PRECISION OF CONTINUOUS NEONATAL VENTILATOR RESPIRATORY MECHANICS IS IMPROVED WITH SELECTED OPTIMAL RESPIRATORY CYCLES.

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ABSTRACT

Given their high apparent variability, bedside continuous respiratory mechanics (RM) parameters (excepting tidal volume (V_T)) remain infrequently used for adjustment of neonatal ventilatory settings. RM parameters provided by ventilator (VRC) from 10 recordings of newborns (10 minutes in synchronized intermittent mandatory ventilation and Assist/control (A/C)) were compared to those computed from visually selected assisted leak-free optimal respiratory cycles (SRC). Mean values, variability and ability to distinguish patients were compared between VRC and SRC. Dynamic resistances were more correlated (r^2=0.95) than compliances (r^2=0.42). V_T's were correlated only in A/C (r^2=0.78). C20/C was significantly higher in VRC (1.81±0.67) than in SRC (1.23±0.36) and frequently out of neonatal reference range. In A/C ventilation, V_T was higher in VRC (5.6 ±1.8 ml/kg) than in SRC (4.8 ±1.0 ml/kg) ($p<0.05$). Displayed V_T's don't reflect those found in optimal assisted breaths and therefore have incomplete value in assessing adequacy of ventilator settings. The variability of RM parameters provided by the ventilator is large, and coefficients of variation were significantly lower with optimal respiratory cycles (for Resistance, Compliance, V_T and C20/C: 27, 26, 18, 24% in SRC, 36, 35, 40, 33% in VRC). Selecting optimal cycles yields RM with a 2-3 times higher discriminating power between patients.

Conclusion: **Current ventilator's RM parameters have limited clinical use. Using optimal breaths to calculate RM parameters improves precision and discriminating power. For integration to ventilatory care, automation of this selection must be implemented first.**

Background:

The monitoring of ventilated newborn infants integrates different parameters. Physical examination, oxygen saturation, transcutaneous oxygen and carbon dioxide content, blood gases, chest radiography and ventilator settings assessment are all the classical tools used for that purpose. Ventilatory strategies aiming to reduce mechanical ventilation could beneficiate from additional continuous monitoring tools. Even if neonatal ventilators offer for years numerical values for common on-line respiratory mechanics (RM) parameters, their use seems limited in clinical conditions due to a large apparent variability. The new 2010 European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome in Preterm Infants [21] advocate the use of RM parameters in combination with oxygen requirements and carbon dioxide values to adjust PEEP level. Still, the usefulness and added value of RM in the clinical setting remain to be demonstrated. Actually, the introduction of commercial ventilator monitoring in neonatal intensive care was described by Klimek et al [13]. This new monitoring tool was not associated with changes in the respiratory management. However, they pointed out that their clinical staff was not experienced with the use and interpretation of the values and displays at the time of the study. The NICHD recently reviewed advanced biomedical devices in use in the neonatal intensive care units and the areas where improvement and evaluation of the safety, accuracy and clinical use were warranted [20]. One of the most important needs they identified is simple tools for continuous assessment of vital pulmonary functions at the bedside [20].

In ventilated newborns, dynamic pulmonary function and RM parameters reflect more than the condition of an isolated lung. Measurements are influenced by ventilatory settings including bias flow [15] or by endotracheal tube size [2; 15]. Dynamic parameters are also dependant of ventilatory conditions such as baseline pulmonary volume [19] and high respiratory rate [10]. Even if very compliant, neonatal chest wall influence can be modified by intrinsic or reflex respiratory muscle activity and tone variation [8; 9].

Among the remaining obstacles to a more widespread use of bedside RM parameters is their apparent high variability. The continuous data displayed are modified every breath for tidal volume (V_T), i.e. around 40-70 times per minute (e.g. solid diamonds in Fig.1), or after a few seconds for other parameters. Summarising and integrating those RM parameters for clinical use become therefore complex.

The present study was undertaken first to evaluate data provided by the ventilator in clinical conditions and to appreciate their variability. We also postulated that calculating RM parameters only from selected good quality assisted respiratory cycles not affected by leak or obstruction would decrease the variability of those RM values, therefore improving their precision. The main objective was to compare RM parameters obtained from the ventilator and from selected optimal loops. The abilities of each method to provide RM parameters able to discriminate between patients were assessed. An adequate discriminating power influences the adequacy to provide clinically relevant evaluation of trends or point of care assessment. To evaluate the influence of non assisted breaths, RM parameters differences between ventilatory modes were considered.

