Short cycling and prolonged cycling are calculated by means of a running mean over the last 20 inspiratory times (Ti). Short cycling is identified when Ti of the current breath is 50% shorter than the averaged Ti, and prolongued cycling is identified when it's 200% larger. This is the way we defined them and that's the reason we didn't performed a clinical validation the way we did with IEE. While IEE detection had to be adjusted according to clinicians and experts opinion (to achieve the best sensitivity/specificity), short cycling and prolongued cycling detection responds only to a mathematical criteria (Ti of the current breath versus averaged Ti).

Ti validation was performed by comparing the manually measured Ti (as seen on the Figure S4) against the Ti estimated by the Better Care software. We tested 1000 breaths with Ti covering a range from 0.5 to 3 seconds, and Better Care software estimated Ti with a maximum error of 50 milliseconds versus the manually measured Ti in only 13 of them (98.7% agreement).

The algorithm to detect short cycling and prolongued cycling has some limitations. In the setting of sudden alterations in respiratory mechanics during PSV (short or prolonged Ti), the algorithm will identify short cycling or prolongued cycling as an asynchrony only according to variations, half or double Ti from the running mean of the previous 20 breaths. In the extreme case of alternating breaths of very short Ti together with breaths of prolonged Ti, such as in a one to one sequence, the algorithm will not detect short cycling or prolongued cycling as asynchronies. This constitutes potential major limitation of the algorithm performance in these circumstances.

Double-triggering

To detect double-triggering, the software searches for two consecutively effective cycles that are separated by an expiratory time less than half the mean inspiratory time, the first cycle triggered by the patient [1-6].

Similar to short cycling and prolongued cycling, Double Triggering detection responds only to mathematical criteria. Mainly, the system triggers DT when: 1) Te (Expiration Time) is 50% shorter than the averaged Ti (Inspiration Time) and 2) Two consecutive inspirations (positive flow – zero flow – positive flow) are detected with no expiration (negative flow) before the second Ti. Once Ti was validated (and so beginning and end of inspiration), Te was automatically calculated. No clinical validation was required as DT triggering only depends on the mathematical algorithm implemented.

Aborted Inspirations

During PCV and VCV, inspiratory time is pre-programmed and should be constant. However, for safety, the ventilator aborts inspiration when airway pressure exceeds inspiratory pressure alarm limits. Aborted inspiration is more likely to occur during VCV than during PCV and PSV and coughing is the only cause for this occurrence. In VCV, any sudden increase in respiratory impedance, such as an abrupt increase in airway resistance due to secretions, would originate an aborted inspiration. In PSV and PCV, instead, a decrease in VT would occur. The software classifies as aborted inspirations VCV and PCV breaths in which inspiratory time is less than half the mean inspiratory time (running mean of 20 consecutive breaths).

Autotriggering in PSV

During PSV, the software classifies breaths as machine-triggered (likely autotriggering) and patient-triggered. The proportion of auto-triggered breaths was defined as the number of machine-trigger breaths multiplied by 100 and divided by the total number of ventilator cycles (machine or patient triggered) [1, 4].

Ineffective inspiratory effort during expiration (IEE)

IEE, defined as contractions of the inspiratory muscles (primarily the diaphragm) that are unable to trigger the ventilator to deliver a breath, occur both during the ventilator's inspiratory time and during its expiratory time. Inspiratory muscle contraction decreases alveolar pressure, resulting in an abrupt decrease in expiratory flow. When the inspiratory muscles relax, alveolar pressure increases, resulting in an abrupt increase in expiratory flow. Thus, Better Care™ detects an IEE whenever it identifies an abrupt increase in expiratory flow preceded by an abrupt decrease in expiratory flow [7]. The system detects abrupt decreases or increases in expiratory flow by searching for a positive maximum value followed by a negative minimum value on the first arm of the flow curve and then evaluating the deviations of these values against a monoexponential curve representing the theoretical mean expiratory flow (Figure S5). In a previous study [7], we found a cutoff of 42% yielded the best sensitivity and specificity for IEE: compared to recordings of electrical activity of the diaphragm, the IEE algorithm had 65.2% sensitivity, 99.3% specificity, 90.8% PPV, and 96.5% NPV, with a 73.9% Kappa index [CI (95%) = (71.3%; 76.3%)]. To ensure that an event is an IEE rather than an inspiratory effort that persists beyond the ventilator's inspiratory time, the algorithm disregards events visible during the first 0.1 seconds of the expiratory time [7].