Patients and methods:

Recordings:

Ten minutes RM files recorded in synchronized intermittent mandatory ventilation (SIMV) then in assist/control (A/C) (10 minutes) by a single attending physician were studied retrospectively. Newborn infants ventilated in SIMV were evaluated for clinical management. In order to eliminate most non assisted respiratory cycles and assess RM parameters, the ventilatory mode was briefly switched to A/C, a fully supported mode, and assessment of ventilation was performed after a 5-10 minutes stabilisation period. Attention was made to record the infants in a quiet and undisturbed condition.

A Babylog 8000 ventilator (Dräger Company, Lübeck, Germany) was linked to a computer based Dräger Ventview software that allows exporting collected data. Ventview allowed the recording of continuous (60

Hz) data for pressure (P) and flow ($\dot{V}$) during ten minutes. The ventilator provided RM data on every breath (V_T) or at 5 seconds intervals for other RM parameters. Ventilator V_T corresponds to expiratory tidal volume. Dynamic resistance (Rdyn) and dynamic compliance (Cdyn) are calculated using the linear regression method applied to the single compartment model [6]. Results are discarded if they do not attain a good enough fit, if leak exceeds 20% and in case of high spontaneous respiratory activity. The ratio between compliance during the last 20% of inspiration and total compliance (C20/C) is a lung overdistension index [7]. C20 is computed by the ventilator as C20= ($V_{T\_inspiration}$-$V_{T\_at\_80\%\_of\_inspiration}$)/(0.2 * Peak_Pressure) [6]. Ventview added one set of ventilator RM parameters every ten seconds to an exportable dataset. Cdyn and V_T from that dataset were adjusted for body weight.

Respiratory cycles evaluation and selection:
The 10 minutes duration is short enough to avoid intrinsic evolution in RM, but still provides a large number of respiratory cycles to analyze. With spontaneous respiratory rates in the order of 60 per minute and two 10 minutes recordings (one in each mode) in ten infants, 12000 ventilatory cycles can be assessed.

A new software designed with Nomics (Liège, Belgium) allows for reconstruction of P, $\dot{V}$, and volume (V) waves. P and $\dot{V}$ are obtained from the Ventview continuous recordings. Volume (V) is calculated as the integral of flow. Each respiratory cycle is automatically individualised: a new cycle starts when $\dot{V}$ increases above zero, or when P increases just before $\dot{V}$.

Each individual respiratory cycle is assessed by a single investigator who evaluates P, $\dot{V}$ and V waves, and P-V, P-$\dot{V}$ and V-$\dot{V}$ loops. Assisted breaths are considered as "optimal" if producing good quality waves and loops, and if the P-$\dot{V}$ loop demonstrates adequate diastasis (Fig.2). Visual evaluation leads to inclusion of cycles with no or minimal leak, below 5-10%. Those optimal respiratory cycles are included in the analysis. All cycles showing moderate or significant leak, oscillations, two phased expiratory limb in the V-$\dot{V}$ loop or circuit or tube obstruction signs are excluded, as well as those causing any unusual wave or loop pattern (Fig.2). Non assisted cycles are not included in the analysis.

RM parameters:
RM parameters are calculated for each optimal cycle. Cdyn and Rdyn are calculated using the least square fit technique [22]. V_T is determined as the maximal volume provided during the cycle. C20/C is calculated as [(V_T-$V_{0.8\ Pmax}$)/(Pmax -0.8 P_{max})]/Cdyn, according to Fisher et al. [7]. Cdyn and V_T are adjusted for body weight.

Statistics:
Differences in mean values and coefficients of variation (CV) of RM data provided by the ventilator ("VRC") and calculated from the selected respiratory cycles ("SRC") are evaluated. Correlations between RM parameters from both methods are determined. Data variability and their change are assessed by comparing CV's. CV, a normalized, dimensionless measurement of the variability of a data, is calculated as the ratio between its standard deviation and mean. To assess the influence of the ventilatory mode, mean values and CV's obtained in A/C and SIMV modes are compared between the two datasets. Reproducibility of the results is evaluated by comparing the two 5 minutes' halves of the recordings.

The power to discriminate patients is evaluated with inter-patients comparisons. Rdyn, Cdyn, V_T and C20/C values from each patient are compared with those of all others patients (in total 45 comparisons in A/C and 36 in SIMV) with unpaired t-tests. All "t" values obtained from those t-tests in SRC and VRC are then compared with paired t-tests.

Mean values, CV's and "t" values are compared with two-tailed Student t-tests for paired values, and p values below 0.05 are considered significant.

Ethics:
Institutional ethics committee approved the study.

Results:
Recordings:
Ten ventilated newborns with a mean birth weight of 1276 ±455 g for a gestational age of 29.2 ±3.6 weeks were recorded in both ventilatory modes at a median postnatal age of 3.5 days (range: 0-19). Six babies were ventilated for neonatal respiratory distress syndrome, one for transient tachypnoea, one had severe necrotising enterocolitis and multi-organ failure, one had sepsis-related apnoea and one was intubated prior to cerebral magnetic resonance imaging when recovering from sepsis.

Cycles' selection:
The ventilator (VRC) provided 1234 RM datasets, 633 in A/C and 601 in SIMV. A total of 11724 respiratory cycles were evaluated, 5596 in A/C and 6128 in SIMV. 4847 (41%) cycles were visually selected as optimal for RM calculation (SRC) (3333, 60% in A/C and 1514, 25% in SIMV). Respiratory cycles were considered to be unassisted in 1% and 41% of the A/C and SIMV totals respectively. One patient had only 6 cycles selected in SIMV and was excluded from analysis when studying that ventilatory mode.

RM parameters results: SRC vs. VRC
Mean values of the combined results obtained in both modes of ventilation are gathered in table 1 according to type of analysis, VRC or SRC. Mean values are very similar between both types, with one exception: C20/C is 32% lower in the SRC group ($p<0.001$). In contrast, SRC and VRC Rdyn, Cdyn, V_T, C20/C were differently correlated, with r^2 of 0.95 ($p<0.001$), 0.42 ($p=0.002$), 0.08 (not significant) and 0.01 (not significant) respectively. The CV's for Rdyn, Cdyn, V_T and C20/C in SRC show significant reductions from VRC's. (Table 1) The important scattering of C20/C values in the VRC group compared to SRC results is depicted in Fig.3.

SRC vs. VRC in each ventilatory mode (table 1, horizontal reading)
When comparing SRC and VRC according to ventilatory mode, we find similar mean Rdyn values and high correlations (r^2=0.96 and 0.95 in A/C and SIMV). The

differences in Cdyn are not significant in either ventilatory mode, but significant correlation remains only in A/C (r^2=0.68). V_T shows opposite changes in A/C and SIMV. The A/C V_T is significantly higher for VRC than for SRC (p=0.027). In contrary, the SIMV V_T tend to be lower for VRC than for SRC (p= 0.10). In contrast to combined values, a significant correlation between SRC and VRC V_T's is found in A/C (r^2=0.78). The major decrease in C20/C is similarly observed in both ventilatory modes (p= 0.02 for each mode). No correlation is observed in either mode.

When comparing CV's between SRC and VRC, the major reduction in V_T variability is found again in both modes and is more important in SIMV (A/C: 28 to 17%, p=0.01; SIMV: 52 to 20%, p=0.0004). CV's of all parameters are decreased in both ventilatory modes, and statistically significant decrease in variability is observed for Rdyn in A/C, and for C20/C in both modes.

A/C vs. SIMV (table 1, vertical reading)
Comparing A/C with SIMV modes of ventilation in VRC, there is a significant decrease in V_T, from 5.6 ±1.8 to 4.4 ±1.1ml/kg (p= 0.014). By contrast, in SRC the difference is inversed, with a significant increase in V_T from 4.8 ±0.9 to 5.6 ±1.2 ml/kg (p=0.049). In SRC, there is also a trend for a lower Cdyn in A/C (0.393 ±0.100 ml/hPa·kg) than in SIMV (0.510 ±0.190) (p= 0.10)

Compared to SIMV, the CV of V_T's in VRC is nearly 50% lower in A/C (52% vs.28, p<0.001). By contrast, in SRC the CV's of V_T's are low and similar in the two modes of ventilation: 17% in A/C and 20% in SIMV.

Results reproducibility:
During the two consecutive 5 minutes, the agreement between data from each period is high. Differences between each period related to mean value were small: for Rdyn, Cdyn, V_T and C20/C respectively 0.8, 1.1, 0.4, and 1.7% in SRC, and 0.9, 2.7, 2.7, and 1.9% in VRC. Agreement of the CV's between the 5 minutes segments is also high, without significant difference.

Discriminating power:
The ability of SRC to differentiate RM's from different patients in this unselected population of the study is high. "t" values were significantly higher in SRC than VRC for all parameters (Table 2). Figure 4 illustrates this by showing decreased standard deviations in SRC for individual patients in A/C.