Figure S1.

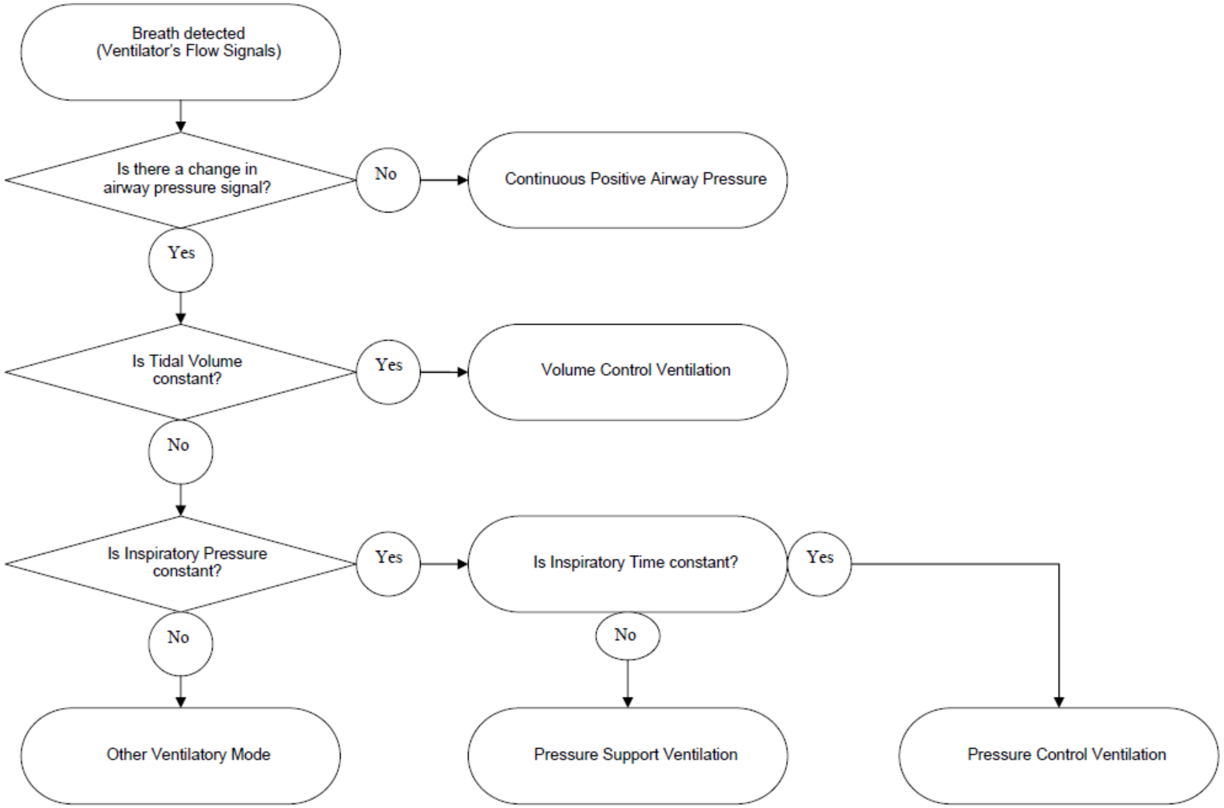


Figure S1. The system classifies ventilatory modes according to the behavior of airway pressure and flow. Inspiratory airway pressure is considered to be constant when no changes larger than 3 cmH2O are detected. Tidal volume is considered to be constant when no changes larger than 10% are detected. Inspiratory time is considered to be constant when no changes larger than 10% are detected. Note that Pressure Synchronized Intermittent Mandatory Ventilation plus Pressure Support (SIMV(p)+PS) breaths would be classified as Pressure Support Ventilation (PSV) if inspiratory pressure under spontaneous and controlled breaths were the same. To avoid this mistake, the system analyzes the frequency distribution of inspiratory time; in PSV a normal distribution is expected, whereas in SIMV(p)+PS the distribution is expected to have a superimposed peak at the inspiratory time of the controlled breaths.