Discussion:
This study evaluates continuous bedside RM monitoring in newborn infants and suggests a method to improve its precision. We demonstrate that the variability of RM values provided by the ventilator is large, with coefficients of variation well above 30% (range: 33-51%). Given such variability, instant on-line ventilator RM data cannot be a powerful tool in the assessment of the patient respiratory system and in the fine tuning of the ventilatory settings. Our strategy of selecting optimal cycles for calculating RM parameters allows for a significant improvement in data precision (with variability decreased to 18-27%) compared with what the ventilator provides. RM parameters averaged over five minutes are highly reproducible. Optimal respiratory cycles averaged over a short period also improve greatly the power to discriminate RM values between patients. The variety of respiratory conditions of the study patients helps to demonstrate such enhanced ability.

Most studies on passive respiratory mechanics testing in preterm infants made with external devices could be based on a few measurements, as their methods are designed to overcome the effects of spontaneous breathing and of the infant's respiratory efforts, and as they are based only on optimal respiratory cycles. In on-line bedside monitoring, many variables affect results of RM analysis, and strategies must be explored to limit their effects. To incorporate patient's contribution to dynamic RM results, oesophageal pressure is considered an adequate surrogate of pleural pressure. However, oesophageal pressure transducers remain only adapted for point of care assessment, are not designed for continuous monitoring and would be considered too invasive for such purpose. Studies already used selected respiratory cycles without pleural pressure data to evaluate inspiratory time [4] or the effect of a paralysing agent [16].

The displayed tidal volume is likely the parameter most often taken into account when reviewing RM data. V_T values are available in the clinical setting for 84% of the ventilated European neonates [23]. The accuracy of V_T measurement by the Babylog 8000 ventilator has been evaluated in laboratory conditions and shown to be accurate within 0-8.5% when testing V_T's of 4 to 20 ml (neonatal range 4-6 ml/kg) [3]. In A/C ventilation, adequate V_T is often used as a surrogate for adequate pressures difference. The mean decrease of 0.8 ml/kg in A/C (Fig. 4c) and the 1.0 ml/kg increase in SIMV found in optimal cycles' reporting (compared to VRC) are highly relevant, and lead to questioning the use of current ventilator derived V_T. The VRC and the SRC V_T are not similar. VRC gives informations on all breaths, whether supported or not, independently of their synchronization and of the leak. Another difference, the use of inspiratory V_T in the SRC group, seems adequate as V_T affected by leaks are not considered there. Small residual leaks would lead to slight overestimation of inspiratory V_T. Given that higher tidal volumes are considered detrimental [17], such approach could be more conservative. SRC reflects only breaths that are assisted and leak free, and therefore could provide more adequate informations to assist ventilatory management.

The effect of the ventilatory mode is mainly limited to the tidal volume. When studying patients' optimal breaths, V_T significantly increases by 0.8 ml/kg from A/C to SIMV. This finding correlates with a study looking at series of five respiratory cycles in preterm infants ventilated in different modes [11], where assisted respiratory cycles tended to generate higher volumes in SIMV than in A/C, and the patient efforts were higher. Augmented inspiratory efforts were also described in non synchronized ventilation with low ventilatory rates [8]. This could suggest that a higher respiratory drive in SIMV leads to increased volumes when the breath is supported, as long as there is no fatigue. Another explanation may originate from the presence of strong respiratory reflexes in preterm infants. Lung inflation induces the Hering –Breuer expiratory promoting reflex, resulting in post-inflation prolongation of neural expiratory signal [1] and apnea [8]. Nearly all respiratory cycles are preceded by artificial inflation on the previous breath in A/C ventilation. The inhibition of respiratory muscles tone by the Hering-Breuer reflex is therefore likely more pronounced in this mode. With both hypotheses, apparent dynamic compliance should decrease in A/C. Given similar resistances, the inspiratory time constant should also be lower. This is supported by a statistically shorter duration of inspiratory flow in A/C (0.30 ± 0.05 s vs. 0.32± 0.05 s in SIMV, $p<0.0001$).

The high variability in VRC V_T's when analysing SIMV, a partially supported mode (CV= 52% instead of 28% in A/C), is not surprising, as spontaneous non assisted breaths are likely less consistent. Most neonatal ventilators are still not able to display separately mechanical and spontaneous V_T. When studying volume guarantee mode, Keszler et al [12] also showed a high variability in control infants ventilated in pressure limited A/C, with 61% of the V_T's outside their 4-6 ml/kg target. In our study, we have been able to reduce the variability of the V_T monitoring in either ventilatory mode by more than 50% to a level much more compatible with clinical use (CV of 18% only)(Fig. 1).

Changes in pressures setting will affect the pulmonary volume and then the dynamic compliance of the respiratory system. When ventilation occurs at the steepest slope of the inflationary limb of the pulmonary pressure-volume relationship, compliance will be the greatest [5]. The tendency to higher Cdyn in the assisted SIMV cycles is likely to have the same explanation as the increase in V_T. The similarity of VRC-Cdyn in both ventilatory modes is surprising as it should be calculated on assisted breaths only [6]. Thus, it doesn't correspond to the lower VRC/V_T that includes non assisted cycles. Higher inspiratory efforts in SIMV (or decreased in A/C) as inferred from SRC results should also lead to higher Cdyn. While SRC and VRC calculations of Cdyn and Rdyn are based on the same model (Linear regression or least mean square fit analysis [14]), small differences in mathematical formula cannot be excluded. However, correlation is very high between VRC and SRC for Rdyn, and remains good for Cdyn in A/C. Such possible formula difference is unlikely to explain the absence of correlation for SIMV-Cdyn between VRC and ARC values. Increased precision (decreased variability) in provided Cdyn values will improve their discriminating power and help to assess that the pressures used remain in the optimal range with natural evolution of the disease, after surfactant therapy or after modification of ventilatory parameters. It is important to remember that Cdyn provided without pleural pressure estimate is increased with the patient's respiratory effort. Selecting only ventilator respiratory cycles without added spontaneous efforts could be interesting, but at the cost of very infrequent data during weaning.

Rdyn reflects resistances from the respiratory system as a whole, and can be affected at many levels. Inner diameter of the endotracheal tube is a major component of resistance [15]. The Rdyn values found in our patients are close to the values predicted by Manczur [15] for 2.5 and 3 mm endotracheal tubes and 8 L/min bias flow. Other variables such as condensation and subobstruction also play a role. Therefore, the precision of Rdyn needs to be high to obtain useful trends. This could help in assessing the need for suctioning, and in suggesting endotracheal tube change.

C20/C is a marker of excessive inspiratory pressure. When the upper inspiratory pressures lead to less increase in volume, the upper portion of the P-V loops flattens, with a "penguin beak" appearance [5]. The dynamic compliance decreases in the last part of inspiration and the C20/C ratio drops below 1. C20/C reflects peak inspiratory pressure adequacy and with overdistension is typically under 0.8 [7]. The extent of difference between C20/C calculated by the Fisher method [7] and those provided by the ventilator was unexpected. VRC values are often away from classical values (Fig. 3). In cycles affected by leaks, the volume loss may be more pronounced at the end of inspiration, therefore increasing the $V_{T\_inspiration}$ part in the ventilator's C20 equation. A biphasic appearance of the pressure plateau (as found in active expiration against the ventilator) will complicate the selection of the adequate peak pressure. Determination of the pressure component of C20 is therefore not straightforward between maximal pressure and pressure at end inspiration, the latter being used in the SRC group. Revision of the C20/C computation has already been suggested [18].

With its higher precision and discriminating power, respiratory cycles' selection improves the ability to distinguish different ventilatory status. If such selection could be automated and integrated in monitoring devices, this could also improve clinician ability to follow the evolution of an individual patient. It might also offer a better assessment of responses to ventilator fine tuning.

In conclusion, ventilator's RM parameters as currently provided have limited clinical use. Displayed V_T's do not reflect those found in optimal assisted breaths and therefore have limited value in assessing adequacy of ventilator settings. Validity of ventilator Cdyn in SIMV remains uncertain. Ventilator C20/C's are often out of published range and should be revised. The variability of RM values provided by the ventilator is large even in stable conditions, with coefficients of variation well above 30%. Using optimal respiratory cycles to calculate RM parameters seems promising given improved precision and discriminating power, but will need further evaluation. As such analysis is tedious, it will benefit of its automation before implementation in the clinical setting.

Conflict of interest:
The authors declare that they have no conflict of interest.

References

1. Beck J, Tucci M, Emeriaud G, Lacroix J, Sinderby C (2004) Prolonged neural expiratory time induced by mechanical ventilation in infants. Pediatr Res 55:747-754
2. Cappa P, Sciuto SA, Silvestri S (2006) Experimental evaluation of errors in the measurement of respiratory parameters of the newborn