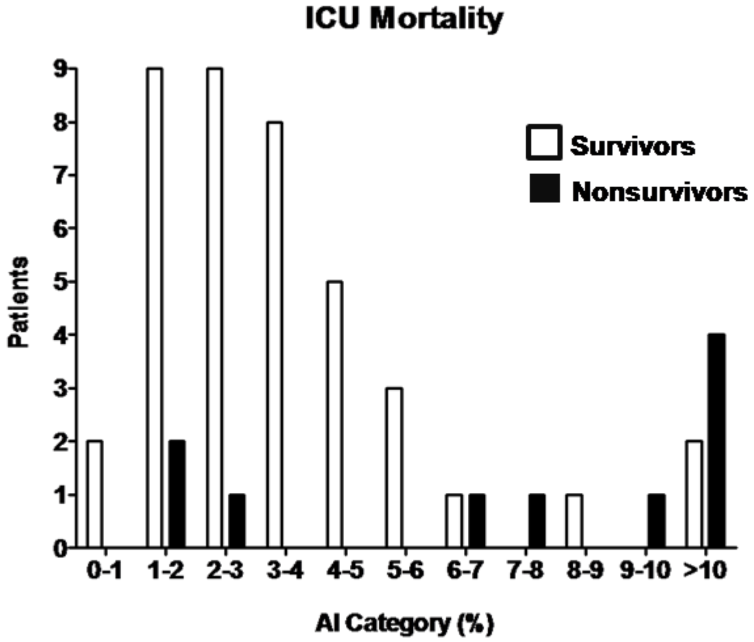
Table S1

Demographic, clinical, and physiologic characteristics	
Total number of patients	50
Age (years)	63.5 [48.7-73.2]
Number of female patients (%)	16 (32%)
Indications for mechanical ventilation - no. of patients (%)	
Severe sepsis	7 (14%)
Pneumonia	14 (28%)
Aspiration	3 (6%)
Acute respiratory distress syndrome	9 (18%)
Postoperative	3 (6%)
Chronic obstructive pulmonary disease	1 (2%)
Cardiogenic pulmonary edema	1 (2%)
Coma	6 (12%)
Others	6(12%)
APACHE II	12 [8.2 - 16.0]
SAPS-3	40 [29.2 - 50]
SOFA	7 [5 - 10]
Length of mechanical ventilation – days	8 [5 - 15]
Length of ICU stay – days	14 [7 - 22]
Patients with tracheostomy[†] - no. of patients (%)	18 (36%)
ICU mortality – no. of patients (%)	10 (20%)
Hospital mortality – no. of patients (%)	14 (28%)
Ventilatory variables	
Applied PEEP (cmH2O)	6.0 [5.0 - 7.9]
Tidal volume (mL/kg PBW)	7.8 [7.3 - 8.3]
Ti (sec)	1.03 [0.79-1.27]
Respiratory physiological variables	
Peak airway pressure (cmH2O)	24.0 [19.4 - 28.6]
Crs (ml/cmH2O)	35.4 [28.6 - 46.3]
Total Rrs (cmH2O/L/s)	10.2 [7.9 - 13.6]

Table S1. Demographic characteristics and median values of different physiologic parameters during the total time on mechanical ventilation.

Abbreviations: APACHE II: Acute Physiology and Chronic Health Evaluation; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment; ICU: intensive care unit; PEEP: positive end-expiratory pressure; PBW: predicted body weight; Crs: respiratory system compliance; Rrs: respiratory system resistance. Ti: Inspiratory time. Crs and Rrs are compliance and resistance of the respiratory system measured with the least squares fitting method in machine-triggered breaths at the initiation of mechanical ventilation. †Two patients were admitted after tracheostomy. Data are expressed as percentages or as medians and interquartile ranges.