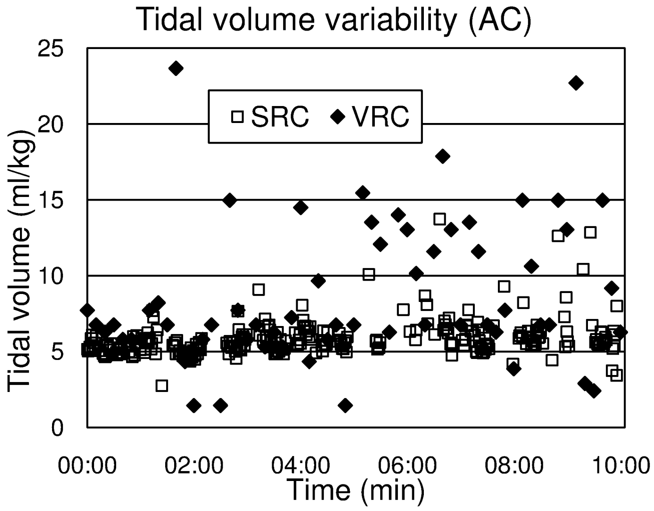
performed by a continuous flow neonatal ventilator. J Med Eng Technol 30:31-40
3. Chow LC, Vanderhal A, Raber J, Sola A (2002) Are tidal volume measurements in neonatal pressure-controlled ventilation accurate? Pediatr Pulmonol 34:196-202
4. De Luca D, Conti G, Piastra M, Paolillo PM (2009) Flow-cycled versus time-cycled sIPPV in preterm babies with RDS: a breath-to-breath randomised cross-over trial. Arch Dis Child Fetal Neonatal Ed 94:F397-401
5. Donn SM, Sinha SK (2006) Minimising ventilator induced lung injury in preterm infants. Arch Dis Child Fetal Neonatal Ed 91:F226-230
6. Dräger Medical (1999) Babylog 8000 plus Infant Care Ventilator. Operating Instructions, Software 5.n.
7. Fisher JB, Mammel MC, Coleman JM, Bing DR, Boros SJ (1988) Identifying lung overdistention during mechanical ventilation by using volume-pressure loops. Pediatr Pulmonol 5:10-14
8. Greenough A, Morley C, Davis J (1983) Interaction of spontaneous respiration with artificial ventilation in preterm babies. J Pediatr 103:769-773
9. Irazuzta J, Pascucci R, Perlman N, Wessel D (1993) Effects of fentanyl administration on respiratory system compliance in infants. Crit Care Med 21:1001-1004
10. Kano S, Lanteri CJ, Pemberton PJ, Lesouef PN, Sly PD (1993) Fast versus slow ventilation for neonates. Am Rev Respir Dis 148:578-584
11. Kapasi M, Fujino Y, Kirmse M, Catlin EA, Kacmarek RM (2001) Effort and work of breathing in neonates during assisted patient-triggered ventilation. Pediatr Crit Care Med 2:9-16
12. Keszler M, Abubakar K (2004) Volume guarantee: stability of tidal volume and incidence of hypocarbia. Pediatr Pulmonol 38:240-245
13. Klimek J, Morley CJ, Lau R, Davis PG (2006) Does measuring respiratory function improve neonatal ventilation? J Paediatr Child Health 42:140-142
14. Lanteri CJ, Kano S, Nicolai T, Sly PD (1995) Measurement of dynamic respiratory mechanics in neonatal and pediatric intensive care: the multiple linear regression technique. Pediatr Pulmonol 19:29-45
15. Manczur T, Greenough A, Nicholson GP, Rafferty GF (2000) Resistance of pediatric and neonatal endotracheal tubes: influence of flow rate, size, and shape. Crit Care Med 28:1595-1598
16. McEvoy C, Sardesai S, Schilling D, Durand M (2007) Acute effects of vecuronium on pulmonary function and hypoxemic episodes in preterm infants. Pediatr Int 49:631-636
17. Miller JD, Carlo WA (2008) Pulmonary complications of mechanical ventilation in neonates. Clin Perinatol 35:273-281
18. Neve V, de la Roque ED, Leclerc F, Leteurtre S, Dorkenoo A, Sadik A, Cremer R, Logier R (2000) Ventilator-induced overdistension in children: dynamic versus low-flow inflation volume-pressure curves. Am J Respir Crit Care Med 162:139-147
19. Neve V, Leclerc F, de la Roque ED, Leteurtre S, Riou Y (2001) Overdistension in ventilated children. Crit Care 5:196-203
20. Raju TN, Stevenson DK, Higgins RD, Stark AR (2009) Safe and effective devices and instruments for use in the neonatal intensive care units: NICHD Workshop summary. Biomed Instrum Technol 43:408-418
21. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R, Saugstad OD, Simeoni U, Speer CP, Halliday HL (2010) European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants - 2010 update. Neonatology 97:402-417
22. Uhl RR, Lewis FJ (1974) Digital computer calculation of human pulmonary mechanics using a least squares fit technique. Comput Biomed Res 7:489-495
23. van Kaam AH, Rimensberger PC, Borensztajn D, De Jaegere AP (2010) Ventilation practices in the neonatal intensive care unit: a cross-sectional study. J Pediatr 157:767-771 e761-763

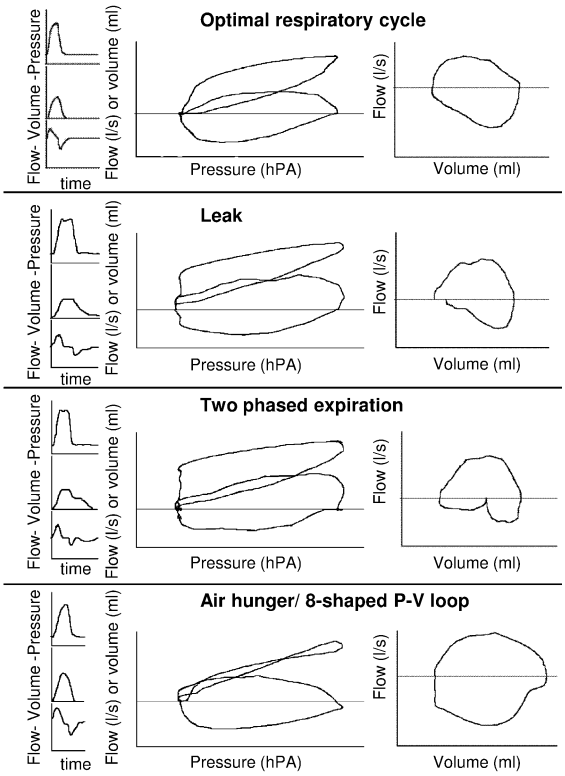
Fig.1 Tidal volumes provided by the ventilator (VRC) [solid diamonds] and derived from selected respiratory cycles (SRC) [squares] in Assist Control ventilation in one patient.

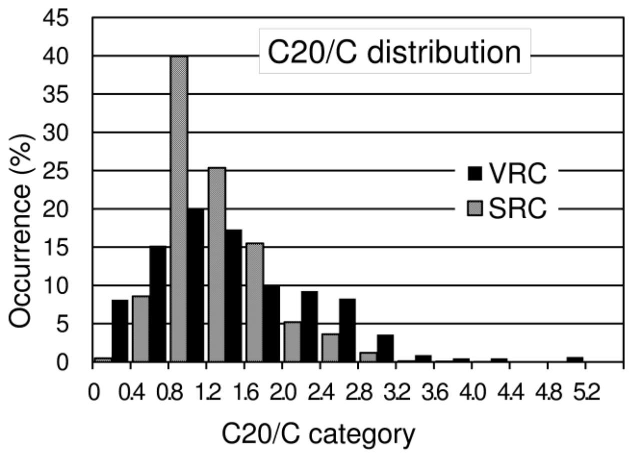
Fig.2 Exemples of pressure, volume, and flow waves (P,V and $\dot{V}$ vs. time) and P-V (upper part), P-$\dot{V}$ (lower part of combined loops) and V-$\dot{V}$ loops. From top to bottom. A) Optimal assisted respiratory cycle. B) Leak, with absence of V wave trace return to baseline and V-$\dot{V}$ loop ending before zero. C) Biphasic expiration, visible on $\dot{V}$ wave and V-$\dot{V}$ loop. D) Air hunger, or bias flow not meeting demand: 8-shaped P-V loop.

Fig.3 Distribution of C20/C provided by the ventilator (VRC) or calculated from selected respiratory cycles (SRC).

Fig. 4 (a-d) RM values (a: Rdyn; b: Cdyn; c: V_T; d: C20/C) of individual patients in A/C for both VRC and SRC groups. Patients are labelled with different letters in the legend. The letter reappears when the RM parameter of another patient is not statistically different from the patient initially labelled with such letter.


Tidal volume variability (AC)
SRC
VRC
Tidal volume (ml/kg)
Time (min)
25
20
15
10
5
0
00:00
02:00
04:00
06:00
08:00
10:00


Optimal respiratory cycle
Leak
Two phased expiration
Air hunger/ 8-shaped P-V loop
Flow- Volume -Pressure
time
Flow (l/s) or volume (ml)
Pressure (hPA)
Flow (l/s)
Volume (ml)