Figure S2.



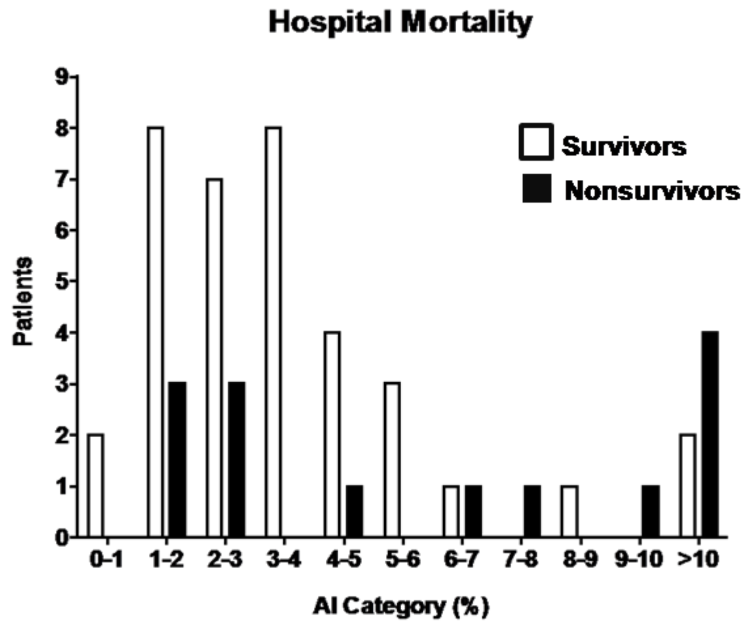


Figure S2. Relationship between individual patient outcome and the median asynchrony index (AI) (broken down into 1% categories) during the total time on mechanical ventilation. A: Intensive care unit (ICU) mortality. B: Hospital mortality. White bars: survivors. Dark bars: nonsurvivors.

Figure S3.

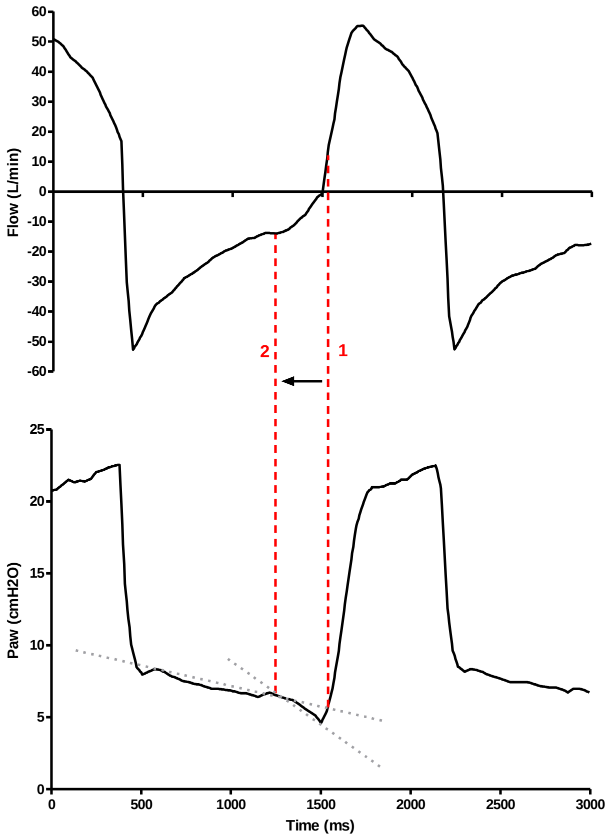


Figure S3. Airflow and airway pressure recordings in a patient in pressure support showing how the system determines the start of inspiration and of expiration. When positive flow is detected (dashed red line 1), the system steps backward to find the patient trigger point, represented by a peak on the first derivative of the pressure curve (dashed red line 2). Depending on the angle set by the two vectors (one defined by the beginning of expiration and the patient trigger point and the other defined by red line 1 and red line 2), the system determines whether the breath is triggered by the ventilator or by the patient. The start of expiration is found by searching for the first negative value after the beginning of the inspiration on the flow signal. Paw: airway pressure.

Figure S4.

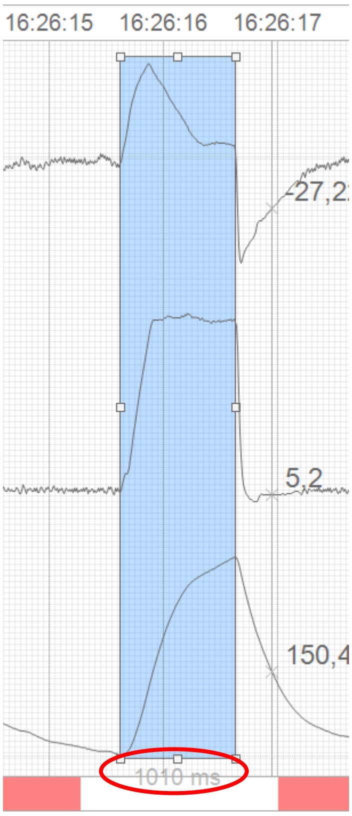


Figure S4. Manually measured inspiratory time (Ti). See ESM text for explanation.

Figure S5

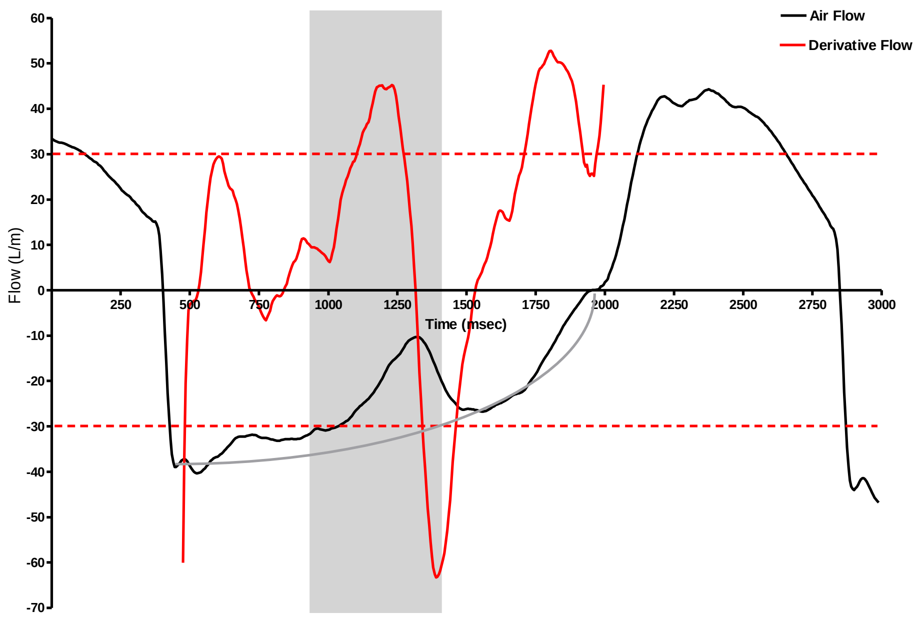


Figure S5. Expiratory airflow recording showing an ineffective inspiratory effort during expiration (IEE). The positive and the negative thresholds (red dotted lines) are determined by the first derivative of the theoretical mean expiratory flow (gray curve). The first derivative of both the actual expiratory flow and the theoretical mean expiratory flow are compared. When an increase followed by a decrease on the expiratory flow is found and the deviation (calculated as the first derivative of the expiratory flow divided by the first derivative of the theoretical mean expiratory flow) is higher than the threshold, the system considers that an IEE has occurred. The gray shaded area marks a region where an IEE occurred.

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