C20/C distribution
VRC
SRC
Occurrence (%)
C20/C category
45
40
35
30
25
20
15
10
5
0
0
0.4
0.8
1.2
1.6
2.0
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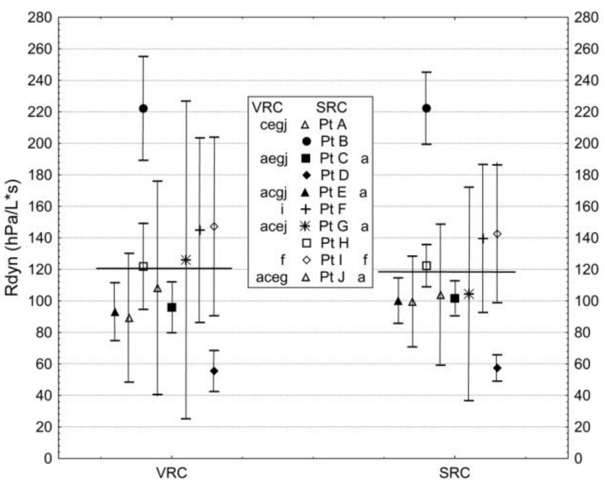
2.8
3.2
3.6
4.0
4.4
4.8
5.2


Rdyn (hPa/L*s)
VRC
SRC
VRC SRC
cegj Pt A
Pt B
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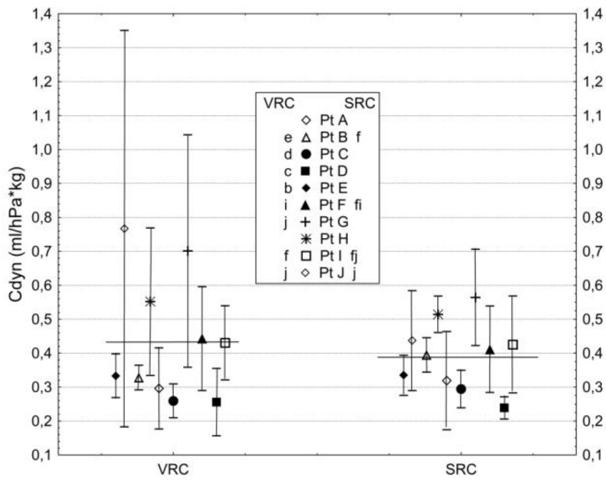
i Pt F
acej Pt G a
Pt H
f Pt I f
aceg Pt J a


Cdyn (ml/hPa*kg)
VRC
SRC
VRC SRC
Pt A
e Pt B f
d Pt C
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b Pt E
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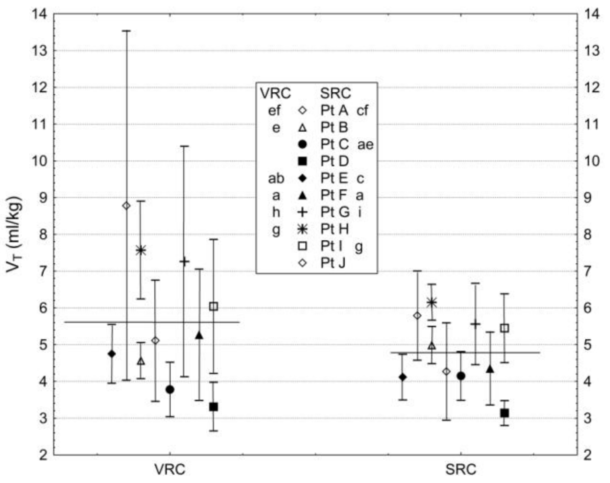
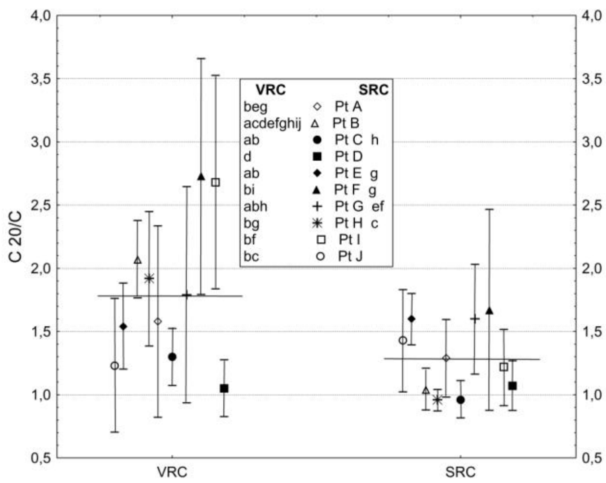
Pt H
f Pt I fj
j Pt J j


V_T (ml/kg)
VRC
SRC
VRC SRC
ef Pt A cf
e Pt B
Pt C ae
Pt D
ab Pt E c
a Pt F a
h Pt G i
g Pt H
Pt I g
Pt J


C 20/C
VRC
SRC
VRC SRC
beg Pt A
acdefghij Pt B
ab Pt C h
d Pt D
ab Pt E g
bi Pt F g
abh Pt G ef
bg Pt H c
bf Pt I
bc Pt